MINUTES OF 322nd MEETING OF REGISTRATION BOARD HELD ON 8th & 10th November, 2022

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Drug Regulatory Authority of Pakistan
T.F. Complex, Mauve Area, G-9/4
Islamabad.

322nd meeting of Registration Board was held on 8th and 10th November, 2022 in the Committee Room, Drug Regulatory Authority of Pakistan, G-9/4, Islamabad. The meeting was chaired by Dr. Obaidullah Director (PE&R Division)/Chairman Registration Board DRAP. The meeting started with recitation of the Holy Verses.

The Chairman, Secretary and members of Registration Board expressed grief and offered Fateha on sad demise of one of the worthy member Meritorious Prof. Dr. Rafiq Alam Khan. The Board appreciated the work and contributions of Prof.Dr. Rafiq Alam Khan and prayed for the eternal peace of the departed soul. The Board also decided to request DRAP to send recognition letter to family of Dr. Rafiq Alam Khan for his rendered services.

The Board decided to co-opt following experts on expiration of their tenure, under Rule 24 (6) of the Drugs (Licensing, Registering & Advertising) Rules, 1976 of the Drugs Act, 1976: -

i. Maj. Gen. (R) Dr. Tahir Mukhtar Sayed, Inspector General (Hospitals), Fauji Foundation, Rawalpindi
ii. Dr. Qurban Ali, Ex-Director General, National Veterinary Laboratories, Islamabad

The Board also decided to co-opt Mr. Hafiz Bilal Bin Akbar, Deputy Director, Legal Affairs Division under Rule 24 (6) of the Drugs (Licensing, Registering & Advertising) Rules, 1976 of the Drugs Act, 1976 on case between M/s Galaxy Pharma, Karachi and M/s AGP, Karachi referred by High Court of Sindh at Karachi,: -

Following members attended the meeting:

1.	Ch. Zeeshan Nazir Bajar, Additional Director (BE&R/PE&R), DRAP.	Member/ Secretary
2.	Lt. Gen.(R) Prof. Dr. Karamat A. Karamat (HI-M.SI-M), Former Surgeon General Pakistan.	Member
3.	Dr. Noor us Saba, Director, Biological Evaluation & Research Division, DRAP	Member
4.	Mr. Ali Ahmad Agha, Director, DTL, Quetta	Member
5.	Mr. Ijaz Alvi, DTL, Rawalpindi	Member
6.	Mr. Muhammad Aslam, Deputy Draftsman-I, Ministry of law & Justice, Islamabad.	Member
7.	Mr. Ghulam Mujtaba, Deputy Director, Representative of IPO	Member
8.	Mr. Ajmal Sohail Asif, Director, QA&LT Division	Member
9.	Mr. Abdullah, Representative of Division of MD&MD	Member
10.	Dr. Imran Khan, Director, DTL, Peshawar	Member (online)
11.	Dr. Qurban Ali, Ex-Director General, National Veterinary Laboratories, Islamabad	Co-opted Member
12.	Dr. Muhammad Akram, Animal Husbandry Commissioner, M/o NFS&R	Co-opted Member
13.	Maj. Gen. (R) Dr. Tahir Mukhtar Sayed, Inspector General (Hospitals), Fauji Foundation, Rawalpindi	Co-opted Member (Online)
14.	Dr. Shabnam Firdous, Secretary/Registrar, Pakistan Veterinary Medical Council	Co-opted Member
15.	Hafiz Bilal Bin Akbar, Deputy Direcor (Legal Affairs Division) for case of M/s Galaxy Pharma, Karaci and M/s AGP, Karachi	Co-opted Member

Mr. Nadeem Alamgir (Pharma Bureau), Hafiz Muhammad Azeem, Mr. Hamid Raza and Mr. Jalal-ud-Din (PPMA) and Mr. Ziaulhaq & Mr. Amir (PCDA) attended the meeting as observers.

Director, BE&R was assisted by respective Additional Director and Assistant Directors for presentation of the agenda.

Item No. I: Confirmation of Minutes of 321st meetings of Registration Board.

321st meeting of Registration Board was held on 20th to 22nd September, 2022. Accordingly, draft minutes of 321st meeting of Registration Board were circulated among all the members of Board on 19th October, 2022 for perusal/approval/comments (if any) by 24th October, 2022 (10:00 am). No comments were received by any member by 24th October, 2022. Accordingly, fair minutes were processed to Chairman, Registration Board for perusal/approval. After approval from Chairman Registration Board, fair minutes of 321st meeting of Registration Board were circulated among concerned Divisions / Sections for implementation of decisions.

Decision: Registration Board noted the information and unanimously confirmed the minutes of 321st meeting of Registration Board.

Item No. II: Division of Pharmaceutical Evaluation & Registration

Pharmaceutical Evaluation Cell (PEC)

Sr. No	Name of Evaluator	Title
1.	Mr. Farooq Aslam	Evaluator PEC-I
2.	Mr. Ammar Ashraf Awan	Evaluator PEC-II
3.	Mr. Muhammad Haseeb Tariq	Evaluator PEC-III
4.	Mst.Farzana Raja	Evaluator PEC-IV
5.	Mst. Iqra Aftab	Evaluator PEC-V
6.	Mr. Ishtiaq Shafique	Evaluator PEC-VI
7.	Dr. Sidra Khalid	Evaluator PEC-VII
8.	Mr. Muhammad Usman	Evaluator PEC-VIII
9.	Mr. Adil Saeed	Evaluator PEC-IX
10.	Mst. Najia Saleem	Evaluator PEC-X
11.	Dr. Farhadullah	Evaluator PEC-XI
12.	Mr. Shahid Nawaz	Evaluator PEC-XIII
13.	Mst. Saima Hussain	Evaluator PEC-XV
14.	Mr. Akbar Ali	Evaluator PEC-XVI
15.	Mr. Zia Ullah	Evaluator PEC-XVII
16.	Mr. Muneeb Ahmed	Evaluator PEC-XVIII
17.	Mst. Sana Kanwal	Evaluator PEC-XX
18.	Mr. Muhammad Zubair	Assistant Director (PE&R)
19.	Mr. Umer Latif	
20.	Mr. Ahsan Hafiz	

Item No. I: Agenda of Evaluator-I (Mr. Farooq Aslam)
Case No. I: Routine applications submitted on Form-5F for Import

1.	Name, address of Applicant / Importer	M/s Lab Diagnostic System (SMC) Pvt. Ltd. 111B, Hali road, Westridge 1, Rawalpindi Cantt.
	Details of Drug Sale License of importer	License No: 01-374-0176-041296D Address: Lab Diagnostic Systems Pvt. Ltd. 111-B, Hali road Westridge 1Cantt, District Rawalpindi. Godown: N/A Validity: 07-03-2023 Status: License to sell drugs as a distributor
	Name and address of marketing authorization holder (abroad)	M/s Actero Middle East, on the cornor of 8th Golestan, Sarvestan Blvd, Baharestan Industrial Zone, Karaj, Iran.
	Name, address of manufacturer(s)	M/s Actero Middle East, on the cornor of 8th Golestan, Sarvestan Blvd, Baharestan Industrial Zone, Karaj, Iran.
	Name of exporting country	Iran
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized CoPP (No. 665/13204 dated 07/06/2021) issued by Food and Drug Administration Tehran, Iran. The applied product is available in the market of exporting country for free sale. The facilities and operations conform to WHO GMP.	
	Details of letter of authorization / sole agency agreement: • Copy of letter of authorization is submitted from Actero Middleast wherein M/s Lab Diagnostic Systems (SMC) is authorized for registration and all other matters pertaining to registration of the product.	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No.33828 : 28/12/2021
	Details of fee submitted	PKR 150,000/- : 01/10/2020
	The proposed proprietary name / brand name	Capecitabine ACTe 500mg oral tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Capecitabine……500mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-cancer

	Reference to Finished product specifications	USP
	Proposed Pack size	10's×10
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xeloda 500mg tablet, USFDA Approved.
	For generic drugs (me-too status)	CAPEGARD-500MG FILM COATED TABLETS by M/s AJ Mirza Pharma, reg. No. 72593
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, detail of impurities and validations studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and product.
	Name, address of drug substance manufacturer	M/s Hetero Labs Limited Unit –I Survey No. 10 IDA Gaddapotharam Village, Jinaram Mandal, Sangareddy district, Telangana, India.
	Module-III Drug Substance:	Official monograph of Capecitabine is present in USP. Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• Real time stability studies have been conducted at 25oC±2 and 60%RH±5% for 36 months of 3 batches • Accelerated stability study is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: (CA0010910, CA0020910, CA0030910)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, compatibility studies of excipients with drug substance manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, detail of impurities and the validation studies, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has submitted pharmaceutical equivalence studies against Xeloda 500mg Tablet by performing all the quality tests. Comparative dissolution prodile is submitted against Xeloda Tablet 500mg batch number X1135 in 4 media that in purified water, acidic pH that is 1.2, Acetate Buffer 4.5pH and Phosphate buffer 6.8pH.
	Analytical method validation/verification of product	The firm has submitted analytical method verification / validation studies for drug substance and drug product including linearity, accuracy, specificity, force degradation, precision etc.
	Container closure system of the drug product	Forming foil: Clear PVC Lidding foil: Aluminium foil
	Stability study data of drug product, shelf life and storage conditions	• Real time stability studies have been conducted at 30oC±2 and65%RH±5% for 24 months of 3 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: (T1924, T1925, T1926)

Evaluation by PEC-I:

Observations	Response
Name and address of the applicant is different form the name and address mentioned in drug sale license, please clarify. Furthermore, submit valid copy of drug sale license.	License No: 01-374-0176-041296D Address: Lab Diagnostic Systems Pvt. Ltd. 111-B, Hali road Westridge 1Cantt, District Rawalpindi. Godown: N/A Validity: 07-03-2023 Status: License to sell drugs as a distributor
Provide details of the reference product against which pharmaceutical equivalence and comparative dissolution profile is submitted including batch number, expiry, date of manufacturing, name of manufacturer and detail of reference authority where the product is registered.	Brand name: Xeloda tablet 500mg, USFDA approved Bacth number: X4955B01 Mfg by: Roche Exp: Sep, 2019
Provide detail of container closure system of the applied product.	Forming foil: Clear PVC Lidding foil: Aluminium foil
Provide stability study data (real time & accelerated) of 03 batches till claimed shelf life conducted under the conditions of zone IV-A.	• Real time stability studies have been conducted at 30oC±2 and65%RH±5% for 24 months of 3 batches • Accelerated stability studies is conducted at 40oC±2 and 75%RH±5% for 6 months of 3 batches Batches: (T1924, T1925, T1926)
Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.	

Case No. II: Routine applications submitted on Form-5F for local manufacturing

2.	Name, address of Applicant /	M/s Herbion Pakistan (pvt) Ltd., Industrial triangle,

	Marketing Authorization Holder	Kahuta road, Humak, Islamabad.
	Name, address of Manufacturing site.	M/s Herbion Pakistan (pvt) Ltd., Industrial triangle, Kahuta road, Humak, Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 5850 dated 03/03/2022
	Details of fee submitted	PKR 30,000/-: dated 07/02/2022
	The proposed proprietary name / brand name	Ista-Met Tablet 50/1000mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin as phosphate monohydrate….. 50mg Metformin HCl……..1000mg
	Pharmaceutical form of applied drug	Immediate release fiml coated tablet
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	14's, 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	Sitaglumet tablet 50/1000 by M/s Hilton Pharma
	GMP status of the Finished product manufacturer	Copy of GMP (for govt supply/institution only) certificate no. F.3-9/2018-Addl.Dir(QA&LT)-49 issued on the basis of inspection conducted on 21/05/2019.
	Section approval	Tablet General Section-Revised
	Name and address of API manufacturer.	**Sitagliptin:** M/s Anhui Haikang Pharmaceutical Co., Ltd.,No. 21, Huancheng west road, Daguan district, Anqing, Anhui China. **Metformin:** M/s Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance (Sitagliptin and Metformin).
	Stability studies	**Sitagliptin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20130421, 20130420, 20130419) **Metfromin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MEF/1510145, MEF/1510146, MEF/1510147)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is established against Sitaglu Met 50/1000mg tablet by Hilton Pharma by performing all the quality tests. (B:141382) CDP testing is performed against Sitaglu Met 50/1000mg tablet by Hilton Pharma in all the 03 media that is 0.1N HCl. Acetate Buffer and Phosphate Bufer.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, Robustness, system suitability etc.
STABILITY STUDY DATA		
Manufacturer of API	**Sitagliptin:** M/s Anhui Haikang Pharmaceutical Co., Ltd.,No. 21, Huancheng west road, Daguan district, Anqing, Anhui China. **Metformin:**	

	M/s Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.		
API Lot No.	Sitaglptin (20010403) Metformin (MEF/10010279)		
Description of Pack (Container closure system)	Alu-Alu blister pakced in secondary unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	ST-001	ST-002	ST-003
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	07/2021	07/2021	07/2021
Date of Initiation	21/08/2021	21/08/2021	21/08/2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has not submitted any response
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Sitagliptin:** Copy of drug manufacturing license number 20190399 valid till 31/12/2025 issued by Food and drug administration of Anhui province china is submitted. **Metformin:** copy of GMP certificate no. 20031933 valid till 19/03/2023 issued by food and drugs control administration, Gujarat.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Sitagliptin:** Copy of attested invoice number WD20200403 dated 03/04/2020. **Metformin:** Copy of attested invoice no. EXP/1490/20-21 dated 21/08/2020 is submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks of Evaluator-I:		

Sr. No.	Observations	Response
1	Provide analytical method verification studies performed by drug product manufacturer for Sitagliptin phosphate monohydrate.	Firm has submitted analytical method verification report including specificity, linearity, precision and accuracy/recovery for Sitagliptin drug substance performed by drug product manufacturer.
2	Provide certificate of analysis for Sitagliptin phosphate monohydrate and Metformin HCl drug substances for those batches which were used for product development from drug product and drug substance manufacturer and batch manufacturing record.	COA for Metformin from drug product manufacturer and drug substance manufacturer is submitted or batch number MEF/10010279. Potency for Metformin HCl is adjusted considering 100% assay value while the assay value for Metformin is 99.19% (on as-is basis). The firm has stated,"We are committed that we will positively consider the "AS-Is" potency adjustment in all upcoming commercial batches". COA for Sitagliptin from drug product manufacturer and drug substance manufacturer is submitted or batch number 20010403.
3	As per submitted dossier, titration method has been used for assay estimation for Metformin HCl while according to latest edition of USP, HPLC method should be used for assay testing, please clarify.	*The provided specifications and test methods by drug product manufacturer is of USP 2020 and the assay of API is conducted by HPLC as claimed in the united states' pharmacopoeia.*
4	Since CDP and pharmaceutical equivalence testing are performed against Sitaglu Met tablet while the said studies are required against innovator's / reference products.	The firm has submitted CDP and pharmaceutical equivalence data against the reference product that is janumet with the following details. Brand: Janumet tablet 50/1000 Batch: HM-21497588A
5	The submitted stability data is till 3rd month time point, please submit stability study data till 6th month.	Data till 6th month time point is submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the submission of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter.**
- **Firm will submit correct calculations for potency adjustment for Metformin HCl considering the assay value on As-Is basis for commercial batches with the submission**

	of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.	
3.	Name, address of Applicant / Marketing Authorization Holder	M/s Herbion Pakistan (pvt) Ltd., Industrial triangle, Kahuta road, Humak, Islamabad.
	Name, address of Manufacturing site.	M/s Herbion Pakistan (pvt) Ltd., Industrial triangle, Kahuta road, Humak, Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 5849 dated 03/03/2022
	Details of fee submitted	PKR 30,000/-: dated 07/02/2022
	The proposed proprietary name / brand name	Ista-Met Tablet 50/500mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin as phosphate monohydrate….. 50mg Metformin HCl……..500mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	14's, 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	Sitaglumet tablet 50/500 by M/s Hilton Pharma
	GMP status of the Finished product manufacturer	Copy of GMP (for govt supply/institution only) certificate no. F.3-9/2018-Addl.Dir(QA&LT)-49 issued on the basis of inspection conducted on 21/05/2019.
	Section approval	Tablet General Section-Revised
	Name and address of API manufacturer.	**Sitagliptin:** M/s Anhui Haikang Pharmaceutical Co., Ltd.,No. 21, Huancheng west road, Daguan district, Anqing, Anhui China. **Metformin:** M/s Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance (Sitagliptin and Metformin).
	Stability studies	**Sitagliptin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20130421, 20130420, 20130419) **Metfromin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MEF/1510145, MEF/1510146, MEF/1510147)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is established against Sitaglu Met 50/500mg tablet by Hilton Pharma by performing all the quality tests. (B:141388) CDP testing is performed against Sitaglu Met 50/500mg tablet by Hilton Pharma in all the 03 media that is 0.1N HCl. Acetate Buffer and Phosphate Bufer.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, Robustness, system suitability etc.
STABILITY STUDY DATA		
Manufacturer of API	**Sitagliptin:**	

	M/s Anhui Haikang Pharmaceutical Co., Ltd.,No. 21, Huancheng west road, Daguan district, Anqing, Anhui China. **Metformin:** M/s Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.		
API Lot No.	Sitaglptin (20010401) Metformin (MEF/10010279)		
Description of Pack (Container closure system)	Alu-Alu blister pakced in secondary unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	ST-001	ST-002	ST-003
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	07/2021	07/2021	07/2021
Date of Initiation	21/08/2021	21/08/2021	21/08/2021
No. of Batches	03		

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has not submitted any response
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Sitagliptin:** Copy of drug manufacturing license number 20190399 valid till 31/12/2025 issued by Food and drug administration of Anhui province china is submitted. **Metformin:** copy of GMP certificate no. 20031933 valid till 19/03/2023 issued by food and drugs control administration, Gujarat.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	**Sitagliptin:** Copy of attested invoice number WD20200403 dated 03/04/2020. **Metformin:** Copy of attested invoice no. EXP/1490/20-21 dated 21/08/2020 is submitted
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
12.	Record of Digital data logger for temperature and humidity	Submitted

	monitoring of stability chambers (real time and accelerated)	

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Provide analytical method verification studies performed by drug product manufacturer for Sitagliptin phosphate monohydrate.	Firm has submitted analytical method verification report including specificity, linearity, precision and accuracy/recovery for Sitagliptin drug substance performed by drug product manufacturer.
2	Provide certificate of analysis for Sitagliptin phosphate monohydrate and Metformin HCl drug substances for those batches which were used for product development from drug product and drug substance manufacturer.	COA for Metformin from drug product manufacturer and drug substance manufacturer is submitted or batch number MEF/10010279. Potency for Metformin HCl is adjusted considering 100% assay value while the assay value for Metformin is 99.19% (on as-is basis). COA for Sitagliptin from drug product manufacturer and drug substance manufacturer is submitted or batch number 20010403.
3	As per submitted dossier, titration method has been used for assay estimation for Metformin HCl while according to latest edition of USP, HPLC method should be used for assay testing, please clarify.	*The provided specifications and test methods by drug product manufacturer is of USP 2020 and the assay of API is conducted by HPLC as claimed in the united states' pharmacopoeia.*
4	Since CDP and pharmaceutical equivalence testing are performed against Sitaglu Met tablet while the said studies are required against innovator's / reference products.	The firm has submitted CDP and pharmaceutical equivalence data against the reference product that is janumet with the following details. Brand: Janumet tablet 50/500 Batch: 21495023A
5	The submitted stability data is till 3rd month time point, please submit stability study data till 6th month.	Data till 6th month time point is submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the submission of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter.**
- **Firm will submit correct calculations for potency adjustment for Metformin HCl considering the assay value on As-Is basis for commercial batches with the submission of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

4.	Name, address of Applicant / Marketing Authorization Holder	M/s Dyson Research Laboratories Pvt. Ltd., 28-km, Ferozepur road, Lahore, Pakistan.
	Name, address of Manufacturing site.	M/s Dyson Research Laboratories Pvt. Ltd., 28-km, Ferozepur road, Lahore, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)+ ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32727 dated 01/12/2021
	Details of fee submitted	PKR 30,000/-: dated 13/09/2021
	The proposed proprietary name / brand name	Vidora Pro 50/500mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vildagliptin…….50mg Meformin HCl…500mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	14's, 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Galvumet 50/500 by M/s Novartis Pharmaceuticals Australia TGA Approved.
	For generic drugs (me-too status)	Galmet 50/500mg tablet by M/s Vision Pharma Reg. No. 81905
	GMP status of the Finished product manufacturer	DML renewal letter no. F.1-7/2003-Lic(Vol-IV) dated 08/06/2021.
	Section approval	Tablet General Section
	Name and address of API manufacturer.	**Vildaglptin:** Fuxin long rui Phramaceutical Co., Ltd., fluoride industrial park, Fumeng County (Yi Ma Tu) Fuxin City, Liaoning province, China. **Metformin HCl:** Aarti drugs Lmted, plot no. 211-213, road no. 2 GIDC Sarigam, District Valsad, Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description

		of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph for Metformin HCl Is present in USP and Vildagliptin is not a pharmacopeoial drug substance. Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance (Mtformin+Vildagliptin).
	Stability studies	**Vildagliptin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20160927, 20161031, 20161123) **Metformin HCl:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MEF/1410027, MEF/1410028, MEF/1410029)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Brand name: Viptin Met 50/500mg Batch: 002F Mfg by: M/s Sami Pharmaceuticals CDP in all the three media with acceptable F2 values and pharmaceutical equivalence by performing quality tests are submitted.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, LOD/LOQ, Robustness, Solution stability, system suitability for drug substance and drug product.
STABILITY STUDY DATA		
Manufacturer of API	**Vildaglptin:**	

	Fuxin long rui Phramaceutical Co., Ltd., fluoride industrial park, Fumeng County (Yi Ma Tu) Fuxin City, Liaoning province, China. **Metformin HCl:** Aarti drugs Lmted, plot no. 211-213, road no. 2 GIDC Sarigam, District Valsad, Gujarat, India.		
API Lot No.	Vildagliptin: WT-20190213-D01-WT03-01 Metformin: MEF/18102464		
Description of Pack (Container closure system)	Alu-Alu blister of 10's packed in printed unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T01	T02	T03
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	Jan, 2020	Jan, 2020	Jan, 2020
Date of Initiation	15/02/2020	15/02/2020	15/02/2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Vildaglitpin: Copy of GMP certificate valid till 27/09/2020 issued by Fuxin Food and Drug Adninistration is submitted. Metformin: copy of GMP certificate no. 20031933 valid till 19/03/2023 issued by food and drugs control administration, Gujarat.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Metformin: Copy of invoice number EXP/289/19-20 dated 06/05/20219 cleared on 16/05/2019 vide dy. No. 6854. Vildagliptin: Copy of invoice number SY190311C dated 11/03/2019 cleared on 20/03/2019 vide dy. No. 3869.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator-I:

Sr. No.	Observations	Response
1	Please provide valid copies of GMP certificates of drug substance manufacturers of Metformin HCL and Vildagliptin.	Vildaglitpin: Copy of GMP certificate valid till 27/09/2020 issued by Fuxin Food and Drug Adninistration is submitted. Metformin: copy of GMP certificate no. 20031933 valid till 19/03/2023 issued by food and drugs control administration, Gujarat.
2	Provide stability study data (Real Time & Accelerated) of 3 batches conducted under the conditions of zone VI-A for Metformin HCl and Vildagliptin.	**Vildagliptin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20160927, 20161031, 20161123) **Metformin HCl:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MEF/1410027, MEF/1410028, MEF/1410029)
3	Please clarify since the analytical method used for Metformin Drug substance is Titration method while the drug substance is compendial and official monograph is present in latest pharmacopoeia.	*We have conducted the studies back in 2019-2020, at that time UV method was mentioned in pharmacopoeia, the HPLC method is published in latest version (2022), we do undertake that for commercial manufacturing we will perform testing as per latest version.*
4	Provide pharmaceutical equivalence studies and comparative dissolution profile against the reference / innovator's product by performing all the quality tests along with the details of manufacturer, batch number, expiry and manufacturing details.	Brand name: Viptin Met 50/500mg Batch: 002F Mfg by: M/s Sami Pharmaceuticals CDP in all the three media with acceptable F2 values and pharmaceutical equivalence by performing quality tests are submitted.
5	Provide documents for the procurement of API (Vildagliptin + Metformin HCl) with approval from DRAP (in case of import).	Metformin: Copy of invoice number EXP/289/19-20 dated 06/05/20219 cleared on 16/05/2019 vide dy. No. 6854. Vildagliptin: Copy of invoice number SY190311C dated 11/03/2019 cleared on 20/03/2019 vide dy. No. 3869.
6	Provide complete batch manufacturing record of the applied product along with the calculation for potency adjustment.	The firm has submitted BMR of the applied product. Potency for Vildagliptin is adjusted by considering 100.18% assay value whereas in

		case of assay more than 100 percent, factor of 100 should be taken for calculations. (50mg with 100% assay & 49.91mg when 100.18% assay value is considered).

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the submission of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter.**
- **Firm will submit correct calculations for potency adjustment for Metformin HCl considering the assay value on As-Is basis for manufacturing of commercial batches with the submission of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

5.	Name, address of Applicant / Marketing Authorization Holder	M/s MartinDow Limited, plot no. 37, Sector 19, Korangi Industrial area, Karachi.
	Name, address of Manufacturing site.	M/s MartinDow Limited, plot no. 37, Sector 19, Korangi Industrial area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 34231 dated 31/12/2021
	Details of fee submitted	PKR 30,000/-: dated 20/05/2021
	The proposed proprietary name / brand name	Migbet PR Tablet 50mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Prolonged Release, Film Coated Tablet contains: Mirabegron…….50mg
	Pharmaceutical form of applied drug	Prolonged Release, Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Beta-3 adrenergic agonist (used for treatment of overactive bladder-OAB)
	Reference to Finished product specifications	In-House
	Proposed Pack size	2×5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved

	For generic drugs (me-too status)	Mibega by Getz Pharma, Reg. No. 089378
	GMP status of the Finished product manufacturer	Last inspection report dated 07/04/2020, Good Level of compliance
	Section approval	Tablet Section (General)
	Name and address of API manufacturer.	M/s Jiangxi synergy Pharmaceutical Co., Ltd., Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi Province China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Mirabegron is non-pharmacopoeial drug substance. Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	• Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20180101V, 20180102V, 20180103V)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is provided against Betigma 50mg PR tablet by M/s Astellas Pharma Europe B.V (Batch Number: 19E2027) by performing all the quality tests including tests for impurities (MBL-ATAH, unspecified impurity, Total Impurity). CDP is submitted against the same product.
	Analytical method validation/verification of product	Analytical method verification / validation studies for drug substance as well as for drug product is submitted.
STABILITY STUDY DATA		
Manufacturer of API	M/s Jiangxi synergy Pharmaceutical Co., Ltd., Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi Province China.	

API Lot No.	20200601V		
Description of Pack (Container closure system)	Au-Alu blister cards made up of cold forming foil (base foil) and Aluminium foil (lid foil) packed in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	NPD-T-1607-S	NPD-T-1627-S	NPD-T-1628-S
Batch Size	2500 tab	5000 tab	5000 tab
Manufacturing Date	29-07-2021	16-08-2021	16-08-2021
Date of Initiation	28-04-2021	24-08-2021	24-08-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empator-M tablet 5mg+500mg (Empaglilozin + Metformin HCl) approved in 312th meeting of Registration Board.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 2022001 valid till 09/01/2027 issued by Jiangxi API Engineering Technology Research Centre, China. Copy of GMP certificate No. 2020002 issued by CFDA valid till 11/03/2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice number JXSG200935 is submitted dated 09/10/2020 Dy. Number 3097.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Please provide valid GMP certificate of Drug Substance manufacturer.	Copy of GMP certificate No. 2022001 valid till 09/01/2027 issued by Jiangxi API Engineering Technology Research Centre, China.

2	Justify the dissolution parameters selected for the applied product including the limits set for release of drug along with the discussion for time points selected for testing (i.e 3hours, 5hours & 8.5hours).	The firm has referred to USFDA dissolution database available on the official website. USP I (basket), Phosphate Buffer pH 6.8, 900mL, sampling time: 3hr, 5hr, 8.5hr.
3	Acceptance criteria for specificity parameter of analytical method validation studies for drug product includes limit for degradation which is ≤5% while the specification of product includes total impurity limit ≤0.8%. Please justify the criteria set for specificity testing which is way broader than the product's specifications. Moreover, provide protocols for analytical method validation studies for the drug product.	Acceptance criteria has been set ≤ 5.0% that is for force degradation study in specificity to control the degradation as more degradation can cause non-homogenous peak (impure peak with purity angle > threshold angle) in assay or degradation peaks can interfere elution zone of active. Force degradation study is conducted for assay specificity. While 5.0% degradation justifiable according to stability significant change criteria in assay.
4	The submitted stability data is till 3rd month time point, please provide stability studies till 6th month time point as per the guidelines provided in 293rd meeting of Registration Board.	The firm has submitted stability summary sheets till 6 months for accelerated and long term stability studies along with the relevant documents.
5	Provide certificate of analysis of relevant batch of drug substance used for product development from drug substance manufacturer and drug product manufacturer.	Copy COAs for batch number from drug product manufacturer as well as from drug substance manufacturer is submitted for batch number 20200601V.
6	Provide documents for the procurement (e.g invoice) of API with approval from DRAP (in case of import).	Copy of attested invoice number JXSG200935 is submitted dated 09/10/2020 Dy. Number 3097.
7	Provide complete batch manufacturing record for the applied product.	The firm has submitted complete batch manufacturing record for the applied product.

Decision: Approved with innovator's specifications. Registration Board further decided that registration letter will be issued after submission of fee Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

6.	Name, address of Applicant / Marketing Authorization Holder	M/s MartinDow Limited, plot no. 37, Sector 19, Korangi Industrial area, Karachi.
	Name, address of Manufacturing site.	M/s MartinDow Limited, plot no. 37, Sector 19, Korangi Industrial area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33103 dated 17/12/2021
	Details of fee submitted	PKR 30,000/-: dated 29/11/2021
	The proposed proprietary name / brand name	Empator-M XR Tablet 25mg+1000mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated, extended release tablet contains: Empagliflozin (immediate release)……..25mg Metformin HCL (extended release)…….1000mg
	Pharmaceutical form of applied drug	Film coated, extended release tablet
	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	14's, 28's
	Proposed unit price	AS per SRO
	The status in reference regulatory authorities	USFDA Approved.
	For generic drugs (me-too status)	Xenglu-Met XR tablet by Hilton Pharma
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 85/2020-DRAP(K) issued on the basis of inspection conducted on 07/05/2019
	Section approval	Table tgeneral section (Regularised)
	Name and address of API manufacturer.	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** IPCA Laboratories Limited, H-4, MIDC, Waluj Aurangabad431136 Maharashtra India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures

		and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substances (i.e Metformin & Empagliflozin).
	Stability studies	Stability study conditions: Empagliflozin: Real time: 25°C ± 2°C / 60% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: EGLZ-20160501, EGLZ-20160502, EGLZ-20160503 Metformin HCl: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: 9002ML2RMI, 9003ML2RMI, 9004ML2RMI
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence studies have been submitted against the innovator's product that is Synjardy XR tablet 25/1000mg mfg by Boehringer Ingelheim USA (Batch number: 3189877) by performing all the quality tests. Comparative dissolution profile is submitted agaisn the innovator's product that is Synjardy XR Tablet (25/1000mg) in 0.1N HCL, Phosphate Buffer and Acetate Buffer. F2 values are in acceptable range.
	Analytical method validation/verification of product	Analytical method verification / validation studies for drug substance as well as for drug product is submitted.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** RUYUAN HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** IPCA Laboratories Limited, H-4, MIDC, Waluj Aurangabad431136 Maharahtra India.
API Lot No.	Empagliflozin: EGLZ-RD202004002 Metformin: 21060ML2ARMI
Description of Pack (Container closure system)	Alu-Alu blisters packed in unit carton
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	NPD-T-1573-S	NPD-T-1616-S	NPD-T-1617-S
Batch Size	4000 tablet	4000 tablet	4000 tablet
Manufacturing Date	07/07/2021	04/08/2021	07/07/2021
Date of Initiation	17/08/2021	17/08/2021	17/08/2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empator-M tablet 5mg+500mg (Empaglilozin + Metformin HCl) approved in 312th meeting of Registration Board.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of GMP Certificate for RUYUAN HEC Pharm Co., Ltd. (Certificate: 2018024) issued by Shaoguan Food and Drug Administration & valid upto 04-12-2021 is submitted. **Metformin HCl:** Copy of GMP certificate No. New-WHO-GMP/Cert/AD/67318/2018/11/24741 issued on 28/08/2018 valid till 27/08/2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of attested invoice (invoice# WIS200034) Dated: 16/04/2020 dy. No. 499 dated 04/05/2020. **Metformin HCl: Copy of attested** Invoice No. MEG2122/1630115 dated 02/04/2021 (diary No. 4247 dated 07/04/2021) imported from IPCA Laboratories limited attested by DRAP Karachi.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted.

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	The submitted stability data is till 3rd month time point, please provide stability study data till 6th month time point.	The firm has submitted stability summary sheets till 6 months for accelerated and long term stability studies along with the relevant documents.
2	As per submitted dossier, titration method has been used for assay estimation for Metformin HCl while according to latest edition of USP, HPLC method should be used for assay testing, please clarify.	*"The method used for assay estimation of Metformin for finished product by FPP manufacturer is HPLC as per latest edition of USP. API manufacturer has used titration method for assay estimation owing to the previous version of USP monograph".*

3	Provide complete batch manufacturing record for the applied product.	Complete batch manufacturing record is submitted.
4	As per submitted dossier, dissolution tests for Metformin core before coating has not been performed. Clarification is required for not establishing the dissolution profile for the tablet core.	*The Dissolution testing for Metformin HCl was performed at core stage before coating and results were well within specified limits. Since Metformin HCl in all strength have same label claim and same formulation, therefore dissolution profile is performed on film coated stage on risk basis. Satisfactory initial and stability results are also evident on Metformin HCl dissolution performance. Following core stage results are also attached herewith.* *Batch No. NPD-T-1108-T (Empagliflozin 5mg + Metformin HCl 1000 mg XR Tablet)* *Batch No. NPD-T-1107-T (Empagliflozin 12.5mg + Metformin HCl 1000 mg XR Tablet)*
5	Provide detail of manufacturing method for the applied product.	The firm has submitted complete batch manufacturing record for the applied product.

6. Scientific justification is require regarding addition of 100% overage for Empagliflozin for compensating the loss during coating.

Response:

Empagliflozin + Metformin HCl 25 + 1000 mg XR tablet is an API (Empagliflozin) coated tablet. Hence, the API is part of the coating suspension. As per label claim, 25 mg of Empagliflozin is coated on the tablet as mentioned in the Batch Production Record of Empagliflozin + Metformin HCl 25 + 1000 mg XR tablet, pp# 25 and is evident through the tablet weight that is 1479.0 mg, pp #43 95mg was coated on the tablet of 1384.0 mg thus taking it to 1479.00mg. Breakup is given below:

API Coating			
S.No.	*Raw Material*	*Quantity/tablet*	*Quantity/Batch*
1	*Empagliflozin*	*25.000 mg*	*250.000 g*
2	*Sheffcoat D white 5Y00692*	*42.000 mg*	*420.000 g*
3	*Talc*	*3.000 mg*	*30.000 g*
4	*Polysorbate 80 (Tween 80)*	*20.000 mg*	*200.000 g*
5	*Polyethylene Glycol 6000*	*5.000 mg*	*500.000 g*

Thus, no overages of the API are added which can be seen via the content increase of tablet before and after API coating mentioned above.

- *The 100% excess quantity mentioned in the BPR is for the clarity of the reviewer and the document itself.*
- *Excess quantity was added in coating material i.e., Sheffcoat D white 5Y00692, Polyethylene Glycol 6000, Talc, Polysorbate 80 (Tween 80) along with it is the **API Empagliflozin** to compensate for the process loss faced while Coating operation is being carried out, as it is an API coated tablet.*

*As it is understood that losses are observed/experienced during coating and thus extra quantities are added as a recompense. These extra quantities do not become part of the final film coated product, as is evident in the **Assay** results of **Empagliflozin** which are well within limits as per label claim.*

Decision: Registration Board deferred the case for;

- **Scientific justification regarding addition of 100% overage for Empagliflozin for**

	compensating the loss during coating. • **Clarification for not establishing the dissolution profile of the extended release core tablet before coating.**	
7.	Name, address of Applicant / Marketing Authorization Holder	M/s Dynatis Pakistan (Pvt.) Ltd. Plot No. 710, Sunder Industrial Estate, Lahore
	Name, address of Manufacturing site.	M/s Dynatis Pakistan (Pvt.) Ltd. Plot No. 710, Sunder Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29202 dated 26/10/2021
	Details of fee submitted	PKR 30,000/-: dated 30/07/2021
	The proposed proprietary name / brand name	Gliflo-Met 5/500mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…….5mg Metformin HCl……...500mg
	Pharmaceutical form of applied drug	Immediate release Film coated tablet
	Pharmacotherapeutic Group of (API)	Drugs used in diabetics (Combination of oral blood glucose lowering drugs)
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy (5/500mg) tablet, USFDA Approved.
	For generic drugs (me-too status)	Empagen 5/500 tablet by M/s Ferozsons.
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 29/2021-DRAP(FID-2065251-174) issued on the basis of inspection conducted on 26/03/2021.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Anhui Haikang Pharmaceutical Co., Ltd., No. 21 Huancheng west road, Anqing city, Anhui Province, 246000 China **Metformin HCl:** M/s Shouguang Fukang Pharmaceutical Co., Ltd., North East of Dongwaihuan road, Dongcheng Industrial Area, Shouguang city, Shandong Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to

		nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards container closure system and stability studies of drug substances.
	Stability studies	Empagliflozin: • Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20160301, 20160302, 20160303) Metformin HCl: • 48 months real time stability studies conducted at 30°C ± 2°C / 65% ± 5%RH of 03 batches. • 06 months accelerated stability studies conducted at 40°C ± 2°C / 75% ± 5%RH of 03 batches Batches: A-71411106004, A-71411106005, A-71411106006
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Jardiance Tablet 10mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, USA. by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that Jardiance Tablet 10mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, USA. in HCl buffer pH 1.2, Acetate Buffer pH 4.5 and Phosphate buffer pH 6.8. Calculation for f2 value is not required since the release is more than 85% in 15 minutes for innovator's as well as the applied product.
	Analytical method validation/ verification of product	Method validation / verification studies have submitted including accuracy/recovery, precision, specificity etc for drug substance and drug product is submitted.
STABILITY STUDY DATA		

Manufacturer of API	**Empagliflozin:** M/s Anhui Haikang Pharmaceutical Co., Ltd., No. 21 Huancheng west road, Anqing city, Anhui Province, 246000 China **Metformin HCl:** M/s Shouguang Fukang Pharmaceutical Co., Ltd., North East of Dongwaihuan road, Dongcheng Industrial Area, Shouguang city, Shandong Province, China.		
API Lot No.	20190703		
Description of Pack (Container closure system)	Alu-Alu blister strips pack packed in unit carton with leaf insert		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TCZ-002	TCZ-003	TCZ-004
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	06-11-2020	06-11-2020	06-11-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of drug manufacturing license no. 20190399 valid till 31/12/2025 is submitted. **Metformin HCl:** Copy of GMP certificate No. SD20190888 valid till 12/03/2024 is submitted by the applicant.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: Copy of attested invoice No. IND-19-0404, dy. No. 14544/2019DRAP dated 11-11-2019. Metformin HCl: Copy of attested invoice no. 419FK07Z057 dy. No. 11177/2019DRAP dated 22-08-2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity	Submitted

	monitoring of stability chambers (real time and accelerated)	

Remarks of Evaluator:

Sr. no.	Observations	Response
1	The official monograph of Metformin HCl (drug substance) is present in USP-43 wherein the HPLC method of analysis for assay of active has been described, whereas you have used titration method for the analysis. Therefore, a clarification is required for not performing the analysis by HPLC method or otherwise submit the said performance using HPLC method for analysis of Metformin drug substance.	The firm has stated that B.P monograph have been adopted for the said testing which is titration method by drug product manufacturer as well as by the drug substance manufacturer.
2	The test for specificity parameter of analytical method validation studies for drug product is performed by taking placebo solution while it should have been performed by spiking, please clarify.	*We have done stressed studies using following conditions.* *Acid-Base Hydrolysis, oxidation and heat treatment* If impurity or degradation product standards are not available, specificity testing may be demonstrated by comparing the test results of samples containing impurities or degradation products to a second well characterized procedure. This should include samples stored under relevant stress conditions that is light, heat, humidity, acid/base hydrolysis, oxidation (ICH Q1R2).
3	Please provide real time stability data of Metformin HCl drug substance conducted under the conditions of zone IV-A.	The firm has submitted real time stability data for Metformin drug substance for 60 months under the conditions of zone IV-A of 03 batches.
4	Provide batch number, expiry and date of manufacturing of the reference product (Synjardy) against which the pharmaceutical equivalence of the applied product is established.	Reference product: Synjardy 5/500mg tablet Bacth no.: C84685 EXiry: May, 2023 Mfg by: Boehringer Ingelheim
5	Provide the quantities (with rational) used for the preparation of 70%, 80%, 100%, 120% etc dilutions of sample solution for testing the accuracy/linearity parameters of validation studies for drug product. **Empagliflozin (Linearity):**	

Concentration (%)	Concentration (ppm)
70	3.5
80	4
90	4.5
100	5
110	5.5
120	6
130	6.5

Metformin (Linearity):

	Concentration (%) / Concentration (ppm) 70 / 700 80 / 800 90 / 900 100 / 1000 110 / 1100 120 / 1200 130 / 1300 **Accuracy:** **Concentration (%)** / **Concentration (mg) Empagliflozin** / **Concentration (mg) Metformin** 80 / 4mg / 800 100 / 5mg / 1000 120 / 6mg / 1200 *****Each sample concentration was dissolved in 100mL of solvent.	
6	Provide batch manufacturing record of all the 03 stability batches along with the calculations for potency adjustment considering the assay values (Empagliflozin 99.8% & Metformin 100.7%) of drug substances.	The firm has submitted complete batch manufacturing record along with the potency adjustment.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the submission of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter along with the submission of Rs. 7,500/- as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

8.	Name, address of Applicant / Marketing Authorization Holder	M/s Pharmevo (Pvt) Ltd., A-29, North Wesyern Industrial Zon Port Qasim Karachi.
	Name, address of Manufacturing site.	M/s Pharmevo (Pvt) Ltd., A-29, North Wesyern Industrial Zon Port Qasim Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32567 dated 13/12/2021
	Details of fee submitted	PKR 30,000/-: dated 26/10/2021
	The proposed proprietary name /	Erli Plus 12.5/850mg Tablet

	brand name	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin……..12.5mg Metformin HCl……850mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-diabetic
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	14's, 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy 12.5/850mg, EM approved.
	For generic drugs (me-too status)	Xenglu-met tablet by M/s Hilton Pharma
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 119/2020-DRAP(K) issued on t basis of inspection conducted on 16/09/2020.
	Section approval	Tablet General Section
	Name and address of API manufacturer.	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical Co., Limited, No. 18, 2 provincial road, economic development zone, Huaian Jiangs China. **Metformin HCl:** M/s Shouguang Fukang Pharmaceutical co. ltd., North-east Dongwaihuan road, Dongchend Industrial area, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD templat Summarized information related to nomenclature, structur general properties, solubilities, physical form, manufacture description of manufacturing process and controls, impuritie specifications, analytical procedures and its verification, bat analysis and justification of specification, reference standar container closure system and stability studies of drug substan and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related nomenclature, structure, general properties, solubility, physic form, manufacturers, description of manufacturing process a controls, impurities, residual solvents, specifications, analytic procedures and its complete validation studies, batch analys and justification of specification, details of reference standard container closure system and stability studies of drug substanc
	Stability studies	**Empagliflozin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months Batches: (130701, 130702, 130703) **Metfromin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (A-72611405016, A-72611405017, A-72611405018)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description manufacturing process and controls, impurities, specification analytical procedure and its validation studies, batch analysis a justification of specification, reference standard, contain closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Product: Diampa-M 12.5/850mg tablet Mfg date: 06/2021 Batch #: 004FF1 Mfg by: M/s Getz Pharma Pharmaceutical equivalence and CDP studies have be performed against the above described product.
	Analytical method validation/verification of product	Method validation / verification studies have submitt including, accuracy/recovery, precision, specificity, , syste suitability etc for drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical Co., Limited, No. 18, 237 provincial roa economic development zone, Huaian Jiangsu, China. **Metformin HCl:** M/s Shouguang Fukang Pharmaceutical co. ltd., North-east of Dongwaihu road, Dongchend Industrial area, China.		
API Lot No.	Empgliflozn (5920) Metformin (6415)		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20PD-3330-02-T	20PD-3330-03-T	20PD-3330-04-T
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	08/2020	08/2020	08/2020
Date of Initiation	22/09/2020	22/09/2020	22/09/2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Empagliflozin: Copy of GMP certificate valid till 14/01/2024 issued by **Huai'a Pharmaceutical Industry association**, China. Copy of Drug Manufacturing License no. Su 20160324 issued Jiangsu Drug Administration (Huai'an Inspection Branch) val till 06-12-2025. Metformin HCl;

		Copy of GMP certificate No. SD20190888 valid till 12/03/202 issued by CFDA.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: Copy of attested invoice number ZY19100801G/W date 18/10/2019 cleared on 22/10/2019 vide dy. No. 11623. Metformin HCl; Copy of attested invoice number 419FK08Z092-2 date 10/10/2019 dy. No. 11552 dated 21/10/2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Please provide analytical method verification studies performed by drug product manufacturer for empaglflozin drug substance.	Analytical method verification studies for empagliflozin is submitted.
2	Provide GMP certificate / drug manufacturer license issued by relevant authority for empagliflozin drug substance.	Empagliflozin: Copy of GMP certificate valid till 14/01/2024 issued by **Huai'an Pharmaceutical Industry association**, China. Copy of Drug Manufacturing License no. Su 20160324 issued by Jiangsu Drug Administration (Huai'an Inspection Branch) valid till 06-12-2025.
3	Provide Documents for the procurement of API with approval from DRAP (in case of import) for Empagliflozin drug substance.	Empagliflozin: Copy of attested invoice number ZY19100801G/W dated 18/10/2019 cleared on 22/10/2019 vide dy. No. 11623
4	Titration method is adopted for analysis of Metformin HCl while HPLC method has been described for the estimation of Metformin in latest edition of USP, please clarify. Moreover, analytical method verification studies are required for Metformin drug	The firm has submitted that they had used the method available in USP at the time of development of the applied product. Now the firm has submitted revised method for assay estimation of Metformin according to latest edition

	substance according to latest USP monograph performed by drug product manufacturer.	of USP and performed the verification studies.
5	Provide results of pharmaceutical equivalence studies against the reference / innovator's product by performing all the quality tests along with the results of comparative dissolution profile against reference / innovator's product. Moreover, provide batch number, expiry and date of manufacturing of the innovator's / reference product.	Product: Diampa-M 12.5/850mg tablet Mfg date: 06/2021 Batch #: 004FF1 Mfg by: M/s Getz Pharma Pharmaceutical equivalence and CDP studies have been performed against the above described product.
6	Provide detailed analytical method for the drug product along with analytical method validation studies.	Analytical method for the applied product and the validation studies including specificity, linearity/range, robustness, precision, accuracy etc have been submitted.
7	Justify the dissolution parameters since the selected RPM is 75 while as per USFDA dissolution data base, the RPM should be 50.	The firm has referred to Empagliflozin tablet's literature review where the speed 75rpm has been selected while as per the assessment report of Synjardy tablet the speed is 50rpm.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughou proposed shelf life and on accelerated studies for six months as per the commitment submitted the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitme submitted in the registration application.**
- **Firm will submit analytical method verifications studies for Metformin HCl drug substance as p latest edition of USP (including specificity, accuracy and method precision) before the issuance registration letter along with the submission of Rs. 7,500/- as pre-registration variation fee as p notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will revise the dissolution specifications for the applied product as per t innovator's product (i.e. paddle speed 50rpm) along with the submission of dissolution testing commercial batch.**

9.	Name, address of Applicant / Marketing Authorization Holder	M/s Sami Pharmaceuticals, F-95, Off Hub river Road, S.I.T. Karachi.
	Name, address of Manufacturing site.	M/s Sami Pharmaceuticals, F-95, Off Hub river Road, S.I.T. Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 4176 dated 14/02/2022
	Details of fee submitted	PKR 75,000/-: dated 23/09/2021
	The proposed proprietary name /	Bemdo 180mg tablet

	brand name	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Bempedoic Acid……180mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Cholesterol lowering agent
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	7's, 10's, 14's, 20's, 28's 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nexletol film coated tablet 180 mg, USFDA Approved. Nilemdo 180mg film ocated tablet, MHRA Approved. Nilemdo 180mg film coated tablet, Austria Approved Nilemdo 180mg film ocated tablet, SPAIN Approved
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	Inspection date: 26-03-2020 & 13-04-2020 Based on the areas inspected, people met, processes observe and intention of the firm for continuous improvement at t time of inspection it is concluded that the firm is operating a Good level of GMP compliance.
	Section approval	Tablet Section (General)
	Name and address of API manufacturer.	M/s Metrochem API private Limited, Unit IV pot no. 34B, 40 & 60B, J.N. Pharma city, Thanam village Parwada Mand Visakhapatnam District, Andhra Pradesh, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD templat Summarized information related to nomenclature, structur general properties, solubilities, physical form, manufacture description of manufacturing process and controls, impuritie specifications, analytical procedures and its verification, bat analysis and justification of specification, reference standar container closure system and stability studies of drug substan and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related nomenclature, structure, general properties, solubility, physic form, manufacturers, description of manufacturing process a controls, impurities, residual solvents, specificatio analytical procedures and its complete validation studies, bat analysis and justification of specification, details of referen standards, container closure system and stability studies drug substance.
	Stability studies	• Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (HAN-P/21003, HAN-P/21004, HAN-P/21005)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description manufacturing process and controls, impurities, specificatio analytical procedure and its validation studies, batch analys and justification of specification, reference standard, contain closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	The firm has submitted pharmaceutical equivalence studi against the innovator's product Nexletol Tablet 180mg (bat number 1708634) by performing quality tests. Comparative dissolution profile against the innovator product (Nexletol 180 mg Tablet) in all the three med including Acetate Buffer (4.5pH), Phosphat eBuffer (6.8p and 0.1N HCl (1.2pH). F2 values are within the acceptab range for 0.1N HCl and Acetate buffer whereas for Phospha Buffer more than 85% drug is released in 15 minutes.
	Analytical method validation/verification of product	Method validation studies have submitted including linearit range, accuracy/recovery, precision, specificity, LOD/LO Robustness, Solution stability, system suitability

STABILITY STUDY DATA

Manufacturer of API	M/s Metrochem API private Limited, Unit IV pot no. 34B, 40B 60B, J.N. Pharma city, Thanam village Parwada Manda Visakhapatnam District, Andhra Pradesh, India.		
API Lot No.	PD/BMP-P/20010		
Description of Pack (Container closure system)	Alu-PVC blister pakced in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	1000 tablets	1000 tablets	1000 tablets
Manufacturing Date	04/2021	04/2021	04/2021
Date of Initiation	17/05/2021	17/05/2021	17/05/2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not provided by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate no. L.Dis.No: 152042/DD/DCA/VSP/2021 dated 29/10/2021 issued by dru control Administration.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copies of packing list, form 3 and for 7. Copy of Invoice number DE/20/0149 dated 19/01/2021 clear on 26/01/2021 vide dy. No. 0306/2021 is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Indications:

Bempedoic Acid is an adenosine triphosphate-citrate lyase (ACL) inhibitor indicated as an adjunct to diet a
maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolem
or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.

Sr. No.	Observations	Response
1	Provide detailed method of analysis for drug substance along with the specifications.	Submitted.
2	Tests for reproducibility parameter (inter-day precision) of analytical method verification studies have not been performed, please clarify.	The firm has submitted revised analytical method validation report including day variation analyst variation and equipment variation.
3	Provide attested copy of invoice for procurement of drug substance.	Copy of Invoice number DE/20/0149 dated 19/01/2021 cleared on 26/01/2021 vide dy. No. 0306/2021 is submitted.
4	Provide complete batch manufacturing record.	Submitted.
5	The limit for disintegration time included in finished product specifications is 30 minutes while dissolution specifications include 80%(Q) of labelled amount of drug at 20 minutes. Please clarify or otherwise revise the specifications for disintegration time.	*We set the disintegration specs according to USP general monograph which specifies NMT 30mins for film coated tablet. Our product is fast dissolving with a dissolution specs of NLT 80% in 20 minutes and disintegration time of our product is found within 10 minutes which correlates with dissolution. We have revised the specifications for DT from NMT 30mins to NMT 15minuts.*

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughou proposed shelf life and on accelerated studies for six months as per the commitment submitted the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitme submitted in the registration application.**
- **Firm will submit fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/202 B&A/DRAP dated 07-05-2021.**

10.	Name, address of Applicant / Marketing Authorization Holder	M/s Genix Pharma (pvt) Ltd. 44, 45-B, Korangi Creek Road, Karachi.
	Name, address of Manufacturing site.	M/s Genix Pharma (pvt) Ltd. 44, 45-B, Korangi Creek Road, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 34240 dated 31/12/2021
	Details of fee submitted	PKR 30,000/-: dated 08/12/2021
	The proposed proprietary name / brand name	Rebamipide 100mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Rebamipide……100mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-gastritis
	Reference to Finished product specifications	JP
	Proposed Pack size	7's, 14's, 28's, 30's, 60's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Mucosta film coated tablet 100mg
	For generic drugs (me-too status)	Mucosta 100mg tablet by Otsuka, Reg. No. 078129
	GMP status of the Finished product manufacturer	Copy of GMP certificate no. 46/2021-DRAP(K) issu on the basis of inspection conducted on 15/06/2021.
	Section approval	Tablet general section (Revised)
	Name and address of API manufacturer.	M/s Jiangxi Synergy Pharmaceutical Co.,Ltd., Jiang Fengxin Industrial Park, Jiangxi Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD templat Summarized information related to nomenclatur structure, general properties, solubilities, physical forn manufacturers, description of manufacturing process ar controls, impurities, specifications, analytical procedur and its verification, batch analysis and justification specification, reference standard, container closu system and stability studies of drug substance and dru product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data relate to nomenclature, structure, general properties, solubilit physical form, manufacturers, description manufacturing process and controls, impurities, residu solvents, specifications, analytical procedures and i complete validation studies, batch analysis ar justification of specification, details of referen standards, container closure system and stability studi of drug substance.
	Stability studies	• Real time: 30˚C ± 2˚C / 65% ± 5%RH for 36 mont • Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for months Batches: (20100704, 20100705, 20100706)
	Module-III (Drug Product):	The firm has submitted detail of manufacturer description of manufacturing process and control

		impurities, specifications, analytical procedure and i validation studies, batch analysis and justification specification, reference standard, container closu system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence studied have bee performed against the innovator's product that Mucosta 100mg Tablet (Batch number MC19607 imported by M/s Otsuka Pakistan Ltd, by performi quality tests. Comparative dissolution profile is submitted again Mucosta 100mg tablet in all the 03 media that is 0.1 HCl, Acetate Buffer and Phosphate Buffer.
	Analytical method validation/verification of product	Method validation / verification studies have submitte including accuracy/recovery, precision, specificity e for drug product and drug substance.

STABILITY STUDY DATA

Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co.,Ltd., Jiangxi Fengx Industrial Park, Jiangxi Province, China.		
API Lot No.	05-20200706C		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21SB(A)-023-01	21SB(A)-023-02	21SB(A)-023-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	04/2021	04/2021	04/2021
Date of Initiation	17/06/2021	17/06/2021	17/06/2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any response.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate no. 2022001 valid t 19/01/2027 issued on 20/01/2022 issued by Jiangxi A Engineering technology research Centre, China submitted. Copy of GMP certificate No. 2020002 issued by CFD valid till 11/03/2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of attested invoice numb JXSG201131 dated 06-11-2020cleared on 02/12/2020.

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator-I:

Sr. No.	Observations	Response
1	Justify the limit (i.e NMT 0.15%) selected for Rebamipide m-chloro isomer since J.P does not describe the limit in terms of percentage for the isomer as well as for the other related substance in the specifications of drug substance.	*As per JP, to calculate the %age of m-chloroisomer as per given acceptance criteria 1.e 3/8 times the area of standard, first calculate the concentration of standard that is 0.0016mg/mL and then sample that is 0.4mg/mL then finally calculate the percentage of m-chloroisomer (0.15%).* Same procedure has been adopted for calculation of other impurities.
2	Real time stability data for of drug substance (batch number 20100706) is not submitted, provide the required data.	The firm has submitted real time stability data of drug substance for batch number 20100706.
3	Provide results of comparative dissolution profile along with the calculations of F2 and F1 factors.	The firm has provided comparative dissolution profile against Mucosta Tablet 100mg by M/s Otsuka Pakistan, batch number MC196077 in all the 3 media. F2 values are in acceptable range.
4	Submitted stability data is till 3rd month time point, provide stability study data till 6 months.	The firm submitted stability data till 6 month time point.
5	Provide Record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) for the applied product	Submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case No. II: Export facilitation

Assistant director PR-I/EFD vide letter No.F.1-6/2019-PR-I (EFD dated 06-10-2022 has informed that DRAP Authority in its 133rd meeting held on 13th April 2022, decided to grant registration on priority basis to the *pharmaceutical* i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year. In compliance to the aforementioned decision of the authority, the following firm have achieved the benchmark of more than 100,000 USD during the fiscal Year 2020-2021 and submitted their applications for priority consideration in lieu of export facilitation for Registration Board please.,

11.	Name, address of Applicant / Marketing Authorization Holder	M/s Novamed Pharmaceuticals (pvt) Ltd. 28-km Ferozepur rod, Lahore.
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals (pvt) Ltd. 28-km Ferozepur rod, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 5104 dated 23/02/2022
	Details of fee submitted	PKR 30,000/-: dated 31/01/2022
	The proposed proprietary name / brand name	Empozin-M 12.5mg+500mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet Contains: Empagliflozin……..12.5mg Metformin HCl…….500mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product specifications	In-house specs
	Proposed Pack size	10’s, 14’s, 20’s, 28’s, 30’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy tablet (5/500, 5/1000, 12.5/500, 12.5/1000), USFDA Approved.
	For generic drugs (me-too status)	Diampa-M 12.5/500 by Getz Pharma
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 68/2021-DRAP(FID-385689549774-222) issued on the basis of inspection conducted on 06/08/2021.
	Section approval	Tablet general section (revised)
	Name and address of API manufacturer.	**Empagliflozin:** M/s Jiangsu Yongan Pharamceutical Co., Ltd., 18, 237 provincial road, economic development zone, Huai’an Jiangsu, China. **Metformin HCl:** Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and

		its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance (Sitagliptin and Metformin).
	Stability studies	**Empagliflozin:** • Real time: 30˚C ± 2˚C / 65% ± 5%RH for 36 months • Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 12 months Batches: (130701, 130702, 130703) **Metfromin:** • Real time: 30˚C ± 2˚C / 65% ± 5%RH for 60 months • Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (MEF/1510145, MEF/1510146, MEF/1510147)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The firm has submitted comparative dissolution profile in all the 03 media that is 0.1N HCl, Phosphate buffer and Acetate buffer against Synjardy 12.5/500mg, mfg by Boehringer ingelheim pharma GmbH & Co. KG Binger Strasse Germany, Batch number C98959. The firm has submitted CDP studies against the innovator's product that is Synjardy (B: C98959) in all the three media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, Robustness, system suitability etc.
STABILITY STUDY DATA		
Manufacturer of API	**Empagliflozin:** M/s Jiangsu Yongan Pharamceutical Co., Ltd., 18, 237 provincial road, economic development zone, Huai'an Jiangsu, China.	

	Metformin HCl: M/s Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.		
API Lot No.	Empgliflozin: 4500-202003001 Metformin HCl:MEF/11041012		
Description of Pack (Container closure system)	Alu-Alu blister pakced in secondary unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD/PR21-100/T1/S1	RD/PR21-100/T1/S2	RD/PR21-100/T1/S3
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	09/2021	09/2021	09/2021
Date of Initiation	28/09/2021	28/09/2021	28/09/2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has not submitted any response
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of GMP certificate valid till 14/01/2024 issued by Huai'an Pharmaceutical industry Association. Copy of DML number Su20160324 issued by Jiangsu Medical Products Administration on 07/12/2020 valid till 06/12/2025 for Empagliflozin drug substance manufacturer. **Metformin HCl:** copy of GMP certificate no. 20031933 valid till 19/03/2023 issued by food and drugs control administration, Gujarat.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of attested invoice No. ZY20052001G/W dated 20th May, 2020 vide diary number 7093/2020-DRAP dated 09/06/2020. **Metformin HCl:** Copy of attested invoice cleared on 15/02/2021 dy. No. 2473/24-DRAP is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity	Submitted

	monitoring of stability chambers (real time and accelerated)	

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Provide certificate of analysis of Empagliflozin & Metformin HCl for those batches which were used for product development from finished product manufacturer and drug substance manufacturer.	Copies of COAs from finished product and drug substance manufacturer is submitted for batch number 4500202003001 (Empagliflozin) and for batch number MEF/11041012 (Metformin HCl) are submitted.
2	Submitted GMP certificate for Empagiflozin is from Huai'an industry association, provide GMP certificate issued by relevant authority.	Copy of DML number Su20160324 issued by Jiangsu Medical Products Administration on 07/12/2020 valid till 06/12/2025 for Empagliflozin drug substance manfuatcurer.
3	Provide documents (i.e invoices) confirming import of Metformin HCl drug substance.	Copy of attested invoice cleared on 15/02/2021 dy. No. 2473/24-DRAP is submitted.
4	Provide analytical method verifiction studies for drug substances (Empagliflozin & Metformin HCl) performed by drug product manufacturer.	The firm has submitted analytical mehto dverification / validations studies for Metformin HCl and Empagliflozin drug substances performed by drug product manufacturer.
5	Provide results of Comparative dissolution profile performed against the innovator's product for Empozin-M 12.5mg/500mg tablet.	The firm has submitted CDP studies against the innovator's product that is Synjardy (B: C98959) in all the three media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer.
6	Clarification is required since as per available literature of the reference product, Q value should be achieved in 20 minutes while you have performed the said studies at 30 minutes in all the five strengths (12.5/1000, 5/500, 5/1000, 5/850, 12.5/500) of the applied product.	The firm has submitted that they will revised the dissolution specifications as per the innovator's product.
7	The submitted stability data is till 3rd month time point, please submit the stability data till 6 months.	The firm has submitted 6th month time point data for all the three batches for accelerated and real time stability studies.

Decision: Approved with innovator's specifications. The Board decided that the manufacturer will submit fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the submission of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter.**
- **Manufacturer will submit revised dissolution specifications as per innovator's product (i.e. sampling time at 20 minutes) along with the performance of testing on commercial**

batches.		
12.	Name, address of Applicant / Marketing Authorization Holder	M/s Novamed Pharmaceuticals (pvt) Ltd. 28-km Ferozepur rod, Lahore.
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals (pvt) Ltd. 28-km Ferozepur rod, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 5105 dated 23/02/2022
	Details of fee submitted	PKR 30,000/-: dated 31/01/2022
	The proposed proprietary name / brand name	Empozin-M 5mg+850mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet Contains: Empagliflozin……..5mg Metformin HCl…….850mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Antidiabetic
	Reference to Finished product specifications	In-house specs
	Proposed Pack size	10’s, 14’s, 20’s, 28’s, 30’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy tablet (5/8508) EMA Approved.
	For generic drugs (me-too status)	Diampa-M 12.5/500 by Getz Pharma
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 68/2021-DRAP(FID-385689549774-222) issued on the basis of inspection conducted on 06/08/2021.
	Section approval	Tablet general section (revised)
	Name and address of API manufacturer.	**Empagliflozin:** M/s Jiangsu Yongan Pharamceutical Co., Ltd., 18, 237 provincial road, economic development zone, Huai’an Jiangsu, China. **Metformin HCl:** Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance (Sitagliptin and Metformin).
	Stability studies	**Empagliflozin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months Batches: (130701, 130702, 130703) **Metfromin:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MEF/1510145, MEF/1510146, MEF/1510147)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The firm has submitted comparative dissolution profile in all the 03 media that is 0.1N HCl, Phosphate buffer and Acetate buffer against Synjardy 5/850mg, mfg by Boehringer ingelheim pharma GmbH & Co. KG Binger Strasse Germany, Batch number 902007. The firm has submitted CDP studies against the innovator's product that is Synjardy (B: 902007) in all the three media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, Robustness, system suitability etc.
STABILITY STUDY DATA		
Manufacturer of API	**Empagliflozin:** M/s Jiangsu Yongan Pharamceutical Co., Ltd., 18, 237 provincial road, economic development zone, Huai'an Jiangsu, China.	

	Metformin HCl: M/s Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.		
API Lot No.	Empgliflozin: 4500-202003001 Metformin HCl:MEF/11041012		
Description of Pack (Container closure system)	Alu-Alu blister pakced in secondary unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD/PR21-099/T1/S1	RD/PR21-099/T1/S2	RD/PR21-099/T1/S3
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	09/2021	09/2021	09/2021
Date of Initiation	28/09/2021	28/09/2021	28/09/2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has not submitted any response
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of GMP certificate valid till 14/01/2024 issued by Huai'an Pharmaceutical industry Association. Copy of DML number Su20160324 issued by Jiangsu Medical Products Administration on 07/12/2020 valid till 06/12/2025 for Empagliflozin drug substance manufacturer. **Metformin HCl:** copy of GMP certificate no. 20031933 valid till 19/03/2023 issued by food and drugs control administration, Gujarat.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of attested invoice No. ZY20052001G/W dated 20th May, 2020 vide diary number 7093/2020-DRAP dated 09/06/2020. **Metformin HCl:** Copy of attested invoice cleared on 15/02/2021 dy. No. 2473/24-DRAP is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity	Submitted

	monitoring of stability chambers (real time and accelerated)	

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Provide certificate of analysis of Empagliflozin & Metformin HCl for those batches which were used for product development from finished product manufacturer and drug substance manufacturer.	Copies of COAs from finished product and drug substance manufacturer is submitted for batch number 4500202003001 (Empagliflozin) and for batch number MEF/11041012 (Metformin HCl) are submitted.
2	Submitted GMP certificate for Empagiflozin is from Huai'an industry association, provide GMP certificate issued by relevant authority.	Copy of DML number Su20160324 issued by Jiangsu Medical Products Administration on 07/12/2020 valid till 06/12/2025 for Empagliflozin drug substance manfuatcurer.
3	Provide documents (i.e invoices) confirming import of Metformin HCl drug substance.	Copy of attested invoice cleared on 15/02/2021 dy. No. 2473/24-DRAP is submitted.
4	Provide analytical method verifiction studies for drug substances (Empagliflozin & Metformin HCl) performed by drug product manufacturer.	The firm has submitted analytical method verification / validations studies for Metformin HCl and Empagliflozin drug substances performed by drug product manufacturer.
5	Clarification is required since as per available literature of the reference product, Q value should be achieved in 20 minutes while you have performed the said studies at 30 minutes in all the five strengths (12.5/1000, 5/500, 5/1000, 5/850, 12.5/500) of the applied product.	The firm has submitted that they will revised the dissolution specifications as per the innovator's product.
6	The submitted stability data is till 3rd month time point, please submit the stability data till 6 months.	The firm has submitted 6th month time point data for all the three batches for accelerated and real time stability studies.

Decision: Approved with innovator's specifications. The Board decided that the manufacturer will submit fee of Rs.7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the submission of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter.**
- **Manufacturer will submit revised dissolution specifications as per innovator's product (i.e. sampling time at 20 minutes) along with the performance of testing on commercial batches.**

A: Registration Applications for which stability data is required submitted on Form 5 / Form 5D

I: M/s Novamed Pharmaceuticals (pvt) ltd.:

Sr. No.	Name & Address of Manufacturer / Applicant	Brand Name (Proprietary Name + Dosage Form + Strength), Composition, Pharmacological Group, Finished Product Specification	Type of Form, Initial Diary & Date, Fee (including differential fee), Demanded Price / Pack size	International Availability GMP Inspection Report Date & Remarks
13.	M/s Novamed Pharmaceuticals (pvt) Ltd. 28-km Ferozepur rod, Lahore.	Empozin-M 12.5mg+1000mg tablet Each film coated tablet Contains: Empagliflozin……..12.5mg Metformin HCl……1000mg Antidiabetic In-house specs	Form 5-D Dy No. 2908 12-04-2017 PKR.50,000/- (copy of fee challan) 15-10-2018 14's, 28's As per SRO	Synjardy tablet (5/500, 5/1000, 12.5/500, 12.5/1000), USFDA Approved. Diampa-M by Get Pharma Copy of GMP certificate No. 68/2021-DRAP(FID-385689549774-222) issued on the basis of inspection conducted on 06/08/2021. Tablet general section (revised)
14.	M/s Novamed Pharmaceuticals (pvt) Ltd. 28-km Ferozepur rod, Lahore.	Empozin-M 5mg+500mg tablet Each film coated tablet Contains: Empagliflozin……..5mg Metformin HCl……500mg Antidiabetic In-house specs	Form 5-D Dy No. 2906 12-04-2017 PKR.50,000/- (copy of fee challan) 15-10-2018 14's, 28's As per SRO	
15.	M/s Novamed Pharmaceuticals (pvt) Ltd. 28-km Ferozepur rod, Lahore.	Empozin-M 5mg+1000mg tablet Each film coated tablet Contains: Empagliflozin……..5mg Metformin HCl……1000mg Antidiabetic In-house specs	Form 5-D Dy No. 2907 12-04-2017 PKR.50,000/- (copy of fee challan) 15-10-2018 14's, 28's As per SRO	

Remarks of Evaluator:
Alternate brand names: Exempa-M, Zampa-M, Gempaz-M
Stability data is submitted on 19/07/2021.
* As per available literature of the reference product, Q value should be achieved in 20 minutes while the firm has performed the said studies at 30 minutes in all the five strengths (12.5/1000, 5/500, 5/1000, 5/850, 12.5/500) of the applied product.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** M/s Jiangsu Yongan Pharamceutical Co., Ltd., 18, 237 provincial road, economic development zone, Huai'an Jiangsu, China.
	Metformin HCl: Aarti Drug limited (unit II) plot no. 211 & 213, road – 2, GIDC at & post: Sarigam 396 155 Dist: Valsad Gujarat India.

API Lot No.	Empgliflozin: 4500-202003001		
	Metformin HCl: MEF/19123234		
Description of Pack (Container closure system)	Alu-Alu foil packed in unit carton		
Stability Storage Condition	Accelerated: 40°C ± 2°C / 75% ± 5%RH Real Time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Accelerated: 6 Months Real Time: 6 Months		
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0, 3, 6 (months)		
Empozin-M 12.5mg+1000mg tablet			
Batch No.	RD/PR20-019/T1/S1	RD/PR20-019/T1/S2	RD/PR20-019/T1/S3
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	11/2020	11/2020	11/2020
Date of Initiation	27/11/2020	27/11/2020	27/11/2020
No. of Batches	03		
Empozin-M 5mg+500mg tablet			
Batch No.	RD/PR21-060/T1/S1	RD/PR21-060/T1/S2	RD/PR21-060/T1/S3
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	04/2021	04/2021	04/2021
Date of Initiation	05/05/2021	05/05/2021	05/05/2021
No. of Batches	03		
Empozin-M 5mg+1000mg tablet			
Batch No.	RD/PR20-018/T1/S1	RD/PR20-018/T1/S2	RD/PR20-018/T1/S3
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	10/2020	10/2020	10/2020
Date of Initiation	03/11/2020	03/11/2020	03/11/2020
No. of Batches	03		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT			
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product Dasvir Tablets (60mg & 90mg) which was conducted on 22/01/2018 for verification stability data and was presented in 278th meeting of Registration Board. The Board approved the cases.	
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	The firm has certificate of analysis for relevant batch used for the product development from drug substance manufacturer for Empagliflozin along with the COA of impurity standards for impurity A and impurity B.	
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Firm has submitted copy of method used for analysis of API from both API Manufacturer and Finished Product manufacturer	

4.	Stability study data of API from API manufacturer	**Empagliflozin:** • Real time: 30˚C ± 2˚C / 65% ± 5%RH for 36 months • Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 12 months Batches: (130701, 130702, 130703) **Metfromin:** • Real time: 30˚C ± 2˚C / 65% ± 5%RH for 60 months • Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (MEF/1510145, MEF/1510146, MEF/1510147)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Copy of GMP certificate valid till 14/01/2024 issued by Huai'an Pharmaceutical industry Association. Copy of DML number Su20160324 issued by Jiangsu Medical Products Administration on 07/12/2020 valid till 06/12/2025 for Empagliflozin drug substance manufacturer. **Metformin HCl:** copy of GMP certificate no. 20031933 valid till 19/03/2023 issued by food and drugs control administration, Gujarat.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of attested invoice No. ZY20052001G/W dated 20th May, 2020 vide diary number 7093/2020-DRAP dated 09/06/2020. **Metformin HCl:** Copy of attested invoice dated 25/12/2019 cleared vide diary number 436/2020-DRAP dated 08/01/2020.
7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of finished product (In-House).
9.	Drug-excipients compatibility studies (where applicable)	Firm has used same excipients as that of the innovator's product therefore compatibility studies are not required
10.	Complete batch manufacturing record of three stability batches.	Firm has provided Batch Manufactu ring Record for all the batches of applied products.
11.	Record of comparative dissolution data (where applicable)	The firm has submitted comparative dissolution profile in all the 03 media that is 0.1N HCl, Phosphate buffer and Acetate buffer against : • Synjardy 12.5/1000mg, mfg by Boehringer ingelheim pharma GmbH & Co. KG Binger Strasse Germany, Batch number 003231. • Synjardy 5/500mg, mfg by Boehringer ingelheim pharma GmbH & Co. KG Binger Strasse Germany, Batch number C98957. • Synjardy 5/1000mg, mfg by Boehringer ingelheim pharma GmbH & Co. KG Binger Strasse Germany, Batch number 004425.

12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and audit trail reports for HPLC analysis for all the three batches.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for both stability chambers for accelerated as well as real time stability studies.

Evaluation by PEC:

Sr. no.	Shortcomings communicated	Response by the firm
1	Please provide certificate of analysis for Empagliflozin drug substance for the batch used for product development from drug product manufacturer.	The firm has provided COAs for Empagliflozin from drug substance and drug product manufacturer for batch number 4500-202003001.
2	Submitted GMP certificate for Empagiflozin is from Huai'an industry association, provide GMP certificate issued by relevant authority.	Copy of DML number Su20160324 issued by Jiangsu Medical Products Administration on 07/12/2020 valid till 06/12/2025 for Empagliflozin drug substance manufacturer.
3	Provide certificate of Analysis of API from both API Manufacturer and Finished Product Manufacturer for Metformin HCl.	The firm has provided COAs for Metformin from drug substance and drug product manufacturer for batch number MEF/19123234.
4	Provide documents (i.e invoice) confirming import of Metformin HCl drug substance.	Copy of attested invoice dated 25/12/2019 cleared vide diary number 436/2020-DRAP dated 08/01/2020.
5	As per provided method of analysis from drug substance manufacturer, titration method has been used for assay estimation while according to latest edition of USP, HPLC method should be used for assay testing, please clarify.	The firm has stated that the drug substance manufacturer and drug product manufacturer have used BP method for analysis of Metformin HCl where the method of assay analysis is titration.

Decision: Registration Board approved the registration applications of Empozin-M 12.5mg+1000mg tablet, Empozin-M 5mg+500mg tablet, Empozin-M 5mg+1000mg tablet with innovator's specifications. The Board further decided that the manufacturer will submit fee of Rs. 7,500/- for revision of specifications for strength as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the submission of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter.**
- **Manufacturer will submit revised dissolution specifications as per innovator's product (i.e. sampling time at 20 minutes) along with the performance of testing on commercial**

batches.

III: M/s Genix Pharma Pvt. Ltd.

Sr. No.	Name & Address of Manufacturer / Applicant	Brand Name (Proprietary Name + Dosage Form + Strength), Composition, Pharmacological Group, Finished Product Specification	Type of Form, Initial Diary & Date, Fee (including differential fee), Demanded Price / Pack size	International Availability GMP Inspection Report Date & Remarks
16.	M/s Genix Pharma (pvt) Ltd. 44, 45-B, Korangi Creek Road, Karachi.	Vonraz 10mg tablet Each film coated tablet contains: Vonoprazan as fumarate…..10mg Potassium-competitive acid blocker In House	Form 5D Dy. No. 11980 dated 06/03/2019 Rs. 50,000/- dated 06/03/2019 10's, 20's, 30's As per SRO	Takecab tablet (10mg & 20mg), PMDA Japan Approved. Copy of GMP certificate no. 46/2021-DRAP(K) issued on the basis of inspection conducted on 15/06/2021.
17.	M/s Genix Pharma (pvt) Ltd. 44, 45-B, Korangi Creek Road, Karachi.	Vonraz 20mg tablet Each film coated tablet contains: Vonoprazan as fumarate…..20mg Potassium-competitive acid blocker In House	Form 5D Dy. No. 11981 dated 06/03/2019 Rs. 50,000/- dated 06/03/2019 10's, 20's, 30's As per SRO	

Remarks of Evaluator:
The firm submitted the stability data on 21/02/2022.
The firm has submitted analytical method validation studeis for drug product including accuracy, linearity, specificity, robustness, precision etc.

STABILITY STUDY DATA			
Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co., Ltd.,, Jiangxi Fengxin Industrial Park 330700 Fengxin County, Jiangxi Province, China.		
API lot number	20201201BD		
Description of Pack (Container closure system)	Alu-Alu blister packed in secondary unit carton		
Stability Storage Condition	Accelerated: 40°C ± 2°C / 75% ± 5%RH Real Time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Accelerated: 6 Months Real Time: 6 Months		
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0, 3, 6 (months)		
Vonraz 10mg tablet			
Batch No.	21SB(A)-155-01	21SB(A)-157-03	21SB(A)-156-02
Batch Size	1500 tab	1500 tab	1500 tab

Manufacturing Date	05/2021	05/2021	05/2021
Date of Initiation	03/06/2021	03/06/2021	03/06/2021
No. of Batches	03		
Vonraz 20mg tablet			
Batch No.	21SB(A)-160-03	21SB(A)-159-02	21SB(A)-158-01
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	05/2021	05/2021	05/2021
Date of Initiation	03/06/2021	03/06/2021	03/06/2021
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to the decision of 281st meeting of Registration Board whereby the product Wymly 25mg (Tenofovir) was approved on the basis of PSI report. Following were endorsed in the report. • 21 CFR complaint system
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Firm has submitted copy of method used for analysis of API from both API Manufacturer and Finished Product manufacturer
4.	Stability study data of API from API manufacturer	• Real time: 30°C ± 2°C / 65% ± 5%RH for 24` months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months Batches: (20190801BD, 20190803BD, 20190801BD)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate no. 2022001 valid till 19/01/2027 issued on 20/01/2022 issued by Jiangxi API Engineering technology research centre, China sis submitted.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of invoice number JXSG210156 dated 28/01/2021 cleared on 17/02/2021.
7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of finished product (In-House).
9.	Drug-excipients compatibility studies (where applicable)	Firm has used same excipients as that of the innovator's product therefore compatibility studies are not required
10.	Complete batch manufacturing record of three stability batches.	Firm has provided Batch Manufacturing Record for all the batches of applied products.
11.	Record of comparative dissolution data (where applicable)	The firm has submitted comparative dissolution profile in all the 03 media that is 0.1N HCl, Phosphate buffer and Acetate buffer against

		Vonozan 10mg (Bbatch number: 005FF8) & 20mg Tablet mfg by M/s Getz Pharma.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and audit trail reports for HPLC analysis for all the three batches .
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for both stability chambers for accelerated as well as real time stability studies.

Evaluation by PEC:

Sr. no.	Shortcomings communicated	Response by the firm
1	Provide copy of valid GMP certificate of drug substance manufacturer issued by relevant authority.	Copy of GMP certificate no. 2022001 valid till 19/01/2027 issued on 20/01/2022 issued by Jiangxi API Engineering technology research centre, China sis submitted. Copy of GMP certificate No. 2020002 issued by CFDA valid till 11/03/2025.
2	Please provide COA of relevant batch of drug substance used for product development from drug product manufacturer.	Submitted.
3	Provide chromatographic conditions along with the complete method of analysis used for drug substance from drug substance manufacturer.	The firm has submitted complete method of analysis along with the specification for the applied product.
4	Comparative dissolution profile is established against the comparator's product while the said study is required against Innovator's / reference product, please provide the required data.	No response is submitted by the firm.
5	Latest inspection report / GMP certificate of drug product manufacturer is required.	Copy of GMP certificate number 46/2021-DRAP(K) issued on the basis of inspection conducted on 15/06/2021.
6	Provide documents confirming import of API with the approval from DRAP.	Copy of invoice number JXSG210156 dated 28/01/2021 cleared on 17/02/2021.
7	Provide detail of container closure system for the drug product.	Alu-Alu blister packed in secondary unit carton
8	Please submit stability summary sheet for batch number 21SB(A)-159-02 of 20mg tablet for 3rd month time point of real time stability studies along with the chromatograms and raw data sheets.	Real time stability study summary sheet for the said batch number along with the chromatograms is submitted for 3rd month time point.

Decision: Approved with innovator's specifications. Registration Board decided that the manufacturer will submit fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies**

throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Sr. No.	Name & Address of Manufacturer / Applicant	Brand Name (Proprietary Name + Dosage Form + Strength), Composition, Pharmacological Group, Finished Product Specification	Type of Form, Initial Diary & Date, Fee (including differential fee), Demanded Price / Pack size	International Availability GMP Inspection Report Date & Remarks
18.	M/s Genix Pharma (pvt) Ltd. 44, 45-B, Korangi Creek Road, Karachi.	Ertozin-M 7.5/500 tablet Each firm cated tablet contains: Ertugliflozin as L-Pyroglutamic acid…….7.5mg Metfromin HCL……500mg Innovator's specifications	Form 5D Dy. No. 33467 dated 09/10/2019 Rs. 50,000/- dated 06/03/2019 60's, 180's, 500's As per SRO	USFDA Approved. (2.5/500, 2.5/1000, 7.5/500, 7.5/1000) Copy of GMP certificate no. 46/2021-DRAP(K) issued on the basis of inspection conducted on 15/06/2021.
19.	M/s Genix Pharma (pvt) Ltd. 44, 45-B, Korangi Creek Road, Karachi.	Ertozin-M 2.5/500 tablet Each firm cated tablet contains: Ertugliflozin as L-Pyroglutamic acid…….2.5mg Metfromin HCL……500mg Innovator's specifications	Form 5D Dy. No. 334655 dated 09/10/2019 Rs. 50,000/- dated 06/03/2019 60's, 180's, 500's As per SRO	

Remarks of Evaluator:
The firm submitted the stability data on 28/03/2021.
The firm has submitted analytical method validation studeis for drug product including accuracy, linearity, specificity, robustness, precision etc.

STABILITY STUDY DATA

Manufacturer of API	Errtugliflozin: M/s Shanghai Pharma Group Changzhou Kony Pharamceutical Co., Ltd., Daixi street, Luoyang town, Wujih district, Changzhou, Jiangsu China. Metformin: M/s Abhilash Chemicals & Pharmaceutical Pvt. Ltd. 34/6A, Nayakkanpatti Village, Madurai North Taluk, Madural-625301, India.
API lot number	Ertugliflozin: ETG20180901 Metformin: MET/01/19030435, MET/01/19030550, MET/B/01/19030070
Description of Pack (Container closure system)	Alu-Alu blister
Stability Storage Condition	Accelerated: 40°C ± 2°C / 75% ± 5%RH Real Time: 30°C ± 2°C / 65% ± 5%RH
Time Period	Accelerated: 6 Months Real Time: 6 Months

Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0, 3, 6 (months)		
Ertozin-M 7.5/500 tablet			
Batch No.	20SB-022-03	20SB-021-02	20SB-020-01
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	02/2020	02/2020	02/2020
Date of Initiation	16/03/2020	16/03/2020	16/03/2020
No. of Batches	03		
Ertozin-M 2.5/500 tablet			
Batch No.	20SB-010-03	20SB-008-01	20SB-0-0
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	01/2020	01/2020	01/2020
Date of Initiation	03/03/2020	03/03/2020	03/03/2020
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to the decision of 281st meeting of Registration Board whereby the product Wymly 25mg (Tenofovir) was approved on the basis of PSI report. Following were endorsed in the report. • 21 CFR complaint system
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Firm has submitted copy of method used for analysis of API from both API Manufacturer and Finished Product manufacturer
4.	Stability study data of API from API manufacturer	• Real time: 30˚C ± 2˚C / 65% ± 5%RH for 24` months • Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 12 months Batches: (ETG20161201, ETG2016202, ETG20170101)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Ertugliflozin: Copy of good manufacturing certificate issued by Jiangsu Food and Drug Administration, Changzhou Pharmaceutical Profession Association, China valid till 27/06/2023. Metformin HCl: Copy of GMP certificate no. 17777/D1/4/2018 dated 18/02/2019 valid till 31/12/2021 issued by Food safety and Drug Control Administration, India.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Ertugliflozin: Copy of invoice cleared on 02/10/2018 dy. No. 2799. Metformin:

		Copy of invoice number GSTE-189/2018-19 cleared on 21/03/2019 dy. No. 3475.
7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of finished product (In-House).
9.	Drug-excipients compatibility studies (where applicable)	Firm has used same excipients as that of the innovator's product therefore compatibility studies are not required
10.	Complete batch manufacturing record of three stability batches.	Firm has provided Batch Manufacturing Record for all the batches of applied products.
11.	Record of comparative dissolution data (where applicable)	The firm has submitted comparative dissolution profile in all the 03 media that is 0.1N HCl, Phosphate buffer and Acetate buffer against the innovator's product: • Seruglumet (2.5/500)mg tablet • Seruglumet (7.5/500)mg tablet
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and audit trail reports for HPLC analysis for all the three batches .
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for both stability chambers for accelerated as well as real time stability studies.

Evaluation by PEC:

Decision: Approved. Registration Board decided that the manufacturer will submit fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the submission of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter.**

Sr. No.	Name & Address of Manufacturer / Applicant	Brand Name (Proprietary Name + Dosage Form + Strength), Composition, Pharmacological Group, Finished Product Specification	Type of Form, Initial Diary & Date, Fee (including differential fee), Demanded Price / Pack size	International Availability GMP Inspection Report Date & Remarks
20.	M/s Genix Pharma (pvt) Ltd. 44, 45-B,	Hypron ER tablet 50mg	Form 5D (Duplicate Dossier)	USFDA Approved

	Korangi Creek Road, Karachi.	Each Prolonged Release, Film Coated Tablet contains: Mirabegron…….50mg Beta-3 adrenergic agonist (used for treatment of overactive bladder-OAB) In-house	Dy. No. 747 dated 05/05/2016 Rs. 1500/- per tablet (10's, 20's, 30's) **The firm has submitted Rs. 50,000/- fee on 24/10/2022 in wrong head that is 1440 (Budget & accounts) for manual fee adjustment for registration of Mirabegron 50mg tablet. The firm is unable to provide old challan.	Mibega by Getz Pharma, Reg. No. 089378 Copy of GMP certificate no. 46/2021-DRAP(K) issued on the basis of inspection conducted on 15/06/2021.

Remarks of Evaluator:
The firm submitted the stability data on 31/05/2021.
The firm has submitted analytical method validation studeis for drug product including accuracy, linearity, specificity, robustness, precision etc.

STABILITY STUDY DATA

Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co., Ltd., Jiangxi Fengxin Industrial Park, Jiangxi province China
API lot number	20190101V
Description of Pack (Container closure system)	Alu-Alu blister packed in secondary unit carton
Stability Storage Condition	Accelerated: 40°C ± 2°C / 75% ± 5%RH Real Time: 30°C ± 2°C / 65% ± 5%RH
Time Period	Accelerated: 6 Months Real Time: 6 Months
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0, 3, 6 (months)

Batch No.	20SB-166-01	20SB-167-02	20SB-168-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	09/2020	09/2020	09/2020
Date of Initiation	14/10/2020	14/10/2020	14/10/2020
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to the decision of 281st meeting of Registration Board whereby the product Wymly 25mg (Tenofovir) was approved on the basis of PSI report. Following were endorsed in the report. • 21 CFR compliant system

2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Firm has submitted copy of method used for analysis of API from both API Manufacturer and Finished Product manufacturer
4.	Stability study data of API from API manufacturer	• Real time: 30˚C ± 2˚C / 65% ± 5%RH for 24` months • Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 12 months Batches: (2015302. 2015303, 2015304)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate no. 2022001 valid till 19/01/2027 issued on 20/01/2022 issued by Jiangxi API Engineering technology research centre, China sis submitted. Copy of GMP certificate No. 2020002 issued by CFDA valid till 11/03/2025. Copy of Pharmaceutical Production License vide No. GAN 20160125 dated 27.11.2020 issued by Jiangxi Provincial Medical Products Administration China valid till 26.11.2025
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of invoice number JXSG200137 dated 15/01/2020 cleared on 24/01/2020 vid dy. No. 0336 is submitted.
7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of finished product (In-House).
9.	Drug-excipients compatibility studies (where applicable)	Firm has used same excipients as that of the innovator's product therefore compatibility studies are not required
10.	Complete batch manufacturing record of three stability batches.	Firm has provided Batch Manufacturing Record for all the batches of applied products.
11.	Record of comparative dissolution data (where applicable)	The firm has submitted comparative dissolution profile in all the 03 media that is 0.1N HCl, Phosphate buffer and Acetate buffer against the innovator's product Myrbetriq 50mg tablet (Batch number G1900197). The F2 values are within the acceptable limits.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and audit trail reports for HPLC analysis for all the three batches.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for both stability chambers for accelerated as well as real time stability studies.

Evaluation by PEC:

Sr. no.	Shortcomings communicated	Response by the firm
1	Provide documents for the procurement of API with approval from DRAP.	Copy of invoice number JXSG200137 dated 15/01/2020 cleared on 24/01/2020 vid dy. No. 0336 is submitted.
2	Stability data for batch number 20SB-166-01 of finished product is submitted while data for 2 more batches is required.	The firm has submitted 6 month accelerated and real time stability data of batch numbers 20SB-167-02 & 20SB-168-03 for 6 months with the following details. Batch size: 1500 tablets Date of Mfg: 09/2020 Date of initiation of stability: 14/10/2020
3	Provide valid copy of GMP certificate for drug substance manufacturer issued by relevant authority.	Copy of GMP certificate no. 2022001 valid till 19/01/2027 issued on 20/01/2022 issued by Jiangxi API Engineering technology research centre, China sis submitted.
4	Provide detail of the innovator's product against which the comparative dissolution profile is submitted including batch number, expiry, manufacturing date and approval granting authority.	The firm has submitted comparative dissolution profile in all the 03 media that is 0.1N HCl, Phosphate buffer and Acetate buffer against the innovator's product Myrbetriq 50mg tablet (Batch number G1900197). The F2 values are within the acceptable limits.
5	As per initially submitted dossier, M/s Optimus Drugs (P) Limited is AP manufacturer while as per the information submitted with stability studies the drug substance manufacturer is M/s Jiangxi Synergy Pharmaceutical Co., Ltd., please clarify.	M/s Jiangxi Synergy Pharmaceutical Co., Ltd., Jiangxi Fengxin Industrial Park, Jiangxi province China is the API supplier. The firm has already submitted the relevant documents including invoice, COAs, GMP certificate etc.
6	Provide stability study data of drug substance according to the conditions of zone IV-A.	• Real time: 30°C ± 2°C / 65% ± 5%RH for 24` months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months Batches: (2015302. 2015303, 2015304)

Decision: Approved with innovator's specifications. Registration Board further decided that the manufacturer will submit fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

B: M/s Wilshire Laboratories (pvt) ltd.

Export facilitation

21.	Name and address of manufacture / Applicant	M/s Wilshire Laboratories Pvt Ltd. 124/1, Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore
	Brand Name + Dosage Form and Strength	P-Pride 1mg Tablet

	Composition	Each Film Coated Tablet Contains: Prucalopride……..…1mg
	Dairy No. date of R &I fee	Form-5D Dy.No 9629 dated 01-03-2019 Rs.50,000/- Dated 01-03-2019
	Pharmacological Group	Other drugs for constipation
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	5's, 7's, 10's, 20's, 30's, 40's, 50's; As per SRO
	Approval status of product in Reference Regulatory Authorities	MOTEGRITY (1mg, 2mg) film coated tablets USFDA Approved
	Me-too-status	
	GMP Status	The firm was inspected on 08-08-2019 and Recommendations/conclusion of inspections was: Keeping in view the findings of inspection proceedings, areas checked including location of premises, production facility, material management, laboratory controls, personnel and documents reviewed, M/s Wilshire Labs Pvt Ltd Lahore is considered to be operating at an acceptable level of compliance with respect to GMP guidelines for pharmaceutical product. The firm was further advised to submit CAPA report with respect to the current inspection proceedings.
	Remark of the Evaluator [XI]	• Letter of deficiencies sent on 21-10-2020 and reminder on 27-01-2021 but no reply received yet • Mention the salt form of Prucalopride in label claim and adjust its weight in master formulation considering the salt form along with submission of applicable fee. • Submission of stability studies data of three batches as per guidelines approved in 293rd meeting of Registration Board.
	Decision of 307thmeeting: Deferred for the following: • Mentioning the salt form of Prucalopride in label claim and adjust its weight in master formulation considering the salt form along with submission of applicable fee. • Submission of stability study data as per the guidelines approved in 293rd meeting of Registration Board. **Submission by the firm:** The firm has submitted revised Form 5D with revised label claim with stability data which presented below. Moreover, Fee of Rs. 7500/- is submitted vide slip number 7360335285 dated 08/12/2021 for 2mg tablet and Rs 7500/- vide slip number 25956780 dated 08/12/2021 for 1mg tablet.	
22.	Name and address of manufacture / Applicant	M/s Wilshire Laboratories Pvt Ltd. 124/1, Quaid-e-Azam Industrial Estate, Kot Lakhpat, Lahore
	Brand Name + Dosage Form and Strength	P-Pride 2mg Tablet
	Composition	Each Film Coated Tablet Contains: Prucalopride…….2mg
	Dairy No. date of R &I fee	Form-5D Dy.No 9630 dated 01-03-2019 Rs.50,000/- Dated 01-03-2019
	Pharmacological Group	Other drugs for constipation
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	5's, 7's, 10's, 20's, 30's, 40's, 50's; As per SRO

	Approval status of product in Reference Regulatory Authorities	MOTEGRITY (1mg, 2mg) film coated tablets USFDA Approved
	Me-too-status	
	GMP Status	The firm was inspected on 08-08-2019 and Recommendations/conclusion of inspections was: Keeping in view the findings of inspection proceedings, areas checked including location of premises, production facility, material management, laboratory controls, personnel and documents reviewed, M/s Wilshire Labs Pvt Ltd Lahore is considered to be operating at an acceptable level of compliance with respect to GMP guidelines for pharmaceutical product. The firm was further advised to submit CAPA report with respect to the current inspection proceedings.
	Remark of the Evaluator [XI]	• Letter of deficiencies sent on 21-10-2020 and reminder on 27-01-2021 but no reply received yet • Mention the salt form of Prucalopride in label claim and adjust its weight in master formulation considering the salt form along with submission of applicable fee. • Submission of stability studies data of three batches as per guidelines approved in 293rd meeting of Registration Board.
	Decision of 307thmeeting: Deferred for the following: • Mentioning the salt form of Prucalopride in label claim and adjust its weight in master formulation considering the salt form along with submission of applicable fee. • Submission of stability study data as per the guidelines approved in 293rd meeting of Registration Board. Submission by the firm: The firm has submitted revised Form 5D with revised label claim with stability data which presented below. Moreover, Fee of Rs. 7500/- is submitted vide slip number 7360335285 dated 08/12/2021 for 2mg tablet and Rs 7500/- vide slip number 25956780 dated 08/12/2021 for 1mg tablet.	

Sr. No.	Name & Address of Manufacturer / Applicant	Brand Name (Proprietary Name + Dosage Form + Strength), Composition, Pharmacological Group, Finished Product Specification	Type of Form, Initial Diary & Date, Fee (including differential fee), Demanded Price / Pack size	International Availability GMP Inspection Report Date & Remarks
a.	M/s Wilshire Laboratories (pvt) Ltd., 124/1 Quaid e Azam Industial Estate, Kot Lakhpat Lahore.	P-Pride 2mg tablet Each film coated tablet contains: Prucalopride as succinate…….2mg Serotonin receptor agonist In-house specs	Form 5-D Dy No. 32446 Dated 10/12/2021 14's, 28's As per SRO	Montegrity (1mg & 2mg) film coated tablet, USFDA Approved Copy of GMP certificate No. 144/2022-DRAP(AD-4119611790) issued on the basis
b.	M/s Wilshire Laboratories (pvt) Ltd., 124/1 Quaid e Azam Industial Estate, Kot Lakhpat Lahore.	P-Pride 1mg tablet Each film coated tablet contains: Prucalopride as succinate…….1mg Serotonin receptor agonist	Form 5-D Dy No. 32446 Dated 10/12/2021 14's, 28's As per SRO	

		In-house spec		of inspection conducted on 14/09/2022.

Remarks of Evaluator:
Stability data is submitted on 10/12/2021. Fee of Rs. 7500/- is submitted vide slip number 7360335285 dated 08/12/2021 for 2mg tablet and slip number 25956780 dated 08/12/2021 for 1mg tablet.

STABILITY STUDY DATA

Manufacturer of API	M/s Zhejiang Guobang Pharmaceutical Co. Ltd., No.6 wei wu road, Hangzhou gulf shangu industrial zone, Zhejiang China.
API Lot No.	190802
Description of Pack (Container closure system)	Alu-Alu blister packed in bleach board unit carton with leaflet.
Stability Storage Condition	Accelerated: 40°C ± 2°C / 75% ± 5%RH Real Time: 30°C ± 2°C / 65% ± 5%RH
Time Period	Accelerated: 6 Months Real Time: 6 Months
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0,1, 2, 3, 4 & 6 (months)

P-Pride 2mg tablet

Batch No.	T001	T002	T003
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	04/2021	04/2021	04/2021
Date of Initiation	14/04/2021	14/04/2021	14/04/2021
No. of Batches	03		

P-Pride 1mg tablet

Batch No.	001	002	003
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	04/2021	04/2021	04/2021
Date of Initiation	17/04/2021	17/04/2021	17/04/2021
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

1.	Reference of previous approval of applications with stability study data of the firm	Panel inspection report for verification of authenticity of stability data of Velbuvir tablet 400/100 by M/s Wilshire conducted on 23/05/2019. The case was presented in 290th and 291st meeting. The Board approved the case in 293rd meeting.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	The firm has certificate of analysis for relevant batch used for the product development from drug substance manufacturer as well as drug product manufacturer.

3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Firm has submitted copy of method used for analysis of API from both API Manufacturer and Finished Product manufacturer
4.	Stability study data of API from API manufacturer	• Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months Batches: (160801, 160802, 160803)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate number ZJ20180112 valid till 09/04/2023 issued by CFDA.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice number ADV-PRU-190302 dated 09/10/2019 issued vide diary number 13786/2009-DRAP dated 28/10/2019 is submitted.
7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of finished product (In-House).
9.	Drug-excipients compatibility studies (where applicable)	Firm has used same excipients as that of the innovator's product therefore compatibility studies are not required
10.	Complete batch manufacturing record of three stability batches.	Firm has provided Batch Manufacturing Record for all the batches of applied products.
11.	Record of comparative dissolution data (where applicable)	The firm has submitted comparative dissolution profile in all the 03 media that is 0.1N HCl, Phosphate buffer and Acetate buffer against: • Resolor 1mg & 2mg tablet
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and HPLC system reports for analysis for all the three batches.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for both stability chambers for accelerated as well as real time stability studies.

Evaluation by PEC:

1	Provide analytical method for analysis of Prucalopride Succinate from drug substance manufacturer.	The firm has submitted detail of analytical method from drug substance manufacturer including detail analytical method for impurities.
2	Valid GMP certificate of drug substance manufacturer issued by relevant authority.	Copy of GMP certificate number ZJ20180112 valid till 09/04/2023 issued by CFDA.
3	Provide the detail of dissolution method and dissolution parameters including	Media: 0.1N HCL Apparatus: Apparatus II (Paddle)

	apparatus, rpm, dissolution medium, etc along with the justification for selection of the parameters.	RPM: 50 Time: 30minutes The firm has referred to FDA's Dissolution Guidance 2018 for development and selection of dissolution parameters. However, the firm has submitted revised dissolution specifications as per the innovator's product that is Montegrity (1mg & 2mg) film coated tablet, USFDA Approved.
4	Provide detail of the reference / innovator's product (batch number, manufacturer, name of approving authority, expiry etc) against which comparative dissolution profile is submitted.	CDP is submitted against P-Pride tablet Manufactured by Janssen approved by European Medicine Agency in all the three media that is 0.1N HCl, Phosphate Buffer pH6.8 and Acetate Buffer pH4.5. Batch number: KLL1P02 (1mg tablet) Expiry: 11/2023 Batch number: KJL3200 (2mg tablet) Expiry: 09/2023
5	Provide detail of container closure system for finished product with detail of outer carton as well.	Alu-Alu blister packed in bleach board unit carton with leaflet.
6	Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Submitted.

Decision: Registration Board approved the registration of P-Pride 1mg and 2mg film coated tablet with change of brand name and with innovator's specifications.

- **Manufacturer will submit differential fee of Rs. 67,000/- for each strength for revision of salt form from Prucalopride to Prucalopride as Succinate.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will perform dissolution testing as per the parameters (i.e sampling time 20 minutes) of innovator's product on commercial batches.**

Case No. III: Deferred Cases submitted on Form 5F
(local manufacturing)

23.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Saffron Pharmaceutical 19 km, Sheikhupura Road, Faisalabad.**
	Name, address of Manufacturing site.	M/s Saffron Pharmaceutical 19 km, Sheikhupura Road, Faisalabad.
	Status of the applicant	☒ Manufacturer √ ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dated 29.12.2021 Dy.No 33995
	Details of fee submitted	Rs.20,000/- dated 13.05.2020 Deposit Slip # 0228310 Rs.10,000/- dated 23.11.2021 Deposit Slip # 88095423419
	The proposed proprietary name / brand name	Doplet-3 Soft Gel Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Soft Gel Capsule contains Cholecalciferol (Vitamin D3)…… 50000 IU
	Pharmaceutical form of applied drug	Oral Capsule
	Pharmacotherapeutic Group of (API)	Vitamin D_3
	Reference to Finished product specifications	USP Specification
	Proposed Pack size	1×10's, 2×7's & 3×10's
	Proposed unit price	As Per SRO
	The status in reference regulatory authorities	Approved **by MHRA**
	For generic drugs (me-too status)	DX3 50,000 IU Oral Capsule of Macter international (Pvt.) Limited.,
	GMP status of the Finished product manufacturer	GMP certificate issued on 03.01.2022 (Good Compliance)
	Name and address of API manufacturer.	**Name:** M/s Zhejiang NHU Company Ltd. **Address:** No.428 Xinchang Dadao West Road, Qixing Street, Xinchang County, Zhejiang Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug substance.
	Stability studies	**Cholecalciferol:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 75 ± 5% RH for 60 months.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence Studies against the reference product of "**Dan D Soft Gel Capsule**".
	Analytical method validation/verification of product	Firm has submitted verification studies of the drug substance and the drug product.

STABILITY STUDY DATA			
Manufacturer of API	**Name:** M/s Zhejiang NHU Company Ltd. **Address:** No.428 Xinchang Dadao West Road, Qixing Street, Xinchang County, Zhejiang Province, China		
API Lot No.	01201103VD		
Description of Pack (Container closure system)	**API Container:** Linear low density polyethylene with aluminum foil bag vacuum packing **Product Container:** Placed in Alu-Alu blister and packed in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-003	T-004	T-005
Batch Size	17000 capsules	17000 capsules	17000 capsules
Manufacturing Date	06.2020	07.2020	07.2020
Date of Initiation	14.07.2020	06.08.2020	06.08.2020
No. of Batches	03		
Administrative Portion			

<table>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm (if any)</td><td>Firm has referred to their last inspection report for Elixa (Apixaban) 2.5mg & 5mg conducted on 08.10.2019, approved in 293rd meeting of Registration Board.
Following are details of few points;
The HPLC software is 21CFR Compliant.
Audit trail reports were available and physically checked by the inspection team.
Firm has adequate monitoring and controls for stability chambers.
Software is installed for continuous monitoring of chambers.</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Copy of GMP certificate (Certificate# ZJ20180077) issued by China Food & Drug Administration valid upto 23.07.2023</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Lahore has been submitted.
Choloecalciferol:<table><tr><th>Batch No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr><tr><td>01201103VD</td><td>06Kg</td><td>14.01.2021</td></tr></table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms,
Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with batch manufacturing record and analytical record.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td>Firm has submitted audit trail reports on product testing.</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated)</td></tr>
<tr><td colspan="3">SUBMITTED DATA REGARDING THE DEFICIENCIES</td></tr>
<tr><td>7.</td><td>3.2.P.2 You are following USP specification. Compare the USP pharmacopoeial test parameters along with specification limits with applied product specification.</td><td>Firm has submitted the USP specification & Comparison of USP pharmacopoeial test parameters along with specification limits</td></tr>
<tr><td>8.</td><td>3.2.P.2 Clarification of the method of analysis of finished drug product for quantification of Vitamin D in Assay test, whether UV spectrophotometric method or HPLC method.</td><td>We performed the Identification & assay method on UV spectrophotometer is internal validated testing method & the validation is performed as per USP general chapter <1225>
We performed has Identification & assay method on HPLC is pharmacopeia testing method & the verification is performed as per USP general Chapter <1226></td></tr>
</table>

9.	Dissolution test for the applied product is not submitted.	Dissolution test is not included in USP monograph so we performed only DT as per USP.

Remarks of Evaluator:

Decision of 316th meeting:

Deferred for justification of applying UV spectrophotometric method, for Assay test of finished drug product, whereas USP monograph specifies HPLC method for the Assay analysis.

Submission by the firm:

The firm has submitted assay results at 18th and 24th month time point. The results are reproduced below.

Assay Contents (%): 90.0 % – 110.0 % (USP)

Assay result is satisfactory on HPLC & UV as shown in table.

Intervals	Batch # T-003		Batch # T-004		Batch # T-005		Performed the stability testing
	Performed date	Results	Performed date	Results	Performed date	Results	
Initial testing	14.07.2020	96.17 (UV)	06.08.2020	105.88 (UV)	06.08.2020	105.82 (UV)	UV
3rd Month	15.10.2020	96.06 (UV)	25.11.2020	102.91 (UV)	25.11.2020	95.21(UV)	UV
6th Month	27.01.2021	95.74 (UV)	18.02.2021	99.86 (UV)	18.02.2021	99.73 (UV)	UV
9th Month	05.05.2021	98.94 (UV)	20.05.2021	98.33 (UV)	20.05.2021	99.29 (UV)	UV
12th Month	10.08.2021	96.04 (UV)	28.09.2021	99.00 (UV)	28.09.2021	98.79 (UV)	UV
18th Month	13.01.2022	96.04 (UV)	21.02.2022	99.45 **(HPLC)**	21.02.2022	99.68 **(HPLC)**	**Now we have performed the stability testing on HPLC as per USP monograph**

Me-too: VITAMIN D3 SOFTGEL CAPSULES 50,000IU soft gel Capsule Reg. no. 59290
RRA Status: Invita D3 50,000 IU soft Gel Capsule, MHRA Approved
Section approval: Soft gel Capsule Section vide letter No.F.1-12/99-Lic(Vol-I) dated 3rd December, 2018.

Decision: Approved with USP specifications. Registration Board further decided that the manufacturer will submit fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Moreover, the firm has submitted audit trail report and revised analytical procedure as per USP 43 along with the analytical method verification studies for HPLC method.

24.	Name, address of Applicant / Marketing Authorization Holder	M/s Citi Pharma pvt ltd, 3km Head Balloki road Phool Nagar District Kasur.
	Name, address of Manufacturing site.	M/s Citi Pharma pvt ltd, 3km Head Balloki road Phool Nagar District Kasur.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 15867 dated 20/06/2022
	Details of fee submitted	PKR 30,000/-: dated 16/04/2022
	The proposed proprietary name / brand name	Panadol Muscle Relaxant Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Paracetamol……..…...650mg Orphenadrine Citrate.…..50mg
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	NSAID, Skeletal muscle relexant
	Reference to Finished product specifications	In-House
	Proposed Pack size	3×5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Norgesic Tablets by M/s Inova Pty Limited, TGAAutralia
	For generic drugs (me-too status)	Nuberol forte by M/s Searle Paksitan ltd
	GMP status of the Finished product manufacturer	Copy of GMP certificate No. 158/2019-DRAP(AD-700521-1099) dated 13-06-2019 is submitted issued on the basis of inspection conducted on 19-03-2019.
	Section approval	Tablet General Section
	Name and address of API manufacturer.	Paracetamol: M/s Citi Pharma (pvt) ltd, 3.5-km, head balloki road, phool nagar Kasur. Orphenadrine Citrate: M/s Harika Drugs Pvt Ltd, Sy. No. 165/A & 165/E, Gummadiadala Village, Sangareddy District, Telangana State, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature,

		structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	**Paracetamol:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (PGP-14-37, PGP-14-38, PGP-14-39) **Orphenadrine Citrate:** • Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months Batches: (HOCAPD005, HOCAPD006, HOCAPD007)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against Nuberol Forte by M/s Searle Pakistan ltd performing all the quality tests. (B:C0560). CDP is submitted against Nuberol Forte by M/s Searle Pakistan ltd. (B:10MPQVO) in all the three media that is 0.1NHCl, Acetate Buffer 4.5pH and Phosphate Buffer 6.8pH.
	Analytical method validation/verification of product	Analytical method verification/validation studies for drug product as well as for drug substance are submitted.

STABILITY STUDY DATA	
Manufacturer of API	Paracetamol: M/s Citi Pharma (pvt) ltd, 3.5-km, head balloki road, phool nagar Kasur. Diphenhydramine hydrochloride: M/s Harika Drugs Pvt Ltd, Sy. No. 165/A & 165/E, Gummadiadala Village, Sangareddy District, Telangana State, India.
API Lot No.	(Paracetamol) HOCCPO024 (Orphenadrine citrate)
Description of Pack	3×5's Blistered in Alu-PVC Packed in standard unit carton.

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5% Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: Accelerated:		
Frequency	Accelerated: 0,1,3, 6, (month) Real Time: 0,1,3, 6, (month)		
Batch No.	TRA-PMR001	TRA-PMR002	TRA-PMR003
Batch Size	10,000 tab	10,000 tab	10,000 tab
Manufacturing Date	12-2021	12-2021	12-2021
Date of Initiation			
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Paracetamol (Citi Pharma): Copy of GMP certificate no. 01/2021-DRAP(FID-2036001-5101) issued on the basis of inspection conducted on 17/12/2020. Orphenadrine (Harika Drugs): Copy of GMP certificate no. L.Dis.No.3390/E1/2019-WHO GMP certificate issued on 20/11/2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Evidence of approval of the applied formulation in reference regulatory authorities provided in 275th meeting of Registration Board could not be confirmed.

Decision of 321st meeting: The Board deferred the case for above mentioned points.

Sr. No.	Observations	Response
1	Valid copies of GMP certificates of manufacturers of drug substance (Paracetamol + Orphenadrine Citrate).	Paracetamol (Citi Pharma): Copy of GMP certificate no. 01/2021-DRAP(FID-2036001-5101) issued on the basis of inspection conducted on 17/12/2020. Orphenadrine (Harika Drugs): Copy of GMP certificate no. L.Dis.No.3390/E1/2019-WHO GMP certificate issued on 20/11/2019.
2	Provide analytical method verification studies including specificity, accuracy and precision for drug substances (Paracetamol & Orphenadrine Citrate) performed by drug product manufacturer.	The firm has submitted analytical method verification / validation studies including specificity, accuracy and precision f or paracetamol and orphenadrine drug substance performed by drug product manufacturer.
3	Provide documents for the procurement of API with approval from DRAP for Orphenadrine Citrate.	The firm has submitted copy of Form 6 Dy. No. 10676/2021DRAP dated 15/07/2021. No invoice is submitted.
4	Justification is required for selection of dissolution parameter including type of apparatus, speed, medium (Phosphate buffer 5.8pH) and time (45mins-NLT75%(Q))	Dissolution medium 5.8 pH (Phosphate Buffer), sampling time 45mins NLT 75% Q. The firm has not provided any reference.
5	Provide date of initiation of stability studies for all the three batches of the applied product.	Not provided.
6	Clarification is required regarding the brand name of the applied product since you have provided two brand name that is Askprol CF Tablets and Panadol Muscle Relaxant Tablet.	*"Askprol CF as applied with our own brand name and Panadol Muscle relaxant is applied after getting NOC from GSK"*
7	The submitted stability study data is till 3rd month time point. Please provide stability study data till 6th month time point for the applied product.	The firm has submitted stability studies till 6 months.
8	Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) and Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted.

Decision: Deferred for evidence of approval of the applied formulation in reference regulatory authorities provided in 275th meeting of Registration Board.

Case No. IV: New Section / New License

b. New Section/New License

M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi is granted New license on 13/09/2021 and has applied for the following products/molecules; In 321st meeting 03 products and 02 molecules were approved by the Board. Total number of products and molecules are provided in the table.

Number of molecules		**Number of products**
04		**08**
25.	Name, address of Applicant / Marketing Authorization Holder	M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi.
	Name, address of Manufacturing site.	M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25620 dated 12/09/2022
	Details of fee submitted	PKR 30,000/-: dated 17/08/2022
	The proposed proprietary name / brand name	Empaxo-M 12.5mg/ 1000mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin……..….12.5mg Metformin HCl…….1000mg
	Pharmaceutical form of applied drug	Blue, Oblong, Film Coated tablet, plain on both sides.
	Pharmacotherapeutic Group of (API)	Antidiabetics, Biguanides, Antidiabetics, SGLT2 Inhibitors
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SYNJARDY 12.5 /1000mg Tablet by BOEHRINGER INGELHEIM PHARMACEUTICALS INC, USFDA Approved.
	For generic drugs (me-too status)	Xenglu-Met 12.5mg/500mg Tablet by Hilton Pharma (Pvt.) Ltd.,
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021

		Tablet (general), Capsule (general), Sachet (general) and Research and Development Laboratory section is approved.
	Section approval	Tablet (general), Capsule (general), Sachet (general) and Research and Development Laboratory section is approved
	Name and address of API manufacturer.	**Empagliflozin** M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China **Metformin Hcl.** M/s. Exemed Pharmaceuticals Co. Ltd. Block No. 628 (A & B) ECP Canal Road, Vill : Luna, Taluka: Padra, District: Vadodara – 391440, Gujarat, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	**Empagliflozin.** Firm has submitted signed and stamped stability data sheets as per zone IV-A in which real time stability data Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH 6 months Batches: L-E-20200409-D01-E06-02, L-E-20200409-D01-E06-03, L-E-20200409-D01-E06-04 **Metformin HCl** Firm has submitted signed and stamped stability data sheets as per zone IV-B in which real time stability data conditions are: Real time: 30°C ± 2°C / 75% ± 5%RH 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH 6 months Batches: MFH11001AFP, MFH11002AFP, MFH11003AFP
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its

		validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence studies with i.e., Xenglu-Met 12.5mg- 1000mg Tablet by M/s Hilton Pharma whereby all the quality tests have been performed. CDP is submitted against the same brand and f2 values are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including System Suitability, Linearity, Accuracy, precision, Specificity, Limit of Quantification, Limit of Detection, Robustness.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin** M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China **Metformin Hcl.** M/s. Exemed Pharmaceuticals Co. Ltd. Block No. 628 (A & B) ECP Canal Road, Vill : Luna, Taluka: Padra, District: Vadodara – 391440, Gujarat, India		
API Lot No.	Empagliflozin H-E-20210605-D01-E06-02 Metformin HCl MFH211237AFP		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5% Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22TTEMM001	22TTEMM002	22TTEMM003
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	02-2022	03-2022	03-2022
Date of Initiation	16-03-2022	16-03-2022	16-03-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Empagliflozin: Copy of GMP certificate No. LN210011 dated26/05/2021 issued by Lioning Drug Administration. Metformin:

		Copy of GMP certificate No. 21082838 dated 07/08/2021 valid till 06/08/2024 issued by Food and Drugs Control Adminsitrtaion Gujarat India.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin : Copy of Form 6 No. 942 dated 10/12/2021 and Copy of attested invoice No. HN20211027-A dated 30/11/2021. Metformin: Copy of attested invoice no. GSTVAD2122427 dated 23/11/2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Observations	**Response**
Provide analytical method verification studies including specificity, accuracy and precision for drug substances (Empaglilozin+Metformin HCl) performed by drug product manufacturer.	Submitted.
Submitted stability study data is till 3rd month time point while the stability studies till 6th month is required.	The firm has submitted stability studies till 6th month time point.
Please provide pharmaceutical equivalence data and CDP for the applied product along with the details of the reference/innovator's product (Batch Number, expiry, manufacturing date etc) against which the said studies have been performed.	Pharmaceutical equivalence studies against Xenglu-Met 12.5mg- 1000mg Tablet whereby all the quality tests have been performed by performing all the quality tests. CDP is submitted against the same brand and f2 values are in the acceptable range in all the 03 media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

26.	Name, address of Applicant / Marketing Authorization Holder	M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi.

	Name, address of Manufacturing site.	M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25629 dated 16/09/2022
	Details of fee submitted	PKR 30,000/-: dated 19/08/2022
	The proposed proprietary name / brand name	Dapamax-M 5mg/ 850mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Dapagliflozin as propanediol monhydrate……5mg Metformin HCl…….850mg
	Pharmaceutical form of applied drug	Blue, Oblong, Film Coated tablet, plain on both sides.
	Pharmacotherapeutic Group of (API)	Antidiabetics, Biguanides, Antidiabetics, SGLT2 Inhibitors
	Reference to Finished product specifications	Inovator's
	Proposed Pack size	3×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	EMA Approved
	For generic drugs (me-too status)	DapaMet 5/850mg by M/s Hilton Pharma
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021 Tablet (general), Capsule (general), Sachet (general) and Research and Development Laboratory section is approved.
	Section approval	Tablet (general), Capsule (general), Sachet (general) and Research and Development Laboratory section is approved
	Name and address of API manufacturer.	**Dapagliflozin:** M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China **Metformin Hcl.** M/s. Exemed Pharmaceuticals Co. Ltd. Block No. 628 (A & B) ECP Canal Road, Vill : Luna, Taluka: Padra, District: Vadodara – 391440, Gujarat, India
	Module-II (Quality Overall	Firm has submitted QOS as per WHO QOS-PD template.

	Summary)	Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	**Dapagliflozin:** Firm has submitted signed and stamped stability data sheets as per zone IV-A in which real time stability data Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH 6 months Batches: DG-20201120-D05-DGM6-01, DG-20201120-D05-DGM6-02, DG-20201120-D05-DGM6-03 **Metformin HCl** Firm has submitted signed and stamped stability data sheets as per zone IV-B in which real time stability data conditions are: Real time: 30°C ± 2°C / 75% ± 5%RH 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH 6 months Batches: MFH11001AFP, MFH11002AFP, MFH11003AFP
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is established against Dapa-Met 5/850mg tablet by M/s Hilton Pharma by performing all the quality tests CDP is submitted against Dapa-Met 5/850mg tablet by M/s Hilton Pharma (Batch number: 142465) in all the 3 media that in Phosphate Buffer, Acetate Buffer and 0.1N HCl.
	Analytical method validation/verification of product	Method validation studies have submitted including System Suitability, Linearity, Accuracy, precision, Specificity, Limit of Quantification, Limit of Detection, Robustness.
STABILITY STUDY DATA		

Manufacturer of API	**Dapagliflozin** M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China **Metformin Hcl.** M/s. Exemed Pharmaceuticals Co. Ltd. Block No. 628 (A & B) ECP Canal Road, Vill : Luna, Taluka: Padra, District: Vadodara – 391440, Gujarat, India		
API Lot No.	Dapagliflozin: L-DG-20210805-D02-DG06-01 Metformin HCl MFH211237AFP		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5% Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22TTDAM003	22TTDAM004	22TTDAM005
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	11/03/2022	11/03/2022	11/03/2022
Date of Initiation	18/03/2022	18/03/2022	18/03/2022
No. of Batches	03		

Administrative Portion

7.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted by the firm
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Dapagliflozin: Copy of GMP certificate No. LN210011 dated26/05/2021 issued by Lioning Drug Administration. Metformin: Copy of GMP certificate No. 21082838 dated 07/08/2021 valid till 06/08/2024 issued by Food and Drugs Control Adminsitrtaion Gujarat India.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Dapagliflozin: Copy of invoice no. HN20211027-A dated 30-11-2021 cleared on 10/12/2021. Metformin: Copy of attested invoice no. GSTVAD2122427 dated 23/11/2021.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Observations	**Response**
Provide analytical method verification studies including specificity, accuracy and precision for drug substances (Dapaglilozin+Metformin) performed by drug product manufacturer.	The firm has submitted analytical method verification studies for Metformin and Dapagliflozin drug substances performed by drug product manufacturer.
Submitted stability study data is till 3rd month time point while the stability studies till 6th month is required.	Submitted.
Please provide pharmaceutical equivalence data and CDP for the applied product along with the details of the reference/innovator's product (Batch Number, expiry, manufacturing date etc) against which the said studies have been performed since submitted data is against the comparator's product.	Pharmaceutical equivalence is established against Dapa-Met 5/850mg tablet by M/s Hilton Pharma by performing all the quality tests CDP is submitted against Dapa-Met 5/850mg tablet by M/s Hilton Pharma (Batch number: 142465) in all the 3 media that in Phosphate Buffer, Acetate Buffer and 0.1N HCl.
Justify the selection of dissolution parameters for the applied product including dissolution media, rpm, sampling time etc.	`The firm has referred to FDA's dissolution guideline 2018 for selection and development of dissolution method, specifications and parameters.
Provide complete batch manufacturing record for the applied product.	Submitted.
Provide Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted.
Provide documents confirming import of Dapagliflozin.	Copy of invoice no. HN20211027-A dated 30-11-2021 cleared on 10/12/2021.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

27.	Name, address of Applicant / Marketing Authorization Holder	M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi.
	Name, address of Manufacturing site.	M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi.
	Status of the applicant	☒ Manufacturer

		☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25817 dated 13/09/2022
	Details of fee submitted	PKR 30,000/-: dated 19/08/2022
	The proposed proprietary name / brand name	Dapamax-M 5mg/ 81000mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Dapagliflozin as propanediol monhydrate……5mg Metformin HCl……1000mg
	Pharmaceutical form of applied drug	Blue, Oblong, Film Coated tablet, plain on both sides.
	Pharmacotherapeutic Group of (API)	Antidiabetics, Biguanides, Antidiabetics, SGLT2 Inhibitors
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	3×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	EMA Approved
	For generic drugs (me-too status)	DapaMet 5/1000mg by M/s Hilton Pharma
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021 Tablet (general), Capsule (general), Sachet (general) and Research and Development Laboratory section is approved.
	Section approval	Tablet (general), Capsule (general), Sachet (general) and Research and Development Laboratory section is approved
	Name and address of API manufacturer.	**Dapagliflozin:** M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China **Metformin Hcl.** M/s. Exemed Pharmaceuticals Co. Ltd. Block No. 628 (A & B) ECP Canal Road, Vill : Luna, Taluka: Padra, District: Vadodara – 391440, Gujarat, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	**Dapagliflozin:** Firm has submitted signed and stamped stability data sheets as per zone IV-A in which real time stability data Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH 6 months Batches: DG-20201120-D05-DGM6-01, DG-20201120-D05-DGM6-02, DG-20201120-D05-DGM6-03 **Metformin HCl** Firm has submitted signed and stamped stability data sheets as per zone IV-B in which real time stability data conditions are: Real time: 30°C ± 2°C / 75% ± 5%RH 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH 6 months Batches: MFH11001AFP, MFH11002AFP, MFH11003AFP
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is established against Dapa-Met 5/1000mg tablet by M/s Hilton Pharma by performing all the quality tests CDP is submitted against Dapa-Met 5/1000mg tablet by M/s Hilton Pharma (Batch number: 142322) in all the 3 media that in Phosphate Buffer, Acetate Buffer and 0.1N HCl.
	Analytical method validation/verification of product	Method validation studies have submitted including System Suitability, Linearity, Accuracy, precision, Specificity, Limit of Quantification, Limit of Detection, Robustness.

STABILITY STUDY DATA	
Manufacturer of API	**Dapagliflozin**

		M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China **Metformin Hcl.** M/s. Exemed Pharmaceuticals Co. Ltd. Block No. 628 (A & B) ECP Canal Road, Vill : Luna, Taluka: Padra, District: Vadodara – 391440, Gujarat, India		
API Lot No.		Dapagliflozin: L-DG-20210805-D02-DG06-01 Metformin HCl MFH211237AFP		
Description of Pack (Container closure system)		Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5% Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		22TTDAM001	22TTDAM002	22TTDAM003
Batch Size		1500 tab	1500 tab	1500 tab
Manufacturing Date		11/03/2022	11/03/2022	11/03/2022
Date of Initiation		18/03/2022	18/03/2022	18/03/2022
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted by the firm		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Dapagliflozin: Copy of GMP certificate No. LN210011 dated26/05/2021 issued by Lioning Drug Administration. Metformin: Copy of GMP certificate No. 21082838 dated 07/08/2021 valid till 06/08/2024 issued by Food and Drugs Control Adminsitrtaion Gujarat India.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Dapagliflozin: Copy of invoice no. HN20211027-A dated 30-11-2021 cleared on 10/12/2021. Metformin: Copy of attested invoice no. GSTVAD2122427 dated 23/11/2021.		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Observations	**Response**
Provide analytical method verification studies including specificity, accuracy and precision for drug substances (Dapaglilozin+Metformin) performed by drug product manufacturer.	The firm has submitted analytical method verification studies for Metformin and Dapagliflozin drug substances performed by drug product manfuactrer.
Submitted stability study data is till 3rd month time point while the stability studies till 6th month is required.	Submitted.
Please provide pharmaceutical equivalence data and CDP for the applied product along with the details of the reference/innovator's product (Batch Number, expiry, manufacturing date etc) against which the said studies have been performed since submitted data is against the comparator's product.	Pharmaceutical equivalence is established against Dapa-Met 5/1000mg tablet by M/s Hilton Pharma by performing all the quality tests CDP is submitted against Dapa-Met 5/1000mg tablet by M/s Hilton Pharma (Batch number: 142322) in all the 3 media that in Phosphate Buffer, Acetate Buffer and 0.1N HCl.
Justify the selection of dissolution parameters for the applied product including dissolution media, rpm, sampling time etc.	`The firm has referred to FDA's dissolution guideline 2018 for selection and development of dissolution method, specifications and parameters.
Provide complete batch manufacturing record for the applied product.	Submitted.
Provide Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted.
Provide documents confirming import of Dapagliflozin.	Copy of invoice no. HN20211027-A dated 30-11-2021 cleared on 10/12/2021.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

May & Baker Pvt. Ltd, Lahore:

28.	Name, address of Applicant / Marketing Authorization Holder	M/s May & Baker (pvt) Ltd., 45km, Dina Nath, Multan road, Lahore.
	Name, address of Manufacturing site.	M/s May & Baker (pvt) Ltd., 45km, Dina Nath, Multan road, Lahore.

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26382 dated 19/09/2022
	Details of fee submitted	PKR 30,000/-: dated 13/09/2022
	The proposed proprietary name / brand name	Fanak 75mg/mL Solution for Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule (3mL) contains: Diclofenac as sodium…….75mg
	Pharmaceutical form of applied drug	Solution for Injection (IV/IM)
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's, 5's, 10's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Voltarol 75mg/3mL Injection, MHRA Approved.
	For generic drugs (me-too status)	Dicloran 75mg/3mL by M/s Sami Pharma
	GMP status of the Finished product manufacturer	DML issued vide letter No.F.1-10/2019-Lic dated 29/04/2022.
	Section approval	Injectable Ampoule Section (General)
	Name and address of API manufacturer.	M/s Henan Dongtai Pharm Co., Ltd., East Changhong road of Tangyin county, Anyang city, Henan province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities,

		residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	• Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (101130-1, 101130-2, 101130-3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is established against Dicloran Injection by performing quality tests. Brand name: Dicloran 75mg/mL Batch number: 066H Mfg date: June, 2022 Mfg by: M/s Sami Pharma
	Analytical method validation/verification of product	Method validation studies have submitted including accuracy/recovery, precision, specificity etc for drug substance and drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Henan Dongtai Pharm Co., Ltd., East Changhong road of Tangyin county, Anyang city, Henan province, China.		
API Lot No.	20200303		
Description of Pack (Container closure system)	Type I glass ampoule packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 01	Trial 02	Trial 03
Batch Size	1000 ampoules	1000 ampoules	1000 ampoules
Manufacturing Date	02/2022	02/2022	02/2022
Date of Initiation	07/02/2022	07/02/2022	07/02/2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No response is submitted.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of Invoice no. 2020FP07013 dated 02/07/2020 cleared on 27/07/2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not Submitted**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	As per submitted dossier, testing for assay of drug substance is done according to USP (titration method) while the submitted verification studies for analytical method is provided for HPLC method, clarify or otherwise provide method verification studies considering USP monograph along with the relevant documents.	The firm has submitted analytical method verification report.
2	Provide detail of the product against which pharmaceutical equivalence has been performed including name of manufacturer, batch number, expiry and manufacturing date.	Brand name: Dicloran 75mg/mL Batch number: 066H Mfg date: June, 2022 Mfg by: M/s Sami Pharma
3	Provide complete manufacturing method for the applied product since the provided method does not provide complete information regarding the process.	Submitted.
4	Provide the required detail of reference standard including COA.	Submitted COA of USP reference standard of Lot# R038G0
5	As per submitted certificate of analysis of drug substance from drug product manufacturer, the assay value on as-is basis is 98.5% and the assay (on dried basis) was calculated and found to be 98.895% which is out of specifications as per the limits defined by USP. Moreover, the calculation of assay value on dried basis is pharmacopoeial requirement and product development has been performed without fulfilling the compendial requirements, please clarify.	*It was a drafting error. The assay was calculated on dried basis and drug product manufacturer has adopted the USP method for assay on dried basis.*
6	Provide documents confirming import of API used for product development.	• Firm has submitted copy of letter from M/s Global

		Pharmaceuticals, for the grant of Loan of API's including Diclofenac sodium for stability and registration purpose. Firm has submitted copy of commercial invoice in name of M/s Global Pharmaceuticals for import of 1000Kg of Diclofenac sodium, attested by AD I&E DRAP, Islamabad dated 27-07-2020.
7	Justification is required since the assay value at initial time points are different for accelerated and real time stability studies.	*It was a drafting error.*
8	As per submitted dossier, the chromatograms were generated from 07/03/2022 and accordingly the rest of the testing was performed but the as per section 3.2.P.8, the stability study was started on 07/02/2022, please clarify and provide audit trail report for establishing the relevancy between the assay values and the provided chromatograms.	*It was a drafting error of dates on the stability data sheets* *We have manual HPLC software. We are now purchasing 21CFR which is in pipeline.*

Decision: Approved.

- **Manufacturer shall follow USP monograph for the drug substance analysis during commercialmanufacturing of drug product.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit pharmaceutical equivalence studies against reference product i.e., Voren 75mg/3mL injection befire issuance of registration letter.**

29.	Name, address of Applicant / Marketing Authorization Holder	M/s May & Baker (pvt) Ltd., 45km, Dina Nath, Multan road, Lahore.
	Name, address of Manufacturing site.	M/s May & Baker (pvt) Ltd., 45km, Dina Nath, Multan road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26379 dated 19/09/2022
	Details of fee submitted	PKR 30,000/-: dated 13/09/2022

	The proposed proprietary name / brand name	Ozole 40mg dry powder vial IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole as sodium……40mg
	Pharmaceutical form of applied drug	Dry powder for solution for IV injection
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved
	For generic drugs (me-too status)	Risek for injection, Getz Pharma
	GMP status of the Finished product manufacturer	DML issued vide letter No.F.1-10/2019-Lic dated 29/04/2022.
	Section approval	Dry Powder Vial Section (General)
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (pvt) ltd., plot no. 22-23, Industrial triangle, Kahuta road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	• Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (1709901, 1607901, 1704901)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference s tandard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence is performed against Risek by Getz Pharma.
	Analytical method validation/verification of product	Method validation studies have submitted including accuracy/recovery, precision, specificity etc for drug substance and drug product.

STABILITY STUDY DATA			
Manufacturer of API	M/s Vision Pharmaceuticals (pvt) ltd., plot no. 22-23, Industrial triangle, Kahuta road, Islamabad.		
API Lot No.	2203902		
Description of Pack (Container closure system)	Amber colored glass vial with rubber stopper		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	1000 vials	1000 vials	1000 vials
Manufacturing Date	01/03/2022	01/03/2022	01/03/2022
Date of Initiation	04-03-2022	04-03-2022	04-03-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	--
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate no. F3-26/2019-Addl.Dir.(QA&LT-I)-56 isued on the basis of inspection conducted on 14-06-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Locally purchased
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not submitted**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator-I:

Sr. No.	Observations	Response
1	Provide compliance Record of HPLC software 21CFR & audit trail reports on product testing.	*We are now purchasing software 21CFR which is in pipeline.*
2	Provide date on which the batches were placed on stability and batch sizes.	Three trial batches were manufactured on 01/03/2022 Batch size: 1000 vials
3	Provide complete batch manufacturing record for the applied product.	The weight of drug substance has not been adjusted. The firm has used 40mg of Omeprazole Sodium as per submitted BMR.
4	As per submitted specification in section 3.2.P.4. the limit of water content is NMT 3% while in stability summary sheets the limit is 4.5-10% and, the results of water content are more than 5% which is not justifiable, please clarify and provide scientific justification for selection of limit of water content.	*We had to do the formulation of ozole according to Omeprazole Sodium but we factored in here whose value is 1.06. According to your query, we keep the value of water more than 5%. Factor wise we put 3% extra, by adding extra our result is 100%.*
5	The drug substance manufacturer has calculated the assay for Omeprazole Sodium on anhydrous basis as well as the limit defined for assay is 36-40% for complete salt while for the applied product the assay has been estimated for Omeprazole (base) only, clarify.	*We had to do the formulation of ozole according to Omeprazole Sodium but we factored in here whose value is 1.06. According to your query, we keep the value of water more than 5%. Factor wise we put 3% extra, by adding extra our result is 100%.*
6	Provide copy of GMP certificate of drug substance manufacturer.	Copy of GMP certificate no. F3-26/2019-Addl.Dir.(QA&LT-I)-56 issued on the basis of inspection conducted on 14-06-2022.
7	The run time for the applied product in 20minutes, 3 standards and 2 samples were analysed for assay calculation from 10:12 am to 10:14am which is not practically possible, clarify. The same observation has been made for subsequent analyses as well.	*This was printing error, the review data is submitted.*

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

• **Firm shall dispense the drug substance based on the potency of Omeprazole (base) on as-is basis for manufacturing of commercial batches.**		
30.	Name, address of Applicant / Marketing Authorization Holder	M/s May & Baker (pvt) Ltd., 45km, Dina Nath, Multan road, Lahore.
	Name, address of Manufacturing site.	M/s May & Baker (pvt) Ltd., 45km, Dina Nath, Multan road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29613 dated 18/10/2022
	Details of fee submitted	PKR 30,000/-: dated 13/09/2022
	The proposed proprietary name / brand name	Ozole 20mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each delayed release capsule contains: Omeprazole……20mg **Source of pellets:** M/s Vision Pharma
	Pharmaceutical form of applied drug	hard capsule containing delayed release pellets
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	USP
	Proposed Pack size	7's, 14's, 28's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	Risek capsule 20mg by Getz Pharma
	GMP status of the Finished product manufacturer	DML issued vide letter No.F.1-10/2019-Lic dated 29/04/2022.
	Section approval	Capsule Section (General)
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (pvt) ltd., plot no. 22-23, Industrial triangle, Kahuta road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure

		system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards, container closure system and stability studies of drug substance.
	Stability studies	• Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (OMP076, OMP073, OMP090)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Brand name: Risek Capsule 20mg Batch #: C03073 Pharmaceutical equivalence nad CDP are submitted.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, LOD/LOQ, Robustness, Solution stability, system suitability

STABILITY STUDY DATA

Manufacturer of API	M/s Vision Pharmaceuticals (pvt) ltd., plot no. 22-23, Industrial triangle, Kahuta road, Islamabad.		
API Lot No.	OMP1059		
Description of Pack (Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	01	02	03
Batch Size	1000 cap	1000 cap	1000 cap
Manufacturing Date	03/2022	03/2022	03/2022
Date of Initiation	06/03/2022	06/03/2022	06/03/2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate no. F3-26/2019-Addl.Dir.(QA&LT-I)-56 isued on the basis of inspection conducted on 14-06-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Locally purchased
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not Submitted**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Provide analytical method verification studies for drug substance.	Submitted.
2	Provide comparative dissolution profile against the reference / innovator's product in three media that is 0.1N HCl, Acetate Buffer and Phosphate Buffer along with the submission of pharmaceutical equivalence studies by performing all the quality tests and provide batch number , expiry, name of manufacturer and approval granting authority of the product against which the said studies have been performed.	Brand name: Risek Capsule 20mg Batch #: C03073 Pharmaceutical equivalence nad CDP are submitted, As per submitted data, the working standard used for the testing of CDP is Omeprazole Sodium.
3	Complete analytical method verification studies are required including specificity, accuracy and precision. Please provide the required studies along with the protocol for analytical method validation studies.	The applied product contains enteric coated pellets of Omeprazole while in submitted method verification studies the peak areas are provided for Omeprazole Sodium.
4	Provide complete details of primary packaging material of the applied product.	Firm has submitted details as Alu-Aluu blister.
5	Provide analytical procedures of finished drug product.	Submitted
6	Provide complete batch manufacturing record along with the detail of potency adjustment.	As per submitted BMR, 2.5% overage has been added without any justification. The firm has submitted calculations for potency adjustment for the trial batches.

7	Provide compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall manufacture commercial batches without overage of drug substance.**
- **Registration letter will be issued upon submission of analytical method verification studies for drug substance as well as for drug product from drug product manufacturer shall be submitted.**

Case No. : Priority Applications:
Cases of Paracetamol containing formulations

DRAP Authority in its 147th meeting decided as under:

"In order to ensure the smooth and continuous supply of paracetamol tablets across Pakistan under prevailing circumstances, the Authority, as one-time exercise, approved incentivization to the manufacturers in the form of out-of-queue consideration of applications of registration of:

i) 01 generic (me-too) molecule on manufacturing and immediate distribution of at least 15,000 packs of paracetamol tablets with pack size of 200 tablets.

ii) *All dosage forms of paracetamol & its combination products with the condition of immediate manufacturing and distribution.*

Accordingly following cases have been evaluated and are placed before the Board

Paracetamol:

31.	Name, address of Applicant / Marketing Authorization Holder	M/s Fahmir Pharma Pvt Ltd. Main Mandianwala stop, 26 km, Lahore Jaranwala road, Tehsil Sharaqpur sharif, Distt. Sheikhupura"
	Name, address of Manufacturing site.	M/s Fahmir Pharma Pvt Ltd. Main Mandianwala stop, 26 km, Lahore Jaranwala road, Tehsil Sharaqpur sharif, Distt. Sheikhupura"
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22082 dated 14-06-2022
	Details of fee submitted	PKR 30,000/-: dated 08-06-2022
	The proposed proprietary name / brand name	Panamir 500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical	Each tablet contains: Paracetamol……500mg

	ingredient (API) per unit	
	Pharmaceutical form of applied drug	Immediate release tablet
	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specifications	BP
	Proposed Pack size	1x10's , 2x10's, 3x10's, 5x10's 10x10's, 10x20's, (500's 1000's Jar Pack)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved.
	For generic drugs (me-too status)	Panadol 500mg tablet by GSK.
	GMP status of the Finished product manufacturer	Copy of GMP certificate no. 43/2021-DRAP(FID-1770625428-536) issues on the basis of conducted on 27/05/2021. Tablet general section
	Name and address of API manufacturer.	**Zenith chemical Industry Lahore** 16 km off Ferozpur Road, behind Wapda Grid Station 1 KM of Chandra Road, Lahore
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, impurity testing for impurity A-G, analytical procedure and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months B: P11-001, P11-002, P11-003
	Module-III (Drug Product):	The official monograph of the applied product is present in B.P. The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard,

		container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Panadol 500mg tablet by GSK Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form) (B:PPXI). CDP has been performed against the same brand that is Panadol 500mg Tablet by Fahmir Pharma in 0.1N HCl, Acetate buffer (4.5pH) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range (B:PPXI).
	Analytical method validation/verification of product	Method validation studies are submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API		M/s Zenith chemical Industry Lahore 16 km off Ferozpur Road, behind Wapda Grid Station 1 KM of Chandra Road, Lahore	
API Lot No.		ZPAR20-350	
Description of Pack (Container closure system)		Alu-Pvc blister packed in unit carton (1×10's)	
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH	
Time Period		Real time: 6 months Accelerated: 6 months	
Frequency		Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)	
Batch No.	Trail -1	Trail -2	Trail -3
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	08-09-2021	09-09-2021	10-09-2021
No. of Batches		03	

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 141/2019-DRAP (AD-813875-228 issued by DRAP valid till 16-12-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Invoice No. 00011/0321 dated 05/03/2021 is submitted (Local)
4.	Data of stability batches will be supported by attested respective documents like chromatograms,	Submitted

	Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The assay is performed by UV method as per BP.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator-I:

Sr. No.	Observations	Response
1	Provide 6 months stability study data (Accelerated and Real time) according to the conditions of zone IV_A since 3 months data is submitted.	The firm has submitted stability data till 6th month time point.
2	Analytical method verification studies for drug substance performed by drug product manufacturer.	Analytical method verification studies have been submitted for Paracetamol drug substance performed by drug product manufacturer.
3	The submitted process validation documents describe the process of film coating while the applied product is uncoated, please clarify. Moreover, as per the BMR provided in the submitted dossier, the applied product is film coated while as per the manufacturing method and master formula no step of film coating is involved.	*Our applied product is uncoated tablet. Further, process validation documents and BMRs have been revised and submitted.*
4	Please submit compatibility of excipients with the drug substance.	Compatibility studies of excipients with the drug substance is submitted.
5	Provide record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Submitted.
6	Latest inspection report of drug product manufacturer.	Copy of GMP certificate no. 43/2021-DRAP(FID-1770625428-536) issues on the basis of conducted on 27/05/2021.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case No. IIV: Deferred cases submitted on Form 5

32.	Name and address of manufacturer / Applicant	M/s Hi-Med Pharmaceuticals. 208C Sunder Industrial Estate, Lahore, Pakistan
	Brand Name +Dosage Form + Strength	Hivirin 200mg Capsule

	Composition	Each Hard Gelatin Capsule Contains: Ribavirin…200mg
	Diary No. Date of R& I & fee	Dy No. 25686: 24.07.2018 PKR 20,000/-: 24.07.2018
	Pharmacological Group	Third generation cephalosporins and beta-lactamase inhibitors
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack size & Demanded Price	10's; As per PRC
	Approval status of product in Reference Regulatory Authorities.	REBETOL® (ribavirin USP) Capsules. USFDA approved
	Me-too status	RIVAB 200mg Capsule. Reg. No. 83984
	GMP status	The firm M/s Himed Pharma was inspected on 27.04.2018, wherein grant of DML was recommended for 4 sections.
	Remarks of the Evaluator.	• Form 5 and all relevant documents are from Medpharm Research Lab, which should be from Hi-Med Pharma. The firm was asked for clarification. The firm did not reply.
	Prevoius decision	The Board in its 291st meeting deferred the case for submission of documents.
	Evaluation by PEC	• The firm submitted an unsigned Form 5 and did not submit any other document.
	Decision of 293rd meeting: Deferred for submission signed and stamped form 5 along with all relevant documents. Submission by the firm: The firm has submitted: • Section approval letter for Tablet General Section • Signed and stamped Form 5 along with the relevant documents • Firm has submitted copy of GMP certificate No. 102/2022-DRAP(AD-37320885037) dated 27-06- 2022 issued on the basis of inspection conducted on 10-06-2022.	
	Decision: Approved.	

33.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd., Plot No. 206 & 207. industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Gemnil 1g Injection Lyophilized Powder for Injection
	Diary No. Date of R& I & fee	Dy.No. 5588 dated: 07/02/2019 Rs.20,000/-
	Composition	Each Vial Contains: Gemcitabine as HCL…..…1gm
	Pharmacological Group	Antineoplastic
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1's (26.3mL), Price as per SRO
	Approval Status of Product in Reference Regulatory Authorities	GEMZAR (gemcitabine) for injection, Lyophilized powder (200mg/via & 1gm/vial) by M/s Lilly USA, LLC, USFDA Approved.
	Me-too Status	ONCOGEM 1gm injection by M/s AJ MIRZA PHARMA (PVT) LTD., (Imported) Reg. No. 45672
	GMP Status	Following additional sections were approved vide letter No.F.1-53/2003-Lic.(Vol-I) dated 13th June, 2017.

		• Tablet (oncology) • Capsule (oncology) • Liquid vial SVP (oncology) • Liquid Ampoule SVP (Onclology) • Dry powder vial (oncology) • Capsule (Ceph) • Dry [powder for oral suspension (ceph) • Dry Powder vial (ceph) • Dry Powder vial (Ceph)
	Remarks of the Evaluator.	Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm with same strength and filled volume could not be confirmed.
	Decision: Decision of 293rd meeting: Deferred for confirmation of manufacturing method (powder filling or lyophilization) and requisite facility. Submission by the firm: • The applicant has stated that they had applied for Gemnil 1g & 200mg liquid injection but these products were deferred in 293rd meeting for confirmation of manufacturing facility. • Furthermore, as per the response of the firm, the product will be manufactured in approved Liquid vial SVP Oncology section. • The firm has submitted full fee Rs. 30,000/- vide challan number 17153518278 dated 03/08/2022 along with the duplicate dossiers.. • Copy of GMP certificate No. F.3-55/2020-Addl.Dir.(QA&LT-1) issued on the basis of inspection conducted on12/08/2020. Label Claim: Each vial (26.3mL) contains: Gemcitabine as HCl…….1g Reference: 1. Gemcitabine IV Infusion 1 g/ 26.3 mL (solution for infusion) Hospira, TGA Australia approved 2. Gemcitabine Ebewe 80mg Injection By M/s Novartis Reg. no. 66183 Decision of 320th meeting: The Board discussed that the applied formualtion is approved in reference regualtory authorities as Lyophilised Powder for Injeciton as well as Solution for Injection and the firm has requested the change of dosage form of the applied formualtuion from Lyophilised Powder for Injeciton to Solution for Injection. Keeping in view, the Board deferred the case for furhter clarification of the applied dosage form from the firm. Submission by the firm: The firm has stated that they had applied for Solution for injection and had submitted Rs. 30,000/- as well. **Decision: Registration Board discussed that the applied formulation is approved in reference regulatory authorities as Lyophilized Powder for Injection as well as Solution for Injection. Considering the submission from the applicant that they had applied for solution for injection, the Board deferred the case for confirmation of applied dosage form from the initially submitted dossier**	
34.	**Name and address of manufacturer / Applicant**	**M/s Rotex Pharma Pvt Ltd., Plot No. 206 & 207. industrial Triangle, Kahuta Road, Islamabad**
	Brand Name +Dosage Form + Strength	Gemnil 200mg Injection Powder for Injection
	Diary No. Date of R& I & fee	Dy.No. 5600 dated: 07/02/2019 Rs.20,000/-

	Composition	Each Vial Contains: Gemcitabine as HCL…..…200mg
	Pharmacological Group	Antineoplastic
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	1's, Price as per SRO
	Approval Status of Product in Reference Regulatory Authorities	GEMZAR (gemcitabine) for injection, Lyophilized powder (200mg/via & 1gm/vial) by M/s Lilly USA, LLC, USFDA Approved.
	Me-too Status	ONCOGEM 200mg injection by M/s AJ MIRZA PHARMA (PVT) LTD., (Imported) Reg. No. 45671
	GMP Status	Following additional sections were approved vide letter No.F.1-53/2003-Lic.(Vol-I) dated 13th June, 2017. • Tablet (oncology) • Capsule (oncology) • Liquid vial SVP (oncology) • Liquid Ampoule SVP (Onclology) • Dry powder vial (oncology) • Capsule (Ceph) • Dry [powder for oral suspension (ceph) • Dry Powder vial (ceph) • Dry Powder vial (Ceph)
	Remarks of the Evaluator.	

Decision: Decision of 293rd meeting:

Deferred for confirmation of manufacturing method (powder filling or lyophilization) and requisite facility.

Submission by the firm:

- The applicant has stated that they had applied for Gemnil 1g & 200mg liquid injection but these products were deferred in 293rd meeting for confirmation of manufacturing facility.
- Furthermore, as per the response of the firm, the product will be manufactured in approved Liquid vial SVP Oncology section.
- The firm has submitted full fee Rs. 30,000/- vide challan number 17153518278 dated 03/08/2022 along with the duplicate dossiers.
- Copy of GMP certificate No. F.3-55/2020-Addl.Dir.(QA&LT-1) issued on the basis of inspection conducted on12/08/2020.

Label Claim:

Each vial (5.3mL) contains:

Gemcitabine as HCl…….200mg

Reference:

1. Gemcitabine IV Infusion 200 mg/ 5.3 mL Hospira, TGA Australia approved.
2. Gemcitabine Ebewe 200mg Injection By M/s Novartis Reg. no. 66182

Decision of 320th meeting:

The Board discussed that the applied formualtion is approved in reference regualtory authorities as Lyophilised Powder for Injeciton as well as Solution for Injection and the firm has requested the change of dosage form of the applied formualtuion from Lyophilised Powder for Injeciton to Solution for Injection. Keeping in view, the Board deferred the case for furhter clarification of the applied dosage form from the firm.

Submission by the firm:

The firm has stated that they had applied for Solution for injection and had submitted Rs. 30,000/- as well.

	Decision: Registration Board discussed that the applied formulation is approved in reference regulatory authorities as Lyophilized Powder for Injection as well as Solution for Injection. Considering the submission from the applicant that they had applied for solution for injection, the Board deferred the case for confirmation of applied dosage form from the initially submitted dossier.	
35.	**Name and address of manufacturer / Applicant**	M/s. Surge Laboratories (Pvt.) Ltd, 10 Km Faisalabad Road, Bikhi District, Sheikhupura.
	Brand Name +Dosage Form + Strength	Isofer Injection 1000mg/10ml
	Diary No. Date of R& I & fee	Dy. No. 756, 18-09-2014, Rs. 20,000/- (17-09-2014)
	Composition	Each 10ml contains: Iron as Iron (III) Isomaltoside 1000……1000mg
	Pharmacological Group	Iron parenteral preparation
	Type of Form	Form-5
	Finished Product Specification	As per Innovator‘s specifications
	Pack Size & Demanded Price	10 mL x 5‘s/ As per PRC
	Approval Status of Product in Reference Regulatory Authorities	Monofer injection EMA approved
	Me-too Status	Monofer injection by Allmed Laboratories
	GMP Status	The firm is GMP compliant as per inspection conducted on 26-11-2016.
	Remarks of the Evaluator.	□ The firm has submitted that Atomic absorption spectrophotometer will be procured before commercial launching of Iron isomaltoside injection. Currently, they are using their in-house validated spectrophotometric method for estimation of iron and also taking help from their mother company NABIQASIM INDUSTRIES, having the atomic absorption spectrophotometer for counter testing verification of R&D trials. □ Evidence of same volume already registered with DRAP required to be verified.
	Decision of 270th meeting: Deferred for confirmation of testing method involving atomic absorption spectrophotometer and evidence of already registered formulation in same volume as applied by applicant. Submission by the firm: The firm has submitted: • Me too status: Maltoside Injection 1000mg/10ml by M/s NabiQasim Industries, Reg. No. 112739 • Copy of invoice number 75-04-CI-N0313 dated 29-04-2019 for Atomic Absorption with VGA, copy of goods declaration and copy of packaging list. **Decision: Registration Board deferred the case for confirmation of generic status of the applied product in same strength and volume.**	
36.	Name and address of manufacturer/ Applicant	M/s Ethical Loboratories Pvt Ltd, 14 KM, Multan Road, Lahore

	Brand Name + Dosage Form + Strength	OLO 0.1% eye drop solution
	Composition	Each ml contains: Olopatadine HCL…1mg
	Diary No. Date of R & I & fee	Dy. No. 3456; 25.01.2019 PKR. 20,000/-; 25.01.2019 PKR. 20,000/-; 07.05.2020
	Pharmacological Group	Other antiallergics
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	as per SRO
	Approval status of product in Reference Regulatory Authorities.	Pataday twice daily relief / Patanol (olopatadine hydrochloride ophthalmic solution) 0.1%. USFDA approved.
	Me-too status	Ogate 0.1% Ophthalmic Solution. Reg. No. 75915
	GMP status	The firm was inspected on 21.11.2017, wherein renewal of DML was recommended.
	Remarks of the Evaluator	• The firm revised the dosage form in line with the reference product with submission of Rs. 20000/- fee. The fee challan has not been endorsed by the Division of Budget and accounts. • Undertaking at the end of Form 5 is missing.
	Previous decision	Deferred for following: (M-295th) • Submission of fee for revision of formulation after getting endorsement from Budget and Account Division. • Submission of undertaking of Form 5.
	Evaluation by EPC	The firm submitted the required undertaking and copy of the challan (not been endorsed by the Division of Budget and accounts).
	Decision of 313th meeting: Registration Board referred the case to QA & LT Division to conduct GMP inspection of Firm on priority. Submission by the firm: The firm has submitted copy of last inspection report dated 08-03-2022. The panel recommended the renewal of DML. Eye drops section (Non-Steroidal) approved. **Decision: Registration Board was apprised that the firm had requested change of strength of the applied formulation from 0.1% to 0.2% Ophthalmic solution. The Board discussed that since both of the strengths are approved in reference regulatory authorities, therefore the Board did not accede to the request of firm.**	
37.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Rubidox P 50mg/25ml Injection
	Diary No. Date of R& I & fee	Dy. No 5607 dated 07-02-2019 Rs.20,000/-
	Composition	Each ml contains: Doxorubicin hydrochloride…2mg (as liposomal pegylated)
	Pharmacological Group	Anthracyclines and related substances
	Type of Form	Form-5
	Finished Product Specification	USP

	Pack Size & Demanded Price	1's(25ml): As per SRO
	Approval Status of Product in Reference Regulatory Authorities	USFDA (Doxil Liposomal)
	Me-too Status	Nagun 50 Injection of M/s. Ghani Brothers registered in import (Reg. no. 072574)
	GMP Status	GMP inspection conducted on 19.09.2018 concluded satisfactory level of GMP compliance.
	Remarks of the Evaluator.	Terminal sterilization not mentioned • Packaging material not mentioned submit separate application for diluent
	Previous Decision of Registration Board (M-296)	Deferred for the following: • Submit justification on scientific grounds for not performing terminal sterilization of applied formulation. • Mention type of primary packaging material of applied formulation whether it is type I, II, or III glass container..
	Response of the Firm	• Firm informed that they import ready to fill sterile bulk solution for infusion. • Firm submitted that filling of product done under aseptic condition and prior to filling solution has been filtered for sterilization. • Primary packaging material is Glass vial Type-I.
	Decision of 316th meeting: Deferred for clarification regarding availability of diluent whether, it will be procured or it will be self manufactured. In case of self manufacturing of diluent by M/s Rotex Pharma Pvt Ltd., firm shall submit manufacturing process along with detail of manufacturing area in which the diluent will be manufactured. **Submission by the firm:** • The firm has stated that no diluent is applied and there is no requirement for any diluent as well. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/050718Orig1s060lbl.pdf (Accessed on 21/07/2022 at 1:50pm).	
	Decision of 320th meeting: The Board was apprised that the applied product is in liposomal dispersion and the liposomal carriers used in the applied formulation have a complex composition. The Board after deliberation regarding complexity of manufacturing method decided to defer the case for detail of manufacturing technique and facility including the detail of equipments used in the manufacturing of the applied product. **Submission by the firm:** The firm has submitted, *"We are procuring API in Pegylated Doxorubicin Liposomal in RTF form (2mg/mL) from M/s Praxin Pharma S.A (Argentina) and not doing Pegylation in our manufacturing facility".* The firm has submitted copy of certificate no. 201332022 000001 19 of medicine In bulk manufactured for export for Pegylated Liposomal Doxorubicin Hydrochloride manufactured by M/s Praxis Pharma S.A and COA of the API. (storage conditions: 2-8^{0}C).	
	Decision: Registration Board deliberated that the applied product is Pegylated Doxorubicin Liposomal form with a specific method of manufacturing. Since the firm has not provided any data related to product manufacturing method, stability data etc therefore, the Board decided to defer the case for the following points:	

	• **Submission of stability studies including long term and accelerated stability studies conducted under the conditions of zone IV-A for 03 batches of drug substance that is Pegylated Liposomal Doxorubicin.** • **Submission of complete method of manufacturing of the drug substance.**	
38.	Name and address of manufacturer / Applicant	M/s Winbrains Research Laboratories. Plot No. 69/1, Block B, Phase I-II , Industrial Estate, Hattar, Pakistan.
	Brand Name +Dosage Form + Strength	Flumeth 0.1% Ophthalmic Suspension
	Diary No. Date of R& I & fee	Dy. No 5607 dated 07-02-2019 Rs.20,000/-
	Composition	Each ml Contains: Fluorometholone…1mg
	Pharmacological Group	Corticosteroids
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	5mL, s per SRO
	Approval Status of Product in Reference Regulatory Authorities	FML® (fluorometholone ophthalmic suspension, USP) 0.1% sterile. USFDA approved.
	Me-too Status	Floroptic 0.1% Eye Drops. Reg No. 33873
	GMP Status	
	Remarks of the Evaluator.	Proof of approved section for the applied product was asked form the firm. The firm provided approval of eye drop (general) section..
	Previous Decision of Registration Board (M-293)	Deferred for clarification of the manufacturing facility.
	Response of the Firm: • The firm has submitted section approval letter No.F.3-7/2007-Lic(Vol-I) dated 20-09-2021 for grant of additional section. CLB in its 282nd meeting held on 31st august, 2021 has considered and approved title of Eye Drops (General) section as Eye/Ear/Nasal Drop (General).	
	Decision: Approved.	

Case No. III: Registration applications for which no response is submitted after issuance of letter for shortcomings

New Section / New License:
M/s Jaskan Pharmaceuticals (pvt) Ltd. was granted New Section "Injectable (vial) General Section" vide letter No. F.1-16/2006-Lic (Vol-I) dated 12/03/2021 title of which was corrected in 283rd meeting of Licensing Board as "Injectable (Vial) (General) (LVP) Section" vide even letter No. dated 18/111/2021.
The firm has applied for 03 pr0ducts and 03 molecules which were considered in 316th meeting. Now the firm has applied for 01 product and 01 molecules. The total number applications considered by the board is given in the following:

No. of Molecules	No. of products
05	05

39.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer

		☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 9668 dated 15/04/2022
	Details of fee submitted	PKR 30,000/-: dated 30-03-2022
	The proposed proprietary name / brand name	Cefbo Injection 1gm IM/IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Cefoperazone as Sodium……. 500mg Sulbactam as Sodium.....500mg
	Pharmaceutical form of applied drug	Sterile powder for solution for injection
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	JP (Japanese Pharmacopoeia)
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Pharmaceuticals and Medical Devices Agency (PMDA) of Japan.
	For generic drugs (me-too status)	Sulzone 1.0gm Injection M/s Biocare Pharmaceutical by Dawnrays Pharmaceutical Co,Ltd., Reg. No. 028468
	GMP status of the Finished product manufacturer	
	Name and address of API manufacturer.	Qilu Antibiotics Pharmaceutical CO, Ltd NO.849 DongJia Town Licheng District, Jinan, Shandong, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of the product is present in JP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24s months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(9001HK81NG,9002HK81NG, 9003HK81NG)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the Sulzone 1.0gm Injection M/s Biocare Pharmaceutical by Dawnrays Pharmaceutical Co, Ltd., by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form etc). (B:210312101)
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Qilu Antibiotics Pharmaceutical CO, Ltd NO.849 DongJia Town Licheng District, Jinan , Shandong, China		
API Lot No.	9001HK81NG		
Description of Pack (Container closure system)	Type I 15mL glass vial with fluorobutyl rubber stopper and green color flip off aluminum seal.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0,1, 2, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 ,24 (Months)		
Batch No.	LD 01	LD 02	LD 03
Batch Size	100Vials	100Vials	100Vials
Manufacturing Date	02-10-2021	02-10-2021	02-10-2021
Date of Initiation	18-10-2021	18-10-2021	18-10-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170569 valid till 25/06/2022 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	ADC attested Invoice NO JTRF210911-MQ Diary No. 14373/204DRAP Dated 24-09-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Sr. No.	**Observations**	**Response**
1	Please provide valid copy of GMP certificate of manufacturer of Drug substance.	
2	Provide analytical method verifications studies performed by the drug product manufacturer for drug substance.	
3	Pharmaceutical equivalence should be established against the reference / innovator's product but you have performed the studies against me-too product, please clarify.	
4	As per specifications of drug substance and COA from the drug substance manufacturer, the water content must be less than 4% and 1.9% water content has been determined while according to the specifications as provided by J.P of finished product, the water content should be less than 1%. Keeping in view the allowed percentage of water content, please clarify that how would the finished product comply the specification as described by JP for water content determination if the drug substance has a content higher than 1%.	
5	Submitted stability data is till 3rd month time point, please submit stability studies till 6th month timepoint.	

6	Please justify the stability studies without the performance of sterility and bacterial endo toxins.	
7	Provide complete calculations for potency adjustment considering the COA from the finished product manufacturer.	
8	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	
9	Evidence of relevant manufacturing facility is required.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

40.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 9669 dated 15/04/2022
	Details of fee submitted	PKR 30,000/-: dated 30-03-2022
	The proposed proprietary name / brand name	Cefbo Injection 2gm IM/IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Cefoperazone as Sodium……. 1000mg Sulbactam as Sodium.....1000mg
	Pharmaceutical form of applied drug	Sterile powder for solution for injection
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	JP (Japanese Pharmacopoeia)
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Pharmaceuticals and Medical Devices Agency (PMDA) of Japan.
	For generic drugs (me-too status)	Sulzone 2.0gm Injection M/s Biocare Pharmaceutical by Dawnrays Pharmaceutical Co,Ltd., Reg. No. 028469

	GMP status of the Finished product manufacturer	cGMP No. FID-797667-1346 issued by DRAP valid till 25/10/2022.
	Name and address of API manufacturer.	Qilu Antibiotics Pharmaceutical CO, Ltd NO.849 DongJia Town Licheng District, Jinan, Shandong, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of the product is present in JP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24s months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(9001HK81NG,9002HK81NG, 9003HK81NG)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the Sulzone 2.0gm Injection M/s Biocare Pharmaceutical by Dawnrays Pharmaceutical Co, Ltd., by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form etc). (B:210712201)
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	Qilu Antibiotics Pharmaceutical CO, Ltd	

	NO.849 DongJia Town Licheng District, Jinan , Shandong, China		
API Lot No.	9001HK81NG		
Description of Pack (Container closure system)	Type I 15mL glass vial with fluorobutyl rubber stopper and green color flip off aluminum seal.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0,1, 2, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 ,24 (Months)		
Batch No.	LE 01	LE 02	LE 03
Batch Size	100Vials	100Vials	100Vials
Manufacturing Date	02-10-2021	02-10-2021	02-10-2021
Date of Initiation	18-10-2021	18-10-2021	18-10-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20170569 valid till 25/06/2022 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	ADC attested Invoice NO JTRF210911-MQ Diary No. 14373/204DRAP Dated 24-09-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Observations	Response
1	Please provide valid copy of GMP certificate of manufacturer of Drug substance.	
2	Provide analytical method verifications studies performed by the drug product manufacturer for drug substance.	

3	Pharmaceutical equivalence should be established against the reference / innovator's product but you have performed the studies against me-too product, please clarify.	
4	As per specifications of drug substance and COA from the drug substance manufacturer, the water content must be less than 4% and 1.9% water content has been determined while according to the specifications as provided by J.P of finished product, the water content should be less than 1%. Keeping in view the allowed percentage of water content, please clarify that how would the finished product comply the specification as described by JP for water content determination if the drug substance has a content higher than 1%.	
5	Submitted stability data is till 3rd month time point, please submit stability studies till 6th month timepoint.	
6	Please justify the stability studies without the performance of sterility and bacterial endo toxins.	
7	Provide complete calculations for potency adjustment considering the COA from the finished product manufacturer.	
8	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	
9	Evidence of relevant manufacturing facility is required.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

Routine applications:

41.	Name, address of Applicant / Marketing Authorization Holder	M/s Welmark Pharmaceuticals, plot # 122, Block B, Phase V, Indusrial Estate Hattar, Haripur, KPK.
	Name, address of Manufacturing site.	M/s Welmark Pharmaceuticals, plot # 122, Block B, Phase V, Indusrial Estate Hattar, Haripur, KPK.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 32854 dated 02/12/2021
	Details of fee submitted	PKR 30,000/-: dated 25/11/2021
	The proposed proprietary name / brand name	Tapentawel tablet 75mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tapentadol as hydrochloride…..75mg
	Pharmaceutical form of applied drug	Immediate release film coated tablet
	Pharmacotherapeutic Group of (API)	Analgesic, opioids
	Reference to Finished product specifications	Innovators specifications
	Proposed Pack size	10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	Tapento tablet by M/s Sami Pharmaceuticals, Reg. No. 093064
	GMP status of the Finished product manufacturer	Copy GMP certificate No F.11-96/2021-DRAP-97 issued on the basis of inspection conducted on 11/11/2021.
	Section approval	Tablet General Section
	Name and address of API manufacturer.	M/s Precise Chemipharma Pvt Limited, C384, TTC Industrial area, MIDC, Pawne village, Nawi Mumbai, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, residual solvents, specifications, analytical procedures and its complete validation studies, batch analysis and justification of specification, details of reference standards , container closure system and stability studies of drug substance.
	Stability studies	• Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months • Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6

		months Batches: (6001012013, 6002012013, 6003012013)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence data is submitted against the comparator's product that is Tapento IR 75mg Tablet by M/s Sami Pharmaceuticals by performing all the quality tests. (Batch number: 003F) Comparative dissolution profile is submitted against the same product that is Tapento IR 75mg tablet by M/s Sami Pharmaceuticals. The values of F2 are within the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy/recovery, precision, specificity, LOD/LOQ, Robustness, Solution stability, system suitability

STABILITY STUDY DATA

Manufacturer of API	87.375mg per tablet		
API Lot No.	060034102019		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T013	T014	T015
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	01/2021	01/2021	01/2021
Date of Initiation	27/01/2021	28/01/2021	29/01/2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 6102090 issued valid till 28/09/2022 by FDA Maharashtra.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of attested invoice No. EXPS/0002082/2019-20 dated 26/12/2019 dy. No. 128 dated 09/01/2020 is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator-I:

Sr. No.	Observations	Response
1	As per submitted analytical method for Tapentadol HCl drug substance, the HPLC method is used for assay while analytical method validation report shows UV-performance for validation/verification studies. Please clarify and submit protocol and complete validation/verification studies for analytical method of drug substance. Moreover, correlate the strengths of dilution prepared for calculation of assay with the strengths of dilutions prepared for performing testing of linearity parameter in analytical method verification studies. Furthermore, please state that whether you have used same method of analysis as used by the manufacturer of drug substance or otherwise. Provide method of analysis of drug substance from drug substance manufacturer.	
2	Provide certificate of analysis of the batch of drug substance used for product development from drug substance manufacturer as well as from the drug product manufacturer.	
3	Provide pharmaceutical equivalence data against innovator's / reference product. The submitted data is against the comparator's product.	
4	Justification is required for selection of dissolution parameters including dissolution medium (0.1N HCl), RPM, time etc.	
5	Justify the amount of drug substance that is 87.375/tablet dispensed for potency adjustment by providing detail of calculations along considering the assay value i.e 99.8%.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

42.	Name, address of Applicant / Importer	**M/s** United International Plot No. MR-1/22. 3rd floor Madina Centre Kutchi gali No. 02, Marriot road Karachi.
	Details of Drug Sale License of importer	**License No:** 0657 **Address:** United International GNB-F-18/A Ground floor, F-block, Meher sons estate Karachi. **Validity:** 23/05/2020 **Status:** By way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Shandong Qidu Pharmaceuticals Co. Ltd. No.17, Hongda road, Linzi district Zibo city, Shandong province China.
	Name, address of manufacturer(s)	M/s Shandong Qidu Pharmaceuticals Co. Ltd. No.17, Hongda road, Linzi district Zibo city, Shandong province China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized Free Sale Certificate No. 20190027 issued on 04/12/2019 (validity 2 years) issued by Zibo Market Supervision and Administrative Bureau confirms the free sale of the following products product. 25% Glucose Injection 20ml:5g 0.9% Sodium chloride Injection 20ml:0.18g Metronidazole and sodium Chloride injection 100ml:0.5g:0.9g Ciprofloxacin lactate and Sodium chloride Injection 100ml:0.2g:0.9g • GMP certificate No. SD20170601 valid till 30/08/2022 issued by China Food and Drug Administration.	
	Details of letter of authorization / sole agency agreement • Original legalized Sole agency agreement is attached. M/s Shandong Qidu Pharmaceutical Co., Ltd., 17, Hongda Road, Linzi District, Zibo City, Shandong Province, PR China authorizes M/s United International Plot No. MR-1/22. 3rd floor Madina Centre Kutchi gali No. 02, Marriot road Karachi for the following 04 products; • Metronidazole and sodium chloride injection 100mh:0.5g:0.9g • Ciprofloxacin lactate and sodium chloride injection 100ml:0.2g:0.9g • 0.9% Sodium chloride injection 20ml:0.18g • 25% Glucose injection 20mg:5g	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging

		☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 16558 Dated 09/07/2020
	Details of fee submitted	Rs. 100,000/- Dated 02/03/2020
	The proposed proprietary name / brand name	Glucose Intravenous Infusion 5g/20ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 20ml infusion bottle contains: Glucose…….5g
	Pharmaceutical form of applied drug	IV Infusion
	Pharmacotherapeutic Group of (API)	Antihypoglycemic agent/
	Reference to Finished product specifications	B.P
	Proposed Pack size	20ml
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	Could not be confirmed
	For generic drugs (me-too status)	Could not be confirmed
	Module-II (Quality Overall Summary)	QOS is submitted as per WHO-PD template.
	Name, address of drug substance manufacturer	M/s Xiwang Pharmaceutical Co., Lt., Xiwang Industrial Park, Handian Town, Zouping District, Binzhou City, Shandong province, China.
	Module-III Drug Substance:	The firm has submitted; General information of Drug substance including manufacturing process and process controls, description of critical steps and process validations leading to development of manufacturing process, detail of impurities, specifications and detail of container closure system.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	6 months Accelerated Stability data of 03 batches at 40°C ±2°C / 75% ± 5%. 36 months Real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. Detail of Batches: 201506011, 20150612, 201506013
	Module-III Drug Product:	The firm has submitted
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not provided
	Analytical method validation/verification of product	Verification not provided
	Container closure system of the drug product	Polypropylene ampoule bottle of 20ml
	Stability study data of drug product, shelf life and storage conditions	6 months Accelerated Stability data of 03 batches at 40°C ±2°C / 75% ± 5%. 36 months Real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. Batch Numbers: 3E14040901, 3E14041001, 3E14041101

Evaluation by PEC-I:

- The free sale certificate and CoPP are issued by Zibo Market Supervision and Administration bureau.
- The submitted free sale certificate shows that the product is available for free sale in exporting country while the submitted CoPP clearly states the applied product is not registered in China and it is not authorized to be placed in China, Clarify.
- The address of the applicant, as mentioned in Form 5F, is different from the address mentioned in Drug Sale License, Clarify and submitt sole agency agreement accordingly.
- Provide evidence of approval of applied formulation in same strength and filled volume in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting.
- Provide evidence of applied formulation/drug in same strength and filled volume already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
- The GMP certificate of API manufacturer is not traceable from the official website of P.R. China.
- In section 2.3.S.7.1 (b), the detail of proposed storage conditions, and re-test period/shelf life is not provided.
- For compendial drugs, the analytical method verification studies are performed instead of method validation. In section 3.2.S.4.3 of Module 3 the verification studies are not provided, Clarify. Moreover, the verification studies are applicable on the impurity testing as well.
- According to the monograph provided in British Pharmacopoeia, the assay method for estimation of glucose content HPLC method is provided. Moreover, glucose reference standard has been officially adopted by the Ph. Eur, clarify and taking these facts into account further clarification is required, in section 3.2.S.4.4 of S part of Module III, the assay value for glucose is not given in the submitted certificate of analysis as well as section 2.3.S.4.1 (Specification) of QOS does not describe the assay specifications as described in British Pharmacopoeia, clarify. Likewise, in section 3.2.S.7.3 of S part of Module III, the assay of glucose is required in stability data summary sheets as well. Only value of specific optical rotation is given.
- In section 3.2.P.2.2, the data for formulation development is not provided in detail. Submit the required data as per the guidelines provided in 293rd meeting later amended in 296th meeting of Registration Board.
- Details of container closure system in section 3.2.P.2.4 is required according to the guidelines provided by the Registration Board.
- Clarification is required since section 3.2.P.5.2 describes the assay method where specific optical rotation of glucose solution is measured in degrees and then multiplied by a factor 09477 for calculation of assay value, which is not in line with the British Pharmacopoeial monograph wherein the formulation is analysed for assay value by HPLC method.
- For the drug products present in the official pharmacopoeia, the validation studies are not performed instead verification tests are mandatory. In section 3.2.P.5.3 the verification studies are not provided, clarify.
- Submit electronic copy of dossier.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

43.	Name, address of Applicant / Importer	**M/s** United International Plot No. MR-1/22. 3rd floor Madina Centre Kutchi gali No. 02, Marriot road Karachi.
	Details of Drug Sale License of importer	**License No:** 0657 **Address:** United International GNB-F-18/A Ground floor, F-block, Meher sons estate Karachi. **Validity:** 23/05/2020

		Status: By way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Shandong Qidu Pharmaceuticals Co. Ltd. No.17, Hongda road, Linzi district Zibo city, Shandong province China.
	Name, address of manufacturer(s)	M/s Shandong Qidu Pharmaceuticals Co. Ltd. No.17, Hongda road, Linzi district Zibo city, Shandong province China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized Free Sale Certificate No. 20190027 issued on 04/12/2019 (validity 2 years) issued by Zibo Market Supervision and Administrative Bureau confirms the free sale of the following products product. 25% Glucose Injection 20ml:5g 0.9% Sodium chloride Injection 20ml:0.18g Metronidazole and sodium Chloride injection 100ml:0.5g:0.9g Ciprofloxacin lactate and Sodium chloride Injection 100ml:0.2g:0.9g • Original legalized CoPP No. 20190010 issued on 24/10/2019 by Zibo Marke Supervision and Administration Bureau. **The product is not actually** on the market for free sale, however the product is licensed to be place in market for use in exporting country. • GMP certificate No. SD20170601 valid till 30/08/2022 issued by China Food and Drug Administration.	
	Details of letter of authorization / sole agency agreement • Original legalized Sole agency agreement is attached. M/s Shandong Qidu Pharmaceutical Co., Ltd., 17, Hongda Road, Linzi District, Zibo City, Shandong Province, PR China authorizes M/s United International Plot No. MR-1/22. 3rd floor Madina Centre Kutchi gali No. 02, Marriot road Karachi for the following 04 products; • Metronidazole and sodium chloride injection 100mh:0.5g:0.9g • Ciprofloxacin lactate and sodium chloride injection 100ml:0.2g:0.9g • 0.9% Sodium chloride injection 20ml:0.18g • 25% Glucose injection 20mg:5g	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 16557 Dated 09/07/2020
	Details of fee submitted	Rs. 100,000/- Dated 02/03/2020
	The proposed proprietary name / brand name	Ciprofloxacin Injection 0.2g/100ml

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml infusion bottle contains: Ciprofloxacin lactate……0.2g
	Pharmaceutical form of applied drug	A colorless solution of Ciprofloxacin Lactate in 100ml Ampoule
	Pharmacotherapeutic Group of (API)	Fluoroquinolones
	Reference to Finished product specifications	B.P
	Proposed Pack size	100ml
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	Ciprofloxacin 200mg/20ml, injection by M/s Hikma Farmaceutica, USFDA Aprpoved
	For generic drugs (me-too status)	Bacip Infusion 200mg by M/s Surge Laboratories, Reg No. 59979
	Module-II (Quality Overall Summary)	Submitted as per WHO-PD template.
	Name, address of drug substance manufacturer	M/s Zhejiang Guorang Pharmaceutical Co., Ltd., No. 6 Wei Wu road Hangzhou Gulf ShangYu Industrial Zone, Zhejiang. Certificate is expired on 06/06/2020.
	Module-III Drug Substance:	The firm has submitted; General information of Drug substance including manufacturing process and process controls, description of critical steps and process validations leading to development of manufacturing process, detail of impurities, specifications and detail of container closure system.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	6 months Accelerated Stability data of 03 batches at $40^{o}C \pm 2^{o}C$ / 75% ± 5%. 36 months Real time stability study data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH. Detail of Batches: 120309-1, 120309-2, 120309-3
	Module-III Drug Product:	
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not submitted
	Analytical method validation/verification of product	
	Container closure system of the drug product	Glass
	Stability study data of drug product, shelf life and storage conditions	6 months Accelerated Stability data of 03 batches at $40^{o}C \pm 2^{o}C$ / 75% ± 5%. 36 months Real time stability study data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH. Batch Numbers: 3A14031301, 3A14031302, 3A14031303

Evaluation by PEC-I:

- The free sale certificate and CoPP are issued by Zibo Market Supervision and Administration bureau. Moreover, the product is not actually present in the market for use in exporting country, the reason of which is not provided in CoPP.

- The address of the applicant, as mentioned in Form 5F, is different from the address mentioned in Drug Sale License, Clarify and submit sole agency agreement accordingly.
- Submit Valid copy of Drug Sale License.
- Electronic copy of dossier is required.
- Clarification regarding the primary container is required since according to the submitted SmPC the primary container is glass vial while description and specifications shows that the container is glass ampoule.
- The quantitative aqueous pH solubility profile from pH 1.2 to 6.8 at 37°C should be provided in section 2.3.S.1.3 of quality overall summary (QOS) and in detail in section 3.2.S.1 of module III..
- GMP certificate of API manufacturer is expired. Submit valid GMP certificate of the manufacturer.
- The API used for the manufacturing of the finished product is Ciprofloxacin Lactate which has been tested according to Chines Pharmacopoeia as stated in section 2.3.S.4.1(a) of QOS while Section 2.3.S.4.3 of QOS and 3.2.S.2 of module III state that the API has been developed according to B.P. Moreover, British Pharmacopoeial monograph for Ciprofloxacin Lactate is not available, however, BP describes the monograph for Ciprofloxacin base, Clarify.
- Provide summarized results of validation studies including specificity, accuracy and repeatability performed by drug product manufacturer in section 2.3.S.4.3 of QOS and the detail of the same should be provided in section 3.2.S.4 as the product is not pharmacopoeial.
- COA of drug substance from API manufacturer in section 2.3.S.4.4 should be submitted along with the submission of COA of API from drug product manufacturer for the same batches used in stability studies.
- Justification of specifications is required including the summary of tests included, analytical procedures and acceptance criteria in section 2.3.S.4.5 as the API (Ciprofloxacin Lactate) is not present in USP and B.P.
- Provide COA of reference standard used along with the lot number and source as well as Justify the use of Ciprofloxacin base as reference standard for analysis of API that is Ciprofloxacin lactate.
- Clarification is required regarding the manufacturing of the applied product. As per the submitted dossier, Ciprofloxacin is treated with Lactic Acid to produce Ciprofloxacin Lactate powder. Ciprofloxacin Lactate is then dispensed to be dissolved in 0.9% solution of NaCl. In contrast to this, the reference product is manufactured by taking Ciprofloxacin base as API, with the aid of Lactic Acid which acts as solubilizing agent, aqueous solution of Ciprofloxacin is prepared. The solution contains Hydrochloric acid as well which is added for pH adjustment. Justify the difference of manufacturing method scientifically.
- The reference standard used by the finished product manufacturer is Ciprofloxacin Hydrochloride. Scientifically justify the use of Ciprofloxacin Hydrochloride as Reference Standard for testing Ciprofloxacin Lactate infusion. Moreover, provide COA of the reference standard.
- Provide detail of Critical Quality attributes & Critical Process Parameters and Pharmaceutical Equivalence of applied drug product against reference/comparator/innovator product in section 3.2.P.2 (Pharmaceutical Development).

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

44.	Name, address of Applicant / Importer	**M/s** United International Plot No. MR-1/22. 3rd floor Madina Centre Kutchi gali No. 02, Marriot road Karachi.
	Details of Drug Sale License of importer	**License No:** 0657 **Address:** United International GNB-F-18/A Ground floor, F-block, Meher sons estate Karachi.

		Validity: 23/05/2020 **Status:** By way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Shandong Qidu Pharmaceuticals Co. Ltd. No.17, Hongda road, Linzi district Zibo city, Shandong province China.
	Name, address of manufacturer(s)	M/s Shandong Qidu Pharmaceuticals Co. Ltd. No.17, Hongda road, Linzi district Zibo city, Shandong province China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate) • Original legalized Free Sale Certificate No. 20190027 issued on 04/12/2019 (validity 2 years) issued by Zibo Market Supervision and Administrative Bureau confirms the free sale of the following products product. 25% Glucose Injection 20ml:5g 0.9% Sodium chloride Injection 20ml:0.18g Metronidazole and sodium Chloride injection 100ml:0.5g:0.9g Ciprofloxacin lactate and Sodium chloride Injection 100ml:0.2g:0.9g • GMP certificate No. SD20170601 valid till 30/08/2022 issued by China Food and Drug Administration. • Original legalized CoPP (certificate no. 20190009) issued on 24/10/2019 (valid till 09/08/2020) by Zibo Market Supervision and Administrative Bureau. The product is licensed to be placed in the market of exporting country. However, **the applied product is not available** for free sale in exporting country. Facilities sand operations conform to WHO-GMP as per CoPP.	
	Details of letter of authorization / sole agency agreement • Original legalized Sole agency agreement is attached. M/s Shandong Qidu Pharmaceutical Co., Ltd., 17, Hongda Road, Linzi District, Zibo City, Shandong Province, PR China authorizes M/s United International Plot No. MR-1/22. 3rd floor Madina Centre Kutchi gali No. 02, Marriot road Karachi for the following 04 products; • Metronidazole and sodium chloride injection 100mh:0.5g:0.9g • Ciprofloxacin lactate and sodium chloride injection 100ml:0.2g:0.9g • 0.9% Sodium chloride injection 20ml:0.18g • 25% Glucose injection 20mg:5g	
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No 16555 Dated 09/07/2020

	Details of fee submitted	Rs. 100,000/- Dated 02/03/2020
	The proposed proprietary name / brand name	Metronidazole Infusion 0.5g/100ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml infusion bottle contains: Metronidazole as hydrochloride……0.5g
	Pharmaceutical form of applied drug	Almost colorless or pale yellow solution in a glass vial of 100ml
	Pharmacotherapeutic Group of (API)	
	Reference to Finished product specifications	B.P
	Proposed Pack size	100ml
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	
	For generic drugs (me-too status)	
	Module-II (Quality Overall Summary)	QOS is submitted as per WHO-PD template.
	Name, address of drug substance manufacturer	M/s Hubei Hongyuan Pharmacetuical Co., Ltd., No.126 Dabieshan rod, Industrial and Economic development zone Luotian County, Hubei Province, No.3 Hongyuan Road, Fengshan Town, Loutian County, Huanggang city, Hubei Province, China.
	Module-III Drug Substance:	The firm has submitted complete S part of moule III including general properties of API, manufacturing process and process controls, detail of specifications, detail of reference standard and container closure system.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	6 months Accelerated Stability data of 03 batches at $40^oC \pm 2^oC$ / 75% ± 5%. 36 months Real time stability study data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH. Detail of Batches: 01120120121, 02230230233, 01120120123
	Module-III Drug Product:	Description of drug product along with composition, manufacturing process detail and process development, control of excipients, specifications of finished product with analytical method and its verification studies, batch analysis' report, detail of reference standard and container closure system.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not provided
	Analytical method validation/verification of product	
	Container closure system of the drug product	Metronidazole infusion is presented in glass vials contains 500mg in 100ml.
	Stability study data of drug product, shelf life and storage conditions	6 months Accelerated Stability data of 03 batches at $40^oC \pm 2^oC$ / 75% ± 5%. 36 months Real time stability study data is

		conducted at 30ºC ±2ºC / 65% ± 5% RH. Batch Numbers: 3A15072001, 3A15072002, 3A15072003

Evaluation by PEC-I:

- Submitted CoPP is expired, however it was valid at the time of submission of dossier.
- The free sale certificate and CoPP are issued by Zibo Market Supervision and Administration bureau. Moreover, the product is not actually present in the market for use in exporting country, the reason of which is not provided in CoPP.
- Submit verification studies including specificity, accuracy and repeatability for analytical method for API performed by the finished drug product manufacturer for API and Drug product under relevant sections.
- Provide COAs of the batches API by Drug product manufacturer as well as from the drug substance manufacturer in section 3.2.S.4.4.
- COA of reference standard used for analysis of API is required in relevant sections including detail of lot number and source.
- Clarify since the qualitative composition of the applied product is different from the innovator's product. Dibasic sodium phosphate and Citric acid are added in innovator's product as buffers in addition to Sodium Chloride while the applied product contains Sodium Chloride only as an excipient. Describe the way for adjusting the pH (which should be in a range of 4.5-6.0 as per B.P specifications) in case when dibasic sodium phosphate and Citric acid are not used as buffers.
- Submit verification studies including specificity, accuracy and repeatability for analytical methods performed by the finished drug product manufacturer in section 3.2.P.4.3.
- Provide detail of Critical Quality attributes & Critical Process Parameters and Pharmaceutical Equivalence of applied drug product against reference/comparator/innovator product in section 3.2.P.2 (Pharmaceutical Development).
- Submit COA of reference standard along with the lot number and source.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

Item No. II: Agenda of Evaluator-VIII (Mr. Muhammad Usman)

45.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Getz Pharma (Pvt) Ltd. Plot No. 29-30, Sector 30, Korangi Industrial Area, Islamabad.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt) Ltd. Plot No. 29-30, Sector 30, Korangi Industrial Area, Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Firm has submitted copy of GMP certificate dated 30-10-2019
	Evidence of approval of manufacturing facility	Firm has submitted copy of GMP certificate dated 30-10-2019 which specifies Tablet (General) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale

		☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29986 dated 3/11/2021
	Details of fee submitted	PKR 30,000/-: vide deposit slip# 6117667857
	The proposed proprietary name / brand name	NILAP 20mg/ml solution for Infusion and oral solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1 ml ampoule contains; Caffeine Citrate 20 mg equivalent to caffeine ……10mg
	Pharmaceutical form of applied drug	A clear colourless liquid, free from turbidity and foreign matter; filled in sterilized USP Type-1 ampoule.
	Pharmacotherapeutic Group of (API)	Anti-Hypertensive
	Reference to Finished product specifications	USP
	Proposed Pack size	1 ml x 1s, 1ml x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Peyona 20 mg/mL solution for infusion and oral solution **(MHRA approved).**
	For generic drugs (me-too status)	PEYONA SOLUTION FOR INFUSION. VIA ENRICO FERMI 1, 65020 ALANNO (PE), ITALY.
	Name and address of API manufacturer.	Hebei Guangxiang Pharmaceutical Co, Limited , Cangzhou City, Hebei Province, China by China Food and Drug Administration.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability

		data is conducted at 30°C ± 2°C / 65% ± 5% RH for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Peyona 20mg/ml solution for infusion and oral solution
	Analytical method validation/verification of product	Firm has submitted report of verification studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Haisen Pharmaceutical Co Ltd. Liushi Street, Dongyang city, Zhejiang Province China.		
API Lot No.	B012006006		
Description of Pack (Container closure system)	1 ml Type 1 Glass Ampoule		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	549DS01	549DS02	549DS03
Batch Size	2500 Ampoule	2500 Ampoule	2500 Ampoule
Manufacturing Date	03-09-2020	03-09-2020	03-09-2020
Date of Initiation	21-10-2020	21-10-2020	21-10-2020
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Mirab (Mirabegron) Extended Release Tablets 25mg & 50mg on 12th December 2017. Further, the said panel inspection report was discussed in 277th Drug Registration Board meeting held on 27th – 29th December 2017. The case was approved and the inspection report confirms following points:

		• The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP Certificate No. HE20190094 issued to manufacturer Hebei Guangxiang Pharmaceutical Co, Limited , Cangzhou City, Hebei Province, China by China Food and Drug Administration
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Firm has submitted copy of commercial invoice specifying import of 075 Kg Caffine Anhydrous . The invoice was signed by AD (I&E) DRAP field office Karachi dated 13-08-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Following Documents are found deficient:

1. Submit label claim as per innovator product declaring the equivalent content of Caffeine citrate in terms of the base per unit ml.
2. Submit microbial reports for the sterility testing of drug product during stability studies.
3. USP monograph of "Caffeine citrate injection" mandates use of Theophylline in the standard solution for Assay test, whereas submitted drug product test method form M/s Getz does not include any such details. Justification shall be submitted in this regard.
4. It is evident from the submitted analytical record for stability studies that standard solution preparation & system suitability parameter for Assay test has not been performed as per the recommendations of USP monograph of "Caffeine citrate injection".

Query Items	Getz Pharma Response
Submit label claim as per innovator product declaring the equivalent content of Caffeine citrate in terms of the base per unit ml.	Below is the label claim as per innovator product declaring the equivalent content of Caffeine citrate in terms of the base per unit ml. Each 1ml ampoule contains: Caffeine Citrate… 20mg (equivalent to 10mg Caffeine) Please refer to Annexure-1 for the SmPC of innovator product for label claim.
Submit microbial reports for the sterility testing of drug product during stability studies.	We would like to inform you that we have performed Bacterial Endotoxin Test, Sterility Test and Particulate Matter Test at the time of Release in line with ICH Q6 requirements which shows that NILAP is sterile.

	As per ICH Q1A, stability studies should include testing of those attributes that are susceptible to change during storage and are likely to influence quality, safety and/or efficacy. Since aforementioned tests can be affected by any breach in container closure system, therefore, we have replaced said tests with container closure integrity test during stability studies. Further, this is in line with US-FDA Guidelines "Container and Closure System Integrity Testing in Lieu of Sterility Testing as a Component of the Stability Protocol for Sterile Products" which states in VI. IMPLEMENTATION as follows: 1. A container and closure system integrity test may replace sterility testing in a stability program at time points other than the product sterility test prior to release 2. Container and closure system integrity tests do not replace sterility testing methods for product sterility testing prior to release. Please refer to Annexure-2 for reports of Bacterial Endotoxin Test, Sterility Test, Particulate Matter Test conducted at batch release and Container Closure Integrity Test at initial stability study interval.
USP monograph of "Caffeine citrate injection" mandates use of Theophylline in the standard solution for Assay test, whereas submitted drug product test method form M/s Getz does not include any such details. Justification shall be submitted in this regard.	This is to bring to your kind attention that in USP monograph of "Caffeine Citrate Injection" Theophylline is used only for resolution purpose between Theophylline and Caffeine and not for the calculation purpose. As per USP Theophylline is categorized as dangerous goods, therefore, we are unable to procure it. Further, in USP monograph RRT (relative retention time) of Theophylline is given which is 0.70, consequently Theophylline can easily be identified & reported through its relative retention time (RRT). In sample solution, peak of Theophylline is observed but it is below the reporting threshold (i.e. less than 0.05%) while the resolution between Theophylline (observed at RRT 0.73) and Caffeine is 7.05 (Greater than 6) which fulfills the requirement of USP resolution criteria. Please refer to Annexure-3 for sample chromatogram on enhanced scale showing resolution of 7.05 between Theophylline and Caffeine.

It is evident from the submitted analytical record for stability studies that standard solution preparation & system suitability parameter for Assay test has not been performed as per the recommendations of USP monograph of "Caffeine citrate Injection".	Please refer to above point for system suitability parameter justification.

Decision: Registration Board deferred for clarification of following points:

- **USP monograph of "Caffeine citrate injection" mandates use of Theophylline in the standard solution for Assay test, whereas submitted drug product test method from M/s Getz does not include any such details.**
- **Non-performance of sterility testing at the start and end of stability studies.**
- **Submitted Pharmacological group of applied formulation as "Anti-hypertensive".**

46.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Tabros Pharma Pvt. Ltd. L-20/B, Sector-22, Federal B Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s Tabros Pharma Pvt. Ltd. L-20/B, Sector-22, Federal B Industrial Area, Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Firm has submitted copy of covering letter of renewal of DML No. 000106(Formulation) dated 30-06-2020 on which the approved sections are mentioned including section namely Tablet (General).
	Evidence of approval of manufacturing facility	Firm has submitted copy of covering letter of renewal of DML No. 000106(Formulation) dated 30-06-2020.
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1110 dated 26-11-21
	Details of fee submitted	PKR75000 dated: 26.11.2021bearing Deposit Slip No. 62756762
	The proposed proprietary name / brand name	PIXIZ TABLET 100mg/10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	PIXIZ TABLET 100mg/10mg Each film coated tablet contains: Losartan Potassium … 100mg Amlodipine Besylate equivalent to Amlodipine ……..… 10mg **Tabros Specs.**
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Losartan Potassium: Angiotensin II Receptor Antagonist Amlodipine Besylate: Calcium channel blocker
	Reference to Finished product	Tabros Specifications

	specifications	
	Proposed Pack size	1x14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	LosAmlo Tablet 100mg/10mg Krka d.d Germany/Slowenien. **( ).**
	For generic drugs (me-too status)	Not available
	Name and address of API manufacturer.	**Losartan Potassium:** Zhejiang Huahai Pharmaceutical Co., Ltd. Chunnan, Duqiao, Linhai Zhejiang, China **GMP Certificate issued by CFDA valid till 26-07-2022** **Certificate No. ZJ20170049 (PAGE 18/Corr)** **Amlodipine Besylate** m/s smruthi organics limited a-27, midc, chincholi, tal-mohol, solapur 413255 maharashtra state, india. GMP Certificate issued by Joint Commissioner & Controlling Authority , Food & Drug Administration M.S, Bandra €, Mumbai, India Certificate No. NEW-WHO-GMP/CERT/PD/86368/2019/11/30111 (Page 19)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and	Pharmaceutical Equivalence have been established against

	Comparative Dissolution Profile	the brand leader that is LosAmlo Tablet 100/10mg by Boehringer Ingelheim, by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is LosAmlo Tablet 100/10mg by KRKA, d.d., Novo mesto, Germany in 0.1N HCl (QC medium), Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory.
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Losartan Potassium: USP** Zhejiang Huahai Pharmaceutical Co., Ltd. Chunnan, Duqiao, Linhai Zhejiang, China **Amlodipine Besylate B.P.** M/s SMRUTHI ORGANICS LIMITED A-27, MIDC, CHINCHOLI, TAL-MOHOL, SOLAPUR 413255 MAHARASHTRA STATE, INDIA.		
API Lot No.	Losartin Potassium Batch No. C5458-18-017 Amlodipine Besylate – Batch No. AMBC 014/19		
Description of Pack (Container closure system)	The proposed pack size of Pixiz Tablet 100/10mg is 1x14's in Alu—Alu Blister.		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6(Months) Real Time: 0, 3, 6(Months)		
Batch No.	TR001-4/PIZ	TR002-4/PIZ	TR003-4/PIZ
Batch Size	1200 TABLETS	1200 TABLETS	1200 TABLETS
Manufacturing Date	June 2021	June 2021	June 2021
Date of Initiation	19-07-2021	19-07-2021	19-07-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Mirab (Mirabegron) Extended Release Tablets 25mg & 50mg on 12th December 2017. Further, the said panel inspection report was discussed in 277th Drug Registration Board meeting held on 27th – 29th December 2017. The case

		was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Losartan Potassium** M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Valid till 15.10.2024. **Amlodipine Besylate** M/s SMRUTHI ORGANICS LIMITED Valid till 13.11.2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Losartan Potassium** The firm has importedAPI consignment Zhejiang Huahai Pharmaceutical Co., Ltd. China bearing invoice number HH20200610R dated 22-06-2020. **Amlodipine Besylate** • The firm has imported commercial consignment of API from SMRUTHI ORGANICS LIMITED India, bearing invoice number E-150 dated December 27, 2019 signed by ADC on 03-01-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Following Documents are found deficient:

1. In the standard testing method for testing of DS Losartan Potassium (USP), the wavelength used by DS Manufacturer is 215nm while the wavelength used by the manufacturer of Product is 220nm and the wavelength specified in the USP is different.
2. Stability data of Data Product provided is of three (03) months rather than 06 months.
3. Provide copy of letter of licensed sections of CLB.
4. Date of manufacturing of batches is mentioned as June 21 instead of exact date.

Reply of Observations:

S. No.	Deficiencies / Short-comings	Justification
1.	In the standard testing method for testing of testing of DS Losartan	We have been performed Analysis / testing of Losartan potassium Drug Substance as per USP

	potassium (USP), the wavelength used by DS manufacturer is 215nm while the wavelength used by the manufacturer of drug product is 220nm and the wavelength specified in the USP is different.	monograph and analytical method verification studies as per ICH guidelines, supporting documents are being attached for your kind perusal: i. Drug substance analytical method as per USP. ii. Drug substance analytical method verification studies in accordance with USP. iii. Revised Certificate of analysis of drug substance analyzed by USP method.
2.	Stability data of product provided is of three (03) months rather than 06 months.	Initially we have submitted CTD dossier application with 3 months stability data, later on again we have submitted 6 months stability data accordingly vide letter DRAP/TAB-REG/03-22, dated March 2,2022. Copy of acknowledgment letter is attached for your ready reference.

Decision: Approved with Innovators specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.711/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

47.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Tabros Pharma Pvt. Ltd. L-20/B, Sector-22, Federal B Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s Tabros Pharma Pvt. Ltd. L-20/B, Sector-22, Federal B Industrial Area, Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Firm has submitted copy of covering letter of renewal of DML No. 000106(Formulation) dated 30-06-2020 on which the approved sections are mentioned including section namely Tablet (General).
	Evidence of approval of manufacturing facility	Firm has submitted copy of covering letter of renewal of DML No. 000106(Formulation) dated 30-06-2020.
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33306 dated 13-12-2021
	Details of fee submitted	PKR75000 dated: 26.11.2021 bearing Deposit Slip No. 579938272

	The proposed proprietary name / brand name	PIXIZ TABLET 100mg/5mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	PIXIZ TABLET 100mg/10mg Each film coated tablet contains: Losartan Potassium … 100mg Amlodipine Besylate equivalent to Amlodipine ……...… 5mg Tabros Specs.
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Losartan Potassium: Angiotensin II Receptor Antagonist Amlodipine Besylate: Calcium channel blocker
	Reference to Finished product specifications	Tabros Specifications
	Proposed Pack size	1x14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	LosAmlo Tablet 100mg/10mg Krka d.d Germany/Slowenien. **( ).**
	For generic drugs (me-too status)	Not available
	Name and address of API manufacturer.	**Losartan Potassium:** Zhejiang Huahai Pharmaceutical Co., Ltd. Chunnan, Duqiao, Linhai Zhejiang, China **GMP Certificate issued by CFDA valid till 26-07-2022** **Certificate No. ZJ20170049** **Amlodipine Besylate** m/s smruthi organics limited a-27, midc, chincholi, tal-mohol, solapur 413255 maharashtra state, india. GMP Certificate issued by Joint Commissioner & Controlling Authority , Food & Drug Administration M.S, Bandra €, Mumbai, India Certificate No. NEW-WHO-GMP/CERT/PD/86368/2019/11/30111
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure

		system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 6 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the brand leader that is LosAmlo Tablet 100/10mg by Boehringer Ingelheim, by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is LosAmlo Tablet 100/10mg by KRKA, d.d., Novo mesto, Germany in 0.1N HCl (QC medium), Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory.
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	**Losartan Potassium: USP** Zhejiang Huahai Pharmaceutical Co., Ltd. Chunnan, Duqiao, Linhai Zhejiang, China **Amlodipine Besylate B.P.** M/s SMRUTHI ORGANICS LIMITED A-27, MIDC, CHINCHOLI, TAL-MOHOL, SOLAPUR 413255 MAHARASHTRA STATE, INDIA.
API Lot No.	Losartin Potassium Batch No. C5458-18-017 Amlodipine Besylate – Batch No. AMBC 014/19
Description of Pack (Container closure system)	The proposed pack size of Pixiz Tablet 100/10mg is 1x14's in Alu—Alu Blister.
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 06 months Accelerated: 06 months

Frequency	Accelerated: 0, 3, 6(Months) Real Time: 0, 3, 6(Months)		
Batch No.	TR003-1/PIZ	TR003-2/PIZ	TR003-3/PIZ
Batch Size	1200 TABLETS	1200 TABLETS	1200 TABLETS
Manufacturing Date	June 2021	June 2021	June 2021
Date of Initiation	19-07-2021	19-07-2021	19-07-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Mirab (Mirabegron) Extended Release Tablets 25mg & 50mg on 12th December 2017. Further, the said panel inspection report was discussed in 277th Drug Registration Board meeting held on 27th – 29th December 2017. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Losartan Potassium** M/s Zhejiang Huahai Pharmaceutical Co., Ltd. Valid till 15.10.2024. **Amlodipine Besylate** M/s SMRUTHI ORGANICS LIMITED Valid till 13.11.2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Losartan Potassium** The firm has imported API consignment Zhejiang Huahai Pharmaceutical Co., Ltd. China bearing invoice number HH20200610R dated 22-06-2020. **Amlodipine Besylate** • The firm has imported 5commercial consignment of API from SMRUTHI ORGANICS LIMITED India, bearing invoice number E-150 dated December 27, 2019 signed by ADC on 03-01-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Following Documents are found deficient:

1. In the standard testing method for testing of DS Losartan Potassium (USP) , the wavelength used by DS Manufacturer is 215nm while the wavelength used by the manufacturer of Product is 220nm and the wavelength specified in the USP is different.
2. Stability data of Data Product provided is of three(03) months rather than 06 months.

S. No.	Deficiencies / Short-comings	Justification
1.	In the standard testing method for testing of testing of DS Losartan potassium (USP), the wavelength used by DS manufacturer is 215nm while the wavelength used by the manufacturer of drug product is 220nm and the wavelength specified in the USP is different.	We have been performed Analysis / testing of Losartan potassium Drug Substance as per USP monograph and analytical method verification studies as per ICH guidelines, supporting documents are being attached for your kind perusal: iv. Drug substance analytical method as per USP. v. Drug substance analytical method verification studies in accordance with USP. vi. Revised Certificate of analysis of drug substance analyzed by USP method.
2.	Stability data of product provided is of three (03) months rather than 06 months.	Initially we have submitted CTD dossier application with 3 months stability data, later on again we have submitted 6 months stability data accordingly vide letter DRAP/TAB-REG/03-22, dated March 2,2022. Copy of acknowledgment letter is attached for your ready reference.

Decision: Approved with Innovators specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.711/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

48.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Honig Pharmaceutical Laboratories, 14 km, Adlaya Road, Rawalpindi**
	Name, address of Manufacturing site.	M/s Honig Pharmaceutical Laboratories, 14 km, Adlaya Road, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 23rd June 2020 is provided.
	Evidence of approval of manufacturing facility	Firm has submitted copy of covering letter of renewal of DML No. 000550 (Formulation) for the period commencing on 28-08-2019 and ending on 27-08-2024, however the copy

		of valid DML and status of renewal of DML application is not provided.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1007 Date: 26/10/2021
	Details of fee submitted	PKR 20000 dated: 28-12-20 .
	The proposed proprietary name / brand name	DES-LOR 5mg Tablet.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Desloratidine … 5mg
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Anti-Histamine
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	1x 10's (Alu-Alu Blister)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved Clarinax 5 mg Film coated Tablet
	For generic drugs (me-too status)	Desloreal 5mg Tablet (M/s Winsfield Pharmaceuticals)
	Name and address of API manufacturer.	**Desloratidne:** M/s Glen Mark Life Sciences Ltd, Plot No. 170-172, chandramouli Industrial Estate, MoholBazarpeth Solapur, India **Certificate No. Not Provided**
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure

		system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the brand leader that Clarinax 5 mg Film coated Tablet , by M/s Merck Pharmaceuticals performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is Clarinax 5 mg Film coated Tablet, by M/s Merck Pharmaceuticals in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Glen Mark Life Sciences Ltd, Plot No. 170-172, chandramouli Industrial Estate, MoholBazarpeth Solapur, India GMP Certificate of relevant authorities is **not provided**		
API Lot No.	API lot No is mentioned generally as 40000290161 is mentioned in stability study data sheets		
Description of Pack (Container closure system)	The proposed pack size of DES-LOR 5mg Tablet. is 1x10's in Alu—Alu Blister.		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6(Months) Real Time: 0, 3, 6,9,12,24(Months)		
Batch No.	T001	T002	T003
Batch Size	100000	100000 TABLETS	100000 TABLETS

	TABLETS		
Manufacturing Date	01-2019	01-2019	01-2019
Date of Initiation	01-2019	01-2019	01-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	• **Not Provided**
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Desloratidine:** M/s Glen Mark Life Sciences Ltd, Plot No. 170-172, chandramouli Industrial Estate, MoholBazarpeth Solapur, India GMP Certificate of relevant authorities is **not provided**
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The document regarding import of Tramadol HCL is **not Provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not Submitted.**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	**Not Submitted.**

Following Documents are found deficient:

1. Fee submitted is 20,000 therefore submit remaining 10,000 fee for generic Product.
2. Copy of valid DML and GMP certificate of Drug Product manufacturer is not provided.
3. Submit GMP certificate of Drug Substance manufacturer by relevant authorities.
4. Provide COA of relevant batch(es) of Drug Substance being used during product development and stability studies, of both Drug Product manufacturer & by Drug Substance / /Active Pharmaceutical Ingredient manufacture
5. Documents for the procurement of API (of relevant batch) with approval from DRAP.
6. Provide compatibility study protocol along with reports as the excipients being used are different from the ones mentioned/used in innovator Product (USFDA)
7. The Protocol/method for verification along with detailed reports of analytical method for Drug Product Desloratadine Tablets is not submitted.
8. In analytical assay testing of Desloratadine Tablets the chromatographic condition (wavelength, column and injection volume) are different from the ones specified in USP.
9. The test reports for Dissolution testing of Des-Lor Tablets are not submitted.
10. Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
11. Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)
12. Process validation protocol wherein critical process parameters and sampling plan must be described

	13. Detailed raw data sheets shall be submitted for complete stability studies. 14. Detailed BMR shall be submitted for stability trial batches. 15. Compliance Record of HPLC software 21CFR & audit trail reports on product testing is not submitted.	
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months of issuance of minutes of 322nd meeting. In case Pharmaceutical Evaluation Cell does not receive any response from firm within the given time, the case will be placed before Registration Board for decision.		
49.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Honig Pharmaceutical Laboratories, 14 km, Adlaya Road, Rawalpindi
	Name, address of Manufacturing site.	M/s Honig Pharmaceutical Laboratories, 14 km, Adlaya Road, Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 23rd June 2020 is provided.
	Evidence of approval of manufacturing facility	Firm has submitted copy of covering letter of renewal of DML No. 000550 (Formulation) for the period commencing on 28-08-2019 and ending on 27-08-2024, however the copy of valid DML and status of renewal of DML application is not provided.
	Status of application	☒ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32073 Date: 23/11/2021
	Details of fee submitted	PKR 20000 dated: 20-02020 .
	The proposed proprietary name / brand name	MOLTRA TABLET 325mg/37.5mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Paracetamol … 325mg Tramadol HCl … 37.5mg USP Specs.
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	Alu-Alu/PVC Blisters of 1 x10's Pack
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	The combination of Tramadol HCL/Paracetamol 37.5mg/325mg as Film coated Tablet is MHRA Approved
	For generic drugs (me-too status)	Rama-D Tablet (M/s Global Pharma, Islamabad)

	Name and address of API manufacturer.	**Paracetamol:** M/s Saakh Pharma (Pvt) Ltd, Plot No. C-7/1, NWIZ, Port Qasim Authority, Karachi. **Certificate No. 83/2020-DRAP (K) dated 23-06-2020.** **Tramadol HCL :** Lucent Drugs (Pvt) Ltd, Survey No. 10, Gaddapotharam village Telangana India GMP Certificate of relevant authorities is **not provided**
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40^{o}C ± 2^{o}C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{o}C ± 2^{o}C / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the brand leader that Rama-D Tablet manufactured by M/s Global Pharma, Islamabad), by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is Rama-D Tablet 37.5mg/325 mg by M/s Global Pharma Islamabad in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification	Firm has submitted report of validation studies of analytical

	of product	method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	**Paracetamol:** M/s Saakh Pharma (Pvt) Ltd, Plot No. C-7/1, NWIZ, Port Qasim Authority, Karachi. **Certificate No. 83/2020-DRAP (K) dated 23-06-2020.** **Tramadol HCL :** Lucent Drugs (Pvt) Ltd, Survey No. 10, Gaddapotharam village Telangana India GMP Certificate of relevant authorities is **not provided**		
API Lot No.	API lot No is mentioned generally as 40000290161 but the lot no of individual API(s) is not mentioned.		
Description of Pack (Container closure system)	The proposed pack size of Moltra Tablet 37.5/325mg is 1x10's in Alu—Alu Blister.		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, (Months) Real Time: 0, 3, (Months)		
Batch No.	T001	T002	T003
Batch Size	100000 TABLETS	100000 TABLETS	100000 TABLETS
Manufacturing Date	08-2019	08-2019	08-2019
Date of Initiation	08-2019	08-2019	08-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	• Not Provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Paracetamol:** M/s Saakh Pharma (Pvt) Ltd, Plot No. C-7/1, NWIZ, Port Qasim Authority, Karachi. **Certificate No. 83/2020-DRAP (K) dated 23-06-2020.** **Tramadol HCL :** Lucent Drugs (Pvt) Ltd, Survey No. 10, Gaddapotharam village Telangana India GMP Certificate of relevant authorities is **not provided**
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The document regarding import of Tramadol HCL is **not Provided.**
4.	Data of stability batches will be supported by attested respective documents like	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.

	chromatograms, Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not Submitted.**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	**Not Submitted.**

Evaluation by PEC:

Following Documents are found deficient:

1. Fee submitted is 20,000 therefore submit remaining 10,000 fee.
2. Copy of valid DML and GMP certificate of Drug Product manufacturer is not provided.
3. GMP certificate of Drug Substance manufacturer (Tramadol HCL) by relevant authorities is not Provided.
4. Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture.
5. Documents for the procurement of API with approval from DRAP (for Tramadol HCL).
6. Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)
7. Justify the excipient being used in Product Development as they are different from the ones mentioned in innovator Product (as in MHRA)
8. Process validation protocol wherein critical process parameters and sampling plan must be described
9. Detail Method verification report for drug product shall be submitted.
10. As per submitted analytical record of stability studies the Assay & dissolution test has been performed by UV spectrophotometric method, whereas Pharmacopoeia monograph mandates HPLC method for both tests. Justification shall be submitted in this regard.
11. Detailed raw data sheets shall be submitted for complete stability studies.
12. Detailed BMR shall be submitted for stability trial batches.
13. The results of CDP studies in the dissolution medium of 0.1N HCl are contradictory to the specifications of dissolution test declared in section 3.2.P.5.1.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months of issuance of minutes of 322nd meeting. In case Pharmaceutical Evaluation Cell does not receive any response from firm within the given time, the case will be placed before Registration Board for decision.

3. Cases of Export Facilitation:

50.	**Name, address of Applicant / Marketing Authorization Holder**	M/s FYNK Pharmaceuticals, 19 km, GT Road, Kalashah Kaku, Lahore
	Name, address of Manufacturing site.	M/s FYNK Pharmaceuticals, 19 km, GT Road, Kalashah Kaku, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 08-08-2019 is provided.

	Evidence of approval of manufacturing facility	Firm has submitted copy of covering letter for renewal of DML and approval letters of licensed sections.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11091 Date: 07/5/2022
	Details of fee submitted	PKR 30000 Slip No. 8036710392
	The proposed proprietary name / brand name	TENDOL TABLET 50mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each immediate release Film Coated tablet contains: Tepentadol as Hydrochloride… 50mg
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Opioid Analgesic (ATC code : N02AX06)
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	10's,20's & 30's (Alu-Alu Blister)
	Proposed unit price	Rs.300 for 10's
	The status in reference regulatory authorities	USFDA Approved NUCYNTA 50mg (Tepentadol HCL) Tablet manufactured by Janssen Ortho, LLC, gurabo,
	For generic drugs (me-too status)	Plaxodol Tablet 50mg (M/s Jenner Pharma, Skeikhupura) Registration No. 109504
	Name and address of API manufacturer.	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India. **Certificate No. 19041306 dated 25-04-2019.**
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities,

		specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 24 months. Not Provided on relevant format and date of initiation
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence study is not performed against the innovator / Reference Product CDP has been performed against the same brand that is Plaxodol Tablet 50mg (M/s Jenner Pharma, Skeikhupura) instead of Innovator / Reference Product of same strength.in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India.
API Lot No.	**Not Provided**
Description of Pack (Container closure system)	The proposed pack size is 10's,20's & 30's Alu-Alu Blister.
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months Accelerated: 06 months
Frequency	Accelerated: 0, 3, (Months) Real Time: 0, 3, (Months)

Batch No.	Not Provided	Not Provided	Not Provided
Batch Size	Not Provided	Not Provided	Not Provided
Manufacturing Date	Not Provided	Not Provided	Not Provided
Date of Initiation	Not Provided	Not Provided	Not Provided
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	• Not Provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India. **Certificate No. 19041306 dated 25-04-2019.**
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The document regarding import of Tramadol HCL is **not Provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	**Submitted. However needs to be evaluated in the light of date of initiation till completion of stability**
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Submitted.**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	**Submitted. However needs to be evaluated in the light of date of initiation till completion of stability**

Evaluation by PEC:

Following Documents are found deficient:

1. Provide copy of valid DML.
2. Provide analytical method verification Protocol and test reports for API Tepentadol Hydrochloride as performed by Drug Product manufacturer.
3. CDP studies are performed against Plaxodol Tablet 50mg (M/s Jenner Pharma, Skeikhupura manufactured by instead of Innovator / Reference Product of same strength.
4. RSD is not calculated for Robustness , Precision in method validation test reports.
5. Test of accuracy is not performed in method validation of Product development.
6. Provide stability studies summary sheets on Prescribed format as recommended by the DRB in its 293rd meeting including batch No, batch size, manufacturing date, date of initiation, API lot No and storage conditions etc.
7. Documents for the procurement of API with approval from DRAP (in case of import) along with COA of relevant batch needs to be submitted.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		
51.	**Name, address of Applicant / Marketing Authorization Holder**	M/s FYNK Pharmaceuticals, 19 km, GT Road, Kalashah Kaku, Lahore
	Name, address of Manufacturing site.	M/s FYNK Pharmaceuticals, 19 km, GT Road, Kalashah Kaku, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 08-08-2019 is provided.
	Evidence of approval of manufacturing facility	Firm has submitted copy of covering letter for renewal of DML and approval letters of licensed sections.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11090 Date: 07/5/2022
	Details of fee submitted	PKR 30000 Slip No. 1530874057
	The proposed proprietary name / brand name	TENDOL TABLET 50mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each immediate release Film Coated tablet contains: Tepentadol as Hydrochloride… 50mg
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Opioid Analgesic (ATC code : N02AX06)
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	10’s,20’s & 30’s (Alu-Alu Blister)
	Proposed unit price	Rs.500 for 10’s Rs.1000 for 10’s Rs.1500 for 30’s
	The status in reference regulatory authorities	USFDA Approved NUCYNTA 50mg (Tepentadol HCL) Tablet manufactured by Janssen Ortho, LLC, gurabo,
	For generic drugs (me-too status)	Tapento Tablet 75 mg (M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi) Registration No. 093064
	Name and address of API manufacturer.	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India. **Certificate No. 19041306 dated 25-04-2019.**

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months and data is provided for (batch no. **TPT50040513, TPT50050513, TPT50050513**). The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 24 months. **(TPT50111119, TPT50121119, TPT50131119)**
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence study is not performed against the innovator / Reference Product CDP has been performed against the same brand that is Plaxodol Tablet 50mg (M/s Jenner Pharma, Skeikhupura) instead of Innovator / Reference Product of same strength.in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.
STABILITY STUDY DATA		

Manufacturer of API	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India.		
API Lot No.	Not Provided		
Description of Pack (Container closure system)	The proposed pack size is 10's,20's & 30's Alu-Alu Blister.		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, (Months) Real Time: 0, 3, (Months)		
Batch No.	Not Provided	Not Provided	Not Provided
Batch Size	Not Provided	Not Provided	Not Provided
Manufacturing Date	Not Provided	Not Provided	Not Provided
Date of Initiation	Not Provided	Not Provided	Not Provided
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	• Not Provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India. **Certificate No. 19041306 dated 25-04-2019.**
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The document regarding import of Tramadol HCL is **not Provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	**Submitted. However needs to be evaluated in the light of date of initiation till completion of stability**
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Submitted.**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	**Submitted. However needs to be evaluated in the light of date of initiation till completion of stability**
Evaluation by PEC:		

Following Documents are found deficient:

1. Provide copy of valid DML.
2. Provide analytical method verification Protocol and test reports for API Tepentadol Hydrochloride as performed by Drug Product manufacturer.
3. Pharmaceutical equivalence study and test results are not submitted against Innovator / Reference Product of same strength For Tendol Tablets 100mg.
4. Comparative Dissolution Profile studies are performed for Tendol Tablets 75mg against Tapento Tablet 75mg manufactured by (M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi instead of Innovator / Reference Product of same strength.
5. RSD is not calculated for Robustness test as performed during analytical method validation of Drug Product.
6. Precision and accuracy test and test report in analytical method validation of Drug Product are not submitted.
7. Provide stability studies summary sheets on Prescribed format as recommended by the DRB in its 293rd meeting including batch No, batch size, manufacturing date, date of initiation, API lot No etc.
8. Documents for the procurement of API with approval from DRAP (in case of import) along with COA of relevant batch needs to be submitted.
9. Batch manufacturing record for all batches prepared for stability testing needs to be provided for all strengths.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

52.	**Name, address of Applicant / Marketing Authorization Holder**	M/s FYNK Pharmaceuticals, 19 km, GT Road, Kalashah Kaku, Lahore
	Name, address of Manufacturing site.	M/s FYNK Pharmaceuticals, 19 km, GT Road, Kalashah Kaku, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 08-08-2019 is provided.
	Evidence of approval of manufacturing facility	Firm has **not submitted** copy of valid DML and approval letters of licensed sections
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11092 Date: 07/5/2022
	Details of fee submitted	PKR 30000 Slip No. 32688433
	The proposed proprietary name / brand name	TENDOL TABLET 100mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated immediate release tablet contains: Tepentadol as Hydrochloride… 100mg
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Opioid Analgesic (ATC code : N02AX06)

	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	10's,20's & 30's Alu-Alu Blister
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved NUCYNTA100mg (Tepentadol HCL) Tablet manufactured by Janssen Ortho, LLC, gurabo,
	For generic drugs (me-too status)	Tapento Tablet 75mg (M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi) **The strength is different**
	Name and address of API manufacturer.	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India. **Certificate No. 19041306 dated 25-04-2019.**
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container

		closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the **Tapento 75mg Tablets manufactured by M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi instead of Innovator / Reference Product of same strength**. **CDP has been performed against the same brand that is Tapento 75mg Tablets manufactured by M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi instead of Innovator / Reference Product of same strength**.in Acid media (0.1N HCl),
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India.		
API Lot No.	API lot No is mentioned generally as 40000290161 but the lot no of individual API(s) is not mentioned.		
Description of Pack (Container closure system)	The proposed pack size is 10's,20's & 30's Alu-Alu Blister.		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, (Months) Real Time: 0, 3, (Months)		
Batch No.	TL100-01	TL100-02	TL100-03
Batch Size	1000 TABLETS	1000 TABLETS	1000 TABLETS
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	08-2019	08-2019	08-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	• **Not Provided**
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Tapentadol Hydrochloride:** M/s Ami Life Sciences Private Limited, Block No. 82/B, ECP Road, Taluka Padra, Gujrat, India. **Certificate No. 19041306 dated 25-04-2019.**

3.	Documents for the procurement of API with approval from DRAP (in case of import).	The document regarding import of Tramadol HCL is **not Provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Submitted.**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	**Submitted.**

Evaluation by PEC:

Following Documents are found deficient:

1. Fee submitted is 30,000 therefore submit remaining 45,000 fee for new drug molecule.
2. Provide copy of valid DML along with approval letter of licensed sections.
3. The strength of Proposed Product is different from Tapento Tablet 75mg (M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi)
4. Provide analytical method verification Protocol and test reports for API Tepentadol Hydrochloride as performed by Drug Product manufacturer.
5. Pharmaceutical equivalence and CDP studies are performed against Tapento 75mg Tablets manufactured by M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi instead of Innovator / Reference Product of same strength.
6. RSD is not calculated for Robustness , Precision in method validation test reports.
7. Test of accuracy is not performed in method validation of Product development.
8. Provide stability studies summary sheets on Prescribed format as recommended by the DRB in its 293rd meeting including batch No, batch size, manufacaturing date, date of initiation, API lot No and storage conditions etc.
9. Documents for the procurement of API with approval from DRAP (in case of import).

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months

53.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Next Pharmaceutical Pvt. Ltd. Plot 44,A-B, Sundar Industrial Estate , Lahore
	Name, address of Manufacturing site.	M/s Next Pharmaceutical Pvt. Ltd. Plot 44,A-B, Sundar Industrial Estate , Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	**Firm has submitted copy of DML No. 000847 (Formulation) valid till 25-10-2026.**
	Evidence of approval of manufacturing facility	Firm has submitted copy of covering letter of renewal of DML No. 000847 (Formulation) on which Tablet (General) section is mentioned as approved section.
	Status of application	☒ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale

		☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32067 dated 23-11-2021
	Details of fee submitted	PKR30000 dated: 15-10-2021 bearing Deposit Slip No. 175588966019
	The proposed proprietary name / brand name	Valvet-S 24/26 mg Film Coated Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sacubitril … 24mg Valsartan ……..… 26mg (as sacubitril valsartan sodium salt complex)
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Valsartan : Angiotensin II Receptor Antagonist Sacubitril : Neprilysin inhibitor
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	07's, 14's, 28's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Entresto 24 mg/26 mg film-coated tablets EMA (Europe) approved
	For generic drugs (me-too status)	1. Savesto 50mg of M/s Getz Pharma (Pvt) Ltd, Karachi. 2. Valsatril 50(24/26 mg) of M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi
	Name and address of API manufacturer.	Sacubitril-Valsartan Complex Nantong Chanyoo Pharmatech Co., Ltd, China LCZ696 In-House Specifications
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time

	studies)	conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 06 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 06 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the innovator that is Entresto Tablet 50mg by Novartis Europharm Limited by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is Entresto Tablet 50mg by Novartis Europharm Limited in 0.1N HCl (QC medium), Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory.
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Sacubitril-Valsartan Complex Nantong Chanyoo Pharmatech Co., Ltd, China **In-House Specifications**		
API Lot No.	API Batch No. RD-LCZ696-202010101		
Description of Pack (Container closure system)	The proposed pack size of Valvet- S Tablet 24/26mg is 1x14's in Alu—Alu Blister.		
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 1,2,3,6 (Months) Real Time: 0, 1,2,3, 6(Months)		
Batch No.	T0001-TAS	T0002-TAS	T0003-TAS
Batch Size	2000 TABLETS	2000 TABLETS	2000 TABLETS
Manufacturing Date	06-05-21	06-05-21	06-05-21
Date of Initiation	28-05-21	28-05-21	28-05-21

No. of Batches		03
DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not Provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Nantong Chanyoo Pharmatech Co, Ltd, Yangkou Chemical Industrial Park , Rundong Coastal Economic Development Zone, China. Manufacturing License No.Su 2016512
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**COA of Batch No.** RD-LCZ696-202010101 of API (Valsartan/Sacubitril) of both Drug Substance manufacturer and Drug Product manufacturer is provided
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not submitted**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Following Documents are found deficient:

1. Either Provide valid copy of DML No. 000847(Formulation) or proof of submission of application in Licensing Division, DRAP.
2. **Stability study of Product is of three months , therefore, provide six (06) months stability data of Product.**
3. **Data Log of stability chambers reveals that the average of humidity was 57 % in Real time stability study with minimum reading of 19.4.**
4. Compatibility studies of the Drug Substance(s) with excipients shall be provided if the qualitative composition of the formulation is not similar to innovator / reference product
5. API) lot no. is not provided in stability data sheet and neither the same is mentioned in batch manufacturing.
6. COA of batch (Lot) of API of API manufacturer, Product manufacturer which is being used in manufacturing of relevant batches of Final Product needs to be provided.
7. Clearance of relevant batch of API & of Standard from AD DRAP Lahore needs to be provided.

Reply of the Applicant:

1. Firm has submitted copy of DML No. 000847 (Formulation) valid till 25-10-2026.
2. The stability studies data sheets are provided for six months, however, attested respective documents like chromatograms, for each point of testing (0,1,3 months) respectively are not submitted.
3. The firm has not submitted the Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) instead has provided the Disc for said purpose which contains the said record.
4. The excipients used by the innovator Product Entresto 24mg/26mg are Microcrystalline cellulose, low substituted hydroxypropylcellulose, crospovidone, magnesium stearate, talc, colloidal silicon dioxide while the Product Manufacturer has used are similar.

5. COA of Batch No. RD-LCZ696-202010101 of API (Valsartan/Sacubitril) of both Drug Substance manufacturer and Drug Product manufacturer is provided
6. Document dated 24-11-2020 for the procurement of API with approval from DRAP (in case of import) Batch No. RD-LCZ696-202010101 of API (Valsartan/Sacubitril) is submitted.

Decision: Approved.

- **Firm shall submit attested respective documents like chromatograms, for each time point of stability studies, till 6th month time point, before issuance of registration letter.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

54.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 17-01-2022 is provided.
	Evidence of approval of manufacturing facility	copy of Valid DML No. 000284 (Formulation) is provided along with covering letter is provided.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10948 Date: 30/4/2022
	Details of fee submitted	PKR 30000 dated: 03-2022 . SLIP No. 857472863756
	The proposed proprietary name / brand name	DAPLYZA-M XR TABLET Dapagliflozin + Metformin HCL (5mg/1000mg)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated XR tablet contains: Dapagliflozin … 5mg Metformin HCL … 1000 mg
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Anti-Diabetic
	Reference to Finished product specifications	In-House Specs
	Proposed Pack size	14’s & 28’s (Alu-Alu Blister in a unit carton)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved (Xigduo XR 5mg/1000mg) Film coated extended release tablets by M/s Astra Zenica USA.

	For generic drugs (me-too status)	Dapa-Met XR Tablets (5/1000 mg) by M/s Hilton Pharma (Pvt) Ltd, Karachi.
	Name and address of API manufacturer.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against Dapa-Met XR Tablets (5mg + 1000mg) by M/s Hilton Pharma (Pvt) Ltd, Karachi by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is (Dapa-Met XR Tablets (5mg + 1000mg) by M/s Hilton Pharma (Pvt) Ltd, Karachi in .1N HCL, acetate buffer

		pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023		
API Lot No.	Metformin HCL : API Lot No is 0000185425, 0186833 Dapagliflozin : API Lot No. D02DG0605		
Description of Pack (Container closure system)	The proposed pack size of DAPLYZA-M XR TABLET is 14's & 28's (Alu-Alu Blister in unit carton)		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	580DS01	580DS02	574DS03
Batch Size	1500 TABLETS	1500 TABLETS	1500 TABLETS
Manufacturing Date	14-4-2021	28-05-2021	28-05-2021
Date of Initiation	28-07-2021	28-07-2021	28-07-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine Tablets 10mg & 20mg (Ebastine 10mg& 20mg) on 6th May 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th-16th May 2019. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available.

		• Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin Propionate:** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Dapagliflozin Propanediol :** Commercial Invoice No. HN200109-F Dated 16-01-2020 **Metformin-HCL :** **The invoice of relevant batch** 0187504 **used in Product Development is provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Observations :

1. Documents for the procurement of API with approval from DRAP (in case of import) for **relevant batch (**0000-185425 & 0-186833)**of API Metformin-HCL used in Product Development is not provided**.
2. CDP has been performed against the same brand that is (Dapa-Met XR Tablets (5mg + 1000mg) by M/s Hilton Pharma (Pvt) Ltd, Karachi in .1N HCL, acetate buffer pH 4.5 & Phosphate Buffer pH 6.8 istead of innovator that is (Xigduo XR 5mg/1000mg) Film coated extended release tablets by M/s Astra Zenica USA.

Response of the firm :

Query Items	Response
1.Documents for the procurement of relevant batch (0000-185425 & 0-186833) of Metformin HCl API with approval from DRAP along with COA of said batches as provided by Drug Substance	Please refer to Annex-1 for documents for the procurement of API with approval from DRAP for relevant batches (0000-185425 & 0-186833) of API Metformin HCl.

	manufacturer and Drug product manufacturer.	<table><tr><th>API Batch No. (Getz Pharma)</th><th>API Batch No. M/s Shouguang Fukang Pharmaceutical Co., Ltd.</th><th>Invoice No.</th><th>DRAP Approval Date</th></tr><tr><td>0000-185425</td><td>A-81412010085</td><td>JC202008013-1</td><td>03-12-2020</td></tr><tr><td>0000-186833</td><td>A-22612012009-0150</td><td>JC202008014-1</td><td>05-01-2021</td></tr></table>
	2.Please clarify why the comparative dissolution studies are performed with DAPA-Met XR 5mg + 500mg by M/s Hilton Pharma (Pvt) Ltd, Karachi instead of reference product USFDA Approved Xigduo XR 5mg + 500mg Film coated extended release tablets.	This is to bring to your kind information that as per DRAP guidelines "Guidance document for submission of application on Form 5-F (CTD) for registration of pharmaceutical Drug products for human use", to perform Pharmaceutical Equivalence '*The comparison of the developed formulation and the innovator / reference / comparator product including the results of all the quality tests shall be submitted and discussed'.* We have established Pharmaceutical Equivalence of Daplyza-M XR Tablets 5mg + 500mg (manufactured by Getz Pharma) with Dapa-Met XR Tablets 5mg + 500mg Manufactured by M/s Hilton Pharma (Pvt.) Limite as innovator brand is currently not available in Pakistan.
	3.Provide Pharmaceutical equivalence study and test results of both Daplyza Tablets and reference product USFDA approved Xigduo XR 5mg + 500mg Film coated extended release tablets.	Please refer to Point #02 of this letter.

Decision: Approved with Innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.711/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

55.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 17-01-2022 is provided.
	Evidence of approval of manufacturing facility	copy of Valid DML No. 000284 (Formulation) is provided along with covering letter is provided.

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10720 Date: 28/4/2022
	Details of fee submitted	PKR 30000 dated: 14-03-2022 .
	The proposed proprietary name / brand name	DAPLYZA-M XR TABLET Dapagliflozin + Metformin HCL (5mg/500mg)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated XR tablet contains: Dapagliflozin … 5 mg Metformin HCL … 500 mg
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Anti-Diabetic
	Reference to Finished product specifications	In-House Specs
	Proposed Pack size	14's & 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved (Xigduo XR 5mg/500mg) Film coated extended release tablets
	For generic drugs (me-too status)	New Drug
	Name and address of API manufacturer.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the Dapa-Met XR 5mg/500mg by M/s Hilton Pharma (Pvt) Ltd , Karachi by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is (Dapa-Met XR 5mg/500mg by M/s Hilton Pharma (Pvt) Ltd , Karachi in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
API Lot No.	Metformin HCL : API Lot No is 0187504 Dapagliflozin : API Lot No. D02DG0605
Description of Pack (Container closure system)	The proposed pack size of DAPLYZA-M XR TABLET is 14's & 28's
Stability Storage	Real time : $30^{\circ}C \pm 2^{\circ}C$ / 75% ± 5%RH

Condition	Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	581DS02	581DS03	581DS04
Batch Size	1500 TABLETS	1500 TABLETS	1500 TABLETS
Manufacturing Date	15-06-2021	07-07-2021	07-07-2021
Date of Initiation	11-08-2021	11-08-2021	11-08-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine Tablets 10mg & 20mg (Ebastine 10mg& 20mg) on 6th May 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th-16th May 2019. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin Propionate:** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Dapagliflozin Propanediol :** Commercial Invoice No. HN200109-F Dated 16-01-2020 **Metformin-HCL :** **The invoice of relevant batch** 0187504 **used in Product Development is not provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Following Documents are found deficient:

1. Documents for the procurement of **relevant batch (**0000-185425 & 0-186833) of **Metformin-HCL** API with approval from DRAP.
2. Please clarify since the UV method is used in dissolution testing of drug product for Metformin HCl while the assay of Metformin HCl is performed on HPLC as per supplier's method.
3. Test Protocols for method validation of Dapagliflozin (drug substance) needs to be provided along with detail of test results for Accuracy of analytical method validation performed by drug product manufacturer.
4. The record of digital data logger of stability chambers (accelerated and real time) throughout the 6 months for which stability study data has been submitted, since your submission does not contain complete record of data logger.

Response/Reply of firm:

<table>
<tr><th>Query Items</th><th>Response</th></tr>
<tr><td>1. Documents for the procurement of relevant batch (0000-185425 & 0-186833) of Metformin HCL API with approval from DRAP.</td><td>Please refer to Annex -1 for documents for the procurement of API with approval from DRAP for relevant batches (0000-185425 & 0-186833) of API Metformin HCl.
<table>
<tr><th>API Batch No. (Getz Pharma)</th><th>API Batch No. M/s Shouguang Fukang Pharmaceutical Co., Ltd.</th><th>Invoice No.</th><th>DRAP Approval Date</th></tr>
<tr><td>0000-185425</td><td>A-81412010085</td><td>JC202008013-1</td><td>03-12-2020</td></tr>
<tr><td>0000-186833</td><td>A-22612012009-0150</td><td>JC202008014-1</td><td>05-01-2021</td></tr>
</table></td></tr>
<tr><td>2.Please clarify since the UV method is used in dissolution testing of drug product for Metformin HCl while the assay of Metformin HCl is performed on HPLC as per supplier's method.</td><td>This is bring to your kind attention that as per US-FDA, Dissolution medium for Dapagliflozin + Metformin Extended Release Tablet is phosphate buffer Ph 6.8.During HPLC testing, peak of dissolution medium can merged with peak of Metformin HCl and lead to inaccurate results. Therefore, we have developed UV method for dissolution for Metformin HCl to get the accurate quantitation results.
Further, USP monographs for Metformin HCl extended release tablets used Spectrophotometric determination for dissolution of Metformin HCl whereas its assay is on HPLC.</td></tr>
<tr><td>3.Test Protocols for method validation of Dapagliflozin (drug substance) needs to be provided along with detail of test results for Accuracy of analytical method validation</td><td>Please refer to Annex-2 for Test Protocols for method validation of Dapagliflozin (drug substance) including specificity, linearity, repeatability and range by drug product manufacturer.
Further, with reference to ICH Guidelines "VALIDATION OF ANALYTICAL PROCEDURES: TEXT AND METHODOLOGY Q2 (R1)" it is mentioned in section 4.1.1 Drug</td></tr>
</table>

performed by drug product manufacturer.	Substance "accuracy may be inferred once precision, linearity and specificity have been established". This is bring to your kind attention that since we have performed method verification studies as per ICH Q2 (R1) therefore, requirement of accuracy is not applicable.
4.The record of digital data logger of stability chambers (Accelerated & Real time) throughout the 06 months for which stability data has been submitted, since your submission does not contain complete record of data logger.	Please refer to Annex -3 for record of digital data logger of stability chambers (Accelerated & Real time) throughout the 06 months for which stability data has been submitted.

Decision: Approved with Innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.711/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

56.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 17-01-2022 is provided.
	Evidence of approval of manufacturing facility	copy of Valid DML No. 000284 (Formulation) is provided along with covering letter is provided.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10721 Date: 28/4/2022
	Details of fee submitted	PKR 30000 dated: 14-03-2022 . SLIP No. 987829781
	The proposed proprietary name / brand name	DAPLYZA-M XR TABLET Dapagliflozin + Metformin HCL (2.5mg/1000mg)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated XR tablet contains: Dapagliflozin … 2.5 mg Metformin HCL … 1000 mg
	Pharmaceutical form of applied drug	Tablet (General)

	Pharmacotherapeutic Group of (API)	Anti-Diabetic
	Reference to Finished product specifications	In-House Specs
	Proposed Pack size	14's & 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved (Xigduo XR 2.5mg/1000mg) Film coated extended release tablets by M/s Astra Zenica USA.
	For generic drugs (me-too status)	Dapa-Met XR Tablets (2.5/1000 mg) by M/s Hilton Pharma (Pvt) Ltd, Karachi.
	Name and address of API manufacturer.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of

		specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against Dapa-Met XR Tablets (2.5mg + 1000mg) by M/s Hilton Pharma (Pvt) Ltd, Karachi by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is (Dapa-Met XR Tablets (2.5mg + 1000mg) by M/s Hilton Pharma (Pvt) Ltd, Karachi in .1N HCL, acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023		
API Lot No.	Metformin HCL : API Lot No is 0000185425, 0186833 Dapagliflozin : API Lot No. D02DG0605		
Description of Pack (Container closure system)	The proposed pack size of DAPLYZA-M XR TABLET is 14's & 28's		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	574DS01	574DS02	574DS03
Batch Size	1500 TABLETS	1500 TABLETS	1500 TABLETS
Manufacturing Date	14-4-2021	08-07-2021	28-05-2021
Date of Initiation	28-07-2021	28-07-2021	28-07-2021
No. of Batches	03		
DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA			

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine Tablets 10mg & 20mg (Ebastine 10mg& 20mg) on 6th May 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th-16th May 2019. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin Propionate:** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Dapagliflozin Propanediol :** Commercial Invoice No. HN200109-F Dated 16-01-2020 **Metformin-HCL :** **The invoice of relevant batch** 0187504 **used in Product Development is not provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.
Evaluation by PEC:		
Observations : **1.** Documents for the procurement of **relevant batch (**0000-185425 & 0-186833) of **Metformin-HCL** API with approval from DRAP along with COA of said batches as provided by Drug Substance manufacturer and Drug Product manufacturer. **2.** Please clarify why the comparative dissolution studies are performed with (Dapa-Met XR 5mg/500mg by M/s Hilton Pharma (Pvt) Ltd , Karachi instead of reference Product USFDA Approved Xigduo XR 5mg/500mg) Film coated extended release tablets.		

3. Provide Pharmaceutical equivalence study and test results of both DAPLYZA Tablets and of reference Product USFDA Approved Xigduo XR 5mg/500mg) Film coated extended release tablets.

Reply of the Firm :

<table>
<tr><th>Query Items</th><th>Response</th></tr>
<tr><td>1. Documents for the procurement of relevant batch (0000-185425 & 0-186833) of Metformin HCl API with approval from DRAP along with COA of said batches as provided by Drug Substance manufacturer and Drug product manufacturer.</td><td>Please refer to Annex-1 for documents for the procurement of API with approval from DRAP for relevant batches (0000-185425 & 0-186833) of API Metformin HCl.
<table>
<tr><th>API Batch No. (Getz Pharma)</th><th>API Batch No. M/s Shouguang Fukang Pharmaceutical Co., Ltd.</th><th>Invoice No.</th><th>DRAP Approval Date</th></tr>
<tr><td>0000-185425</td><td>A-81412010085</td><td>JC202008013-1</td><td>03-12-2020</td></tr>
<tr><td>0000-186833</td><td>A-22612012009-0150</td><td>JC202008014-1</td><td>05-01-2021</td></tr>
</table></td></tr>
<tr><td>2.Please clarify why the comparative dissolution studies are performed with DAPA-Met XR 5mg + 500mg by M/s Hilton Pharma (Pvt) Ltd, Karachi instead of reference product USFDA Approved Xigduo XR 5mg + 500mg Film coated extended release tablets.</td><td>This is to bring to your kind information that as per DRAP guidelines “Guidance document for submission of application on Form 5-F (CTD) for registration of pharmaceutical Drug products for human use”, to perform Pharmaceutical Equivalence ‘<u>The comparison of the developed formulation and the innovator / reference / comparator product including the results of all the quality tests shall be submitted and discussed’.</u>
We have established Pharmaceutical Equivalence of Daplyza-M XR Tablets 5mg + 500mg (manufactured by Getz Pharma) with Dapa-Met XR Tablets 5mg + 500mg Manufactured by M/s Hilton Pharma (Pvt.) Limite as innovator brand is currently not available in Pakistan.</td></tr>
<tr><td>3.Provide Pharmaceutical equivalence study and test results of both Daplyza Tablets and reference product USFDA approved Xigduo XR 5mg + 500mg Film coated extended release tablets.</td><td>Please refer to Point #02 of this letter.</td></tr>
</table>

Decision: Approved with Innovator’s specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.711/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

57.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector

		27,Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 17-01-2022 is provided.
	Evidence of approval of manufacturing facility	copy of Valid DML No. 000284 (Formulation) is provided along with covering letter is provided.
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10722 Date: 28/4/2022
	Details of fee submitted	PKR 75000 dated: 14-03-2022 .
	The proposed proprietary name / brand name	DAPLYZA-M XR TABLET Dapagliflozin + Metformin HCL (10mg/500mg)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated XR tablet contains: Dapagliflozin … 10 mg Metformin HCL … 500 mg
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Anti-Diabetic
	Reference to Finished product specifications	In-House Specs
	Proposed Pack size	14’s & 28’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved (Xigduo XR 10mg/1000mg) Film coated extended release tablets
	For generic drugs (me-too status)	New Drug
	Name and address of API manufacturer.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug

		substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the brand leader Xigduo XR 10mg/500mg by M/s Astra Zenica USA), by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is (Xigduo XR 10mg/500mg by M/s Astra Zenica USA in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
API Lot No.	Metformin HCL :

	API Lot No is 0000185425 Dapagliflozin : API Lot No. D02DG0605		
Description of Pack (Container closure system)	The proposed pack size of DAPLYZA-M XR TABLET is 14's & 28's		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	582DS02	582DS03	582DS04
Batch Size	1500 TABLETS	1500 TABLETS	1500 TABLETS
Manufacturing Date	08-07-2021	08-07-2021	08-07-2021
Date of Initiation	11-08-2021	11-08-2021	11-08-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine Tablets 10mg & 20mg (Ebastine 10mg& 20mg) on 6th May 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th-16th May 2019. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin Propionate:** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Dapagliflozin Propanediol :** Commercial Invoice No. HN200109-F Dated 16-01-2020 **Metformin-HCL :**

		The invoice of relevant batch 0187504 **used in Product Development is not provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Observations :

1. Documents for the procurement of **relevant batch (**0000-185425 & 0-186833) of **Metformin-HCL** API with approval from DRAP along with COA of said batches as provided by Drug Substance manufacturer and Drug Product manufacturer.
2. Please clarify why the comparative dissolution studies are performed with (Dapa-Met XR 5mg/500mg by M/s Hilton Pharma (Pvt) Ltd , Karachi instead of reference Product USFDA Approved Xigduo XR 5mg/500mg) Film coated extended release tablets.
3. Provide Pharmaceutical equivalence study and test results of both DAPLYZA Tablets and of reference Product USFDA Approved Xigduo XR 5mg/500mg)

<table>
<tr><th>Query Items</th><th>Response</th></tr>
<tr><td>1. Documents for the procurement of relevant batch (0000-185425 & 0-186833) of Metformin HCl API with approval from DRAP along with COA of said batches as provided by Drug Substance manufacturer and Drug product manufacturer.</td><td>Please refer to Annex-1 for documents for the procurement of API with approval from DRAP for relevant batches (0000-185425 & 0-186833) of API Metformin HCl.
<table>
<tr><th>API Batch No. (Getz Pharma)</th><th>API Batch No. M/s Shouguang Fukang Pharmaceutical Co., Ltd.</th><th>Invoice No.</th><th>DRAP Approval Date</th></tr>
<tr><td>0000-185425</td><td>A-81412010085</td><td>JC202008013-1</td><td>03-12-2020</td></tr>
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</table></td></tr>
<tr><td>2.Please clarify why the comparative dissolution studies are performed with DAPA-Met XR 5mg + 500mg by M/s Hilton Pharma (Pvt) Ltd, Karachi instead of reference product USFDA Approved Xigduo XR 5mg + 500mg Film coated extended release tablets.</td><td>This is to bring to your kind information that as per DRAP guidelines “Guidance document for submission of application on Form 5-F (CTD) for registration of pharmaceutical Drug products for human use”, to perform Pharmaceutical Equivalence ‘<u>The comparison of the developed formulation and the innovator / reference / comparator product including the results of all the quality tests shall be submitted and discussed’.</u>
We have established Pharmaceutical Equivalence of Daplyza-M XR Tablets 5mg + 500mg (manufactured by Getz Pharma) with Dapa-Met XR Tablets 5mg + 500mg</td></tr>
</table>

		Manufactured by M/s Hilton Pharma (Pvt.) Limite as innovator brand is currently not available in Pakistan.
	3.Provide Pharmaceutical equivalence study and test results of both Daplyza Tablets and reference product USFDA approved Xigduo XR 5mg + 500mg Film coated extended release tablets.	Please refer to Point #02 of this letter.

Decision: Approved with Innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.711/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

58.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt) Ltd, Plot No. 29-30, Sector 27,Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 17-01-2022 is provided.
	Evidence of approval of manufacturing facility	copy of Valid DML No. 000284 (Formulation) is provided along with covering letter is provided.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10722 Date: 28/4/2022
	Details of fee submitted	PKR 30000 dated: 14-03-2022 .
	The proposed proprietary name / brand name	DAPLYZA-M XR TABLET Dapagliflozin + Metformin HCL (10mg/1000 mg)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated XR tablet contains: Dapagliflozin … 10 mg Metformin HCL … 1000 mg USP Specs.
	Pharmaceutical form of applied drug	Tablet (General)
	Pharmacotherapeutic Group of (API)	Anti-Diabetic
	Reference to Finished product specifications	In-House Specs

	Proposed Pack size	14's & 28's Tablets
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved (Xigduo XR 10mg/1000mg) Film coated extended release tablets
	For generic drugs (me-too status)	Dapa-Met XR Tablets (10mg + 1000mg) M/s Hilton Pharma (Pvt) Ltd, Karachi
	Name and address of API manufacturer.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the brand leader that Rama-D Tablet

		manufactured by M/s Global Pharma, Islamabad), by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is Rama-D Tablet 37.5mg/325 mg by M/s Global Pharma Islamabad in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory(>50%).
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin :** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023			
API Lot No.	Metformin HCL : API Lot No is 0000185425 Dapagliflozin : API Lot No. D02DG0605			
Description of Pack (Container closure system)	The proposed pack size of DAPLYZA-M XR TABLET is 14's & 28's			
Stability Storage Condition	Real time : 30˚C ± 2˚C / 75% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH			
Time Period	Real time: 06 months Accelerated: 06 months			
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)			
Batch No.	575DS01	575DS02	575DS03	
Batch Size	1500 TABLETS	1500 TABLETS	1500 TABLETS	
Manufacturing Date	14-04-2021	28-05-2021	08-2019	
Date of Initiation	10-08-2021	10-08-2021	08-2019	
No. of Batches	03			

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine Tablets 10mg & 20mg (Ebastine 10mg& 20mg) on 6th May 2019. Further, the said panel inspection report was discussed in 289th Drug

		Registration Board meeting held on 14th-16th May 2019. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Metformin HCL (USP):** M/s Shouguang Fukang Pharmaceutical Co., Ltd, North East of Dongwaihuan Province, China. Certificate No. SD20190888 valid till 12-03-2024. **Dapagliflozin Propionate:** Fuxin Long Rui Pharmaceutical Co., Ltd, GMP Certificate valid till 23-08-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Dapagliflozin Propanediol :** Commercial Invoice No. HN200109-F Dated 16-01-2020 **Metformin-HCL :** **The invoice of relevant batch 0000185425 used in Product Development is not provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.
Evaluation by PEC:		
Observations : 1. Documents for the procurement of **relevant batch (**0000-185425 & 0-186833) of **Metformin-HCL** API with approval from DRAP. 2. Please clarify since the UV method is used in dissolution testing of drug product for Metformin HCl while the assay of Metformin HCl is performed on HPLC as per supplier's method. 3. Test Protocols for method validation of Dapagliflozin (drug substance) needs to be provided along with detail of test results for Accuracy of analytical method validation performed by drug product manufacturer. 4. The record of digital data logger of stability chambers (accelerated and real time) throughout the 6 months for which stability study data has been submitted, since your submission does not contain complete record of data logger.		
Reply of the firm :		

<table>
<tr><th>Query Items</th><th>Response</th></tr>
<tr><td>1. Documents for the procurement of relevant batch (0000-185425 & 0-186833) of Metformin HCL API with approval from DRAP.</td><td>Please refer to Annex -1 for documents for the procurement of API with approval from DRAP for relevant batches (0000-185425 & 0-186833) of API Metformin HCl.

<table>
<tr><th>API Batch No. (Getz Pharma)</th><th>API Batch No. M/s Shouguang Fukang Pharmaceutical Co., Ltd.</th><th>Invoice No.</th><th>DRAP Approval Date</th></tr>
<tr><td>0000-185425</td><td>A-81412010085</td><td>JC202008013-1</td><td>03-12-2020</td></tr>
<tr><td>0000-186833</td><td>A-22612012009-0150</td><td>JC202008014-1</td><td>05-01-2021</td></tr>
</table>
</td></tr>
<tr><td>2.Please clarify since the UV method is used in dissolution testing of drug product for Metformin HCl while the assay of Metformin HCl is performed on HPLC as per supplier’s method.</td><td>This is bring to your kind attention that as per US-FDA, Dissolution medium for Dapagliflozin + Metformin Extended Release Tablet is phosphate buffer Ph 6.8.During HPLC testing, peak of dissolution medium can merged with peak of Metformin HCl and lead to inaccurate results. Therefore, we have developed UV method for dissolution for Metformin HCl to get the accurate quantitation results.

Further, USP monographs for Metformin HCl extended release tablets used Spectrophotometric determination for dissolution of Metformin HCl whereas its assay is on HPLC.</td></tr>
<tr><td>3.Test Protocols for method validation of Dapagliflozin (drug substance) needs to be provided along with detail of test results for Accuracy of analytical method validation performed by drug product manufacturer.</td><td>Please refer to Annex-2 for Test Protocols for method validation of Dapagliflozin (drug substance) including specificity, linearity, repeatability and range by drug product manufacturer.

Further, with reference to ICH Guidelines “VALIDATION OF ANALYTICAL PROCEDURES: TEXT AND METHODOLOGY Q2 (R1)” it is mentioned in section 4.1.1 Drug Substance “accuracy may be inferred once precision, linearity and specificity have been established”.

This is bring to your kind attention that since we have performed method verification studies as per ICH Q2 (R1) therefore, requirement of accuracy is not applicable.

Link of ICH guideline is provided below:

Q2(R1) Guideline.pdf (ich.org)</td></tr>
<tr><td>4.The record of digital data logger of stability chambers (Accelerated & Real time) throughout the 06 months for which stability data has been submitted, since your submission does not contain complete record of data logger.</td><td>Please refer to Annex -3 for record of digital data logger of stability chambers (Accelerated & Real time) throughout the 06 months for which stability data has been submitted.</td></tr>
<tr><td colspan="2">Decision: Approved with Innovator’s specifications.</td></tr>
</table>

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.711/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

3. Cases of New Sections :

59.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Biogen Life Sciences 8 km Chakbeli Road Rawat Rawalpindi
	Name, address of Manufacturing site.	M/s Biogen Life Sciences 8 km Chakbeli Road Rawat Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 17-01-2022 is provided.
	Evidence of approval of manufacturing facility	copy of Valid DML No. 000911 (Formulation) valid till 13-02-2025 along with covering letter is provided.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27912 Date: 03/10/2022
	Details of fee submitted	PKR 30000 dated: 28-07-2022 . SLIP No. 9108432875
	The proposed proprietary name / brand name	**Actogen 100ml Vial**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Paracetamol 10mg/ml solution for infusion
	Pharmaceutical form of applied drug	Solution for Infusion
	Pharmacotherapeutic Group of (API)	Anti-Pyretic
	Reference to Finished product specifications	Innovator Specs
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved
	For generic drugs (me-too status)	**Brand Name:** Provas (10mg/ml) **Registration holder:** M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi.

		Registration Number: 050650
	Name and address of API manufacturer.	M/s Citi Pharma (Pvt) Ltd, 3 km, Head Balloki Road, Phool Nagar, Kasur. GMP Certificate No. 10444/2016-DRAP/2016
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have not been established/submitted with innovator Product, but with Provas Infusion of M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi
	Analytical method validation/verification of product	Firm has submitted report of verification studies of analytical method of drug substance. Firm has submitted report of validation of analytical method (In-House) for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Citi Pharma (Pvt) Ltd, 3 km, Head Balloki Road, Phool Nagar, Kasur. GMP Certificate No. 10444/2016-DRAP/2016
API Lot No.	**Not Provided**
Description of Pack	1's

(Container closure system)			
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	11-2021	11-2021	11-2021
Date of Initiation	20-11-2021	20-11-2021	20-11-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	• Not Submitted. • Firm has stated that Biogen is a new license section and no such data is submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Sun Pharmaceutical Industries Limited, Industrial Area - 3 A.B. Road 455001 Madhya Pradesh , India DML No. 24/24/83 in form no. 25 & 28/15/83 in form no.28
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Not required.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not Submitted.**
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	**Not Submitted.**

Evaluation by PEC :

1. Provide updated GMP certificate of API manufacturer M/s Citi Pharma Kasur as the submitted GMP certificated is dated 2016.
2. API manufacturer (M/s citi Pharma Kasur) has performed melting point test for identification of API but has set specifications different from those as mentioned in BP.
3. API manufacturer (M/s citi Pharma Kasur) has performed impurities testing as mentioned in BP but the acceptance criteria is kept at Not more than 1 % while the one mentioned in BP is max .2%
4. Provide the detailed analytical method with complete detail (method verification) along with test reports of API as performed by the Drug Product manufacturer.
5. The Manufacturing Protocol/Procedure for manufacture/Product Development (including sterility testing) are not submitted.

	6. Batch detail along with BMR (including sterility testing) is not provided for manufacturing of Drug Product. 7. Compliance Record of HPLC software 21CFR & audit trail reports on product testing is not Provided. 8. Submit microbial reports for the sterility testing of drug product along during stability studies. 9. Pharmaceutical Equivalence studies along with test reports results of all the quality tests (mentioned in any official pharmacopoeia or section 3.2.P.5.1 of this application) of the developed formulation and the innovator / reference / comparator product shall be submitted with innovator Product of Drug Product are not submitted. 10. Submit microbial reports for the sterility testing of drug product during stability studies. 11. Provide compatibility study protocol along with reports as the excipients being used are different from the ones mentioned/used in innovator Product (USFDA) 12. In chromatogram of stability studies, study on blank and respective chromatogram of blank is not submitted. 13. Compliance Record of HPLC software 21CFR & audit trail reports on product testing needs to be submitted. 14. Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is not submitted.	
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		
60.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Biogen Life Sciences 8 km Chakbeli Road Rawat Rawalpindi
	Name, address of Manufacturing site.	M/s Biogen Life Sciences 8 km Chakbeli Road Rawat Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 17-01-2022 is provided.
	Evidence of approval of manufacturing facility	copy of Valid DML No. 000911 (Formulation) valid till 13-02-2025 is provided along with covering letter is provided.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28776 Date: 11/10/2022
	Details of fee submitted	PKR 30000 dated: 14-07-2022 . SLIP No. 9829497909
	The proposed proprietary name / brand name	Cilagen 250mg Injection IV (Powder for injection/infusion)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Imipenem (as Monohydrate)---------250mg Cilastatin (as Sodium)---------250mg

	Pharmaceutical form of applied drug	Powder for solution for injection/infusion
	Pharmacotherapeutic Group of (API)	Anti-Biotics (Anti Bacterial)
	Reference to Finished product specifications	USP Specs
	Proposed Pack size	As per SRO **Innovator Product (MHRA) :** Pack sizes: 1 x 250 mg vial 10 x 250 mg vial Not all pack sizes may be marketed.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	**MHRA Approved**
	For generic drugs (me-too status)	**Brand Name:** Cilapen 250mg Injection **Registration holder:** Bosh pharmaceuticals **Registration Number:** 048490
	Name and address of API manufacturer.	Sun Pharmaceutical Industries Limited, Industrial Area - 3 A.B. Road 455001 Madhya Pradesh , India GMP Certificate No. V/WHOGMP/Rev/Sun-17/2019
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^oC \pm 2^oC$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been not been established/submitted.
	Analytical method validation/verification of product	Not Submitted.

STABILITY STUDY DATA			
Manufacturer of API	Sun Pharmaceutical Industries Limited, Industrial Area -3 A.B. Road 455001 Madhya Pradesh , India GMP Certificate No. V/WHOGMP/Rev/Sun-17/2019 valid till 02-10-2022		
API Lot No.	Imipenem Monohydrate & Cilastatin Sodium: API Lot No is AB06493		
Description of Pack (Container closure system)	As per SRO		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	700 vials	700 vials	700 vials
Manufacturing Date	11-2021	11-2021	11-2021
Date of Initiation	04-12-2021	04-12-2021	04-12-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	• Not Submitted. • Firm has stated that Biogen is a new license facility and no such data is submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Sun Pharmaceutical Industries Limited, Industrial Area -3 A.B. Road 455001 Madhya Pradesh , India DML No. 24/24/83 in form no. 25 & 28/15/83 in form no.28
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**The invoice of relevant batch** AB06493 **used in Product Development is not provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not Submitted.**
6.	Record of Digital data logger for temperature and humidity monitoring of	**Not Submitted.**

	stability chambers (real time and accelerated)	

Evaluation by PEC:

1. Provide the analytical method with complete detail as the submitted documents contain ,issing/cutting along with test reports of API as performed by the Drug Substance manufacturer.
2. Provide the analytical method with complete detail along with test reports of API as performed by the Drug Product manufacturer.
3. The Manufacturing Protocol/Procedure for manufacture/Product Development are not submitted.
4. Batch detail along with BMR is not provided for manufacturing of Drug Product.
5. Documents for the procurement of API with approval from DRAP **of relevant batch** AB06493 **used in Product Development is not provided.**
6. Compliance Record of HPLC software 21CFR & audit trail reports on product testing is not Provided.
7. Submit microbial reports for the sterility testing of drug product during stability studies.
8. Pharmaceutical Equivalence studies along with test reports are not submitted.
9. Provide supportive data i.e. attested respective documents like chromatograms specifying whether of standard or sample etc, Raw data sheets, COA, summary data sheets etc.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

61.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Biogen Life Sciences 8 km Chakbeli Road Rawat Rawalpindi
	Name, address of Manufacturing site.	M/s Biogen Life Sciences 8 km Chakbeli Road Rawat Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Copy of current GMP certificate dated 17-01-2022 is provided.
	Evidence of approval of manufacturing facility	copy of Valid DML No. 000911 (Formulation) valid till 13-02-2025 is provided along with covering letter is provided.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28777 Date: 11/10/2022
	Details of fee submitted	PKR 30000 dated: 14-07-2022 . SLIP No. 63961987615
	The proposed proprietary name / brand name	Cilagen 500mg Injection IV (Powder for injection/infusion)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Imipenem (as Monohydrate)---------500mg Cilastatin (as Sodium)---------500mg

	Pharmaceutical form of applied drug	Powder for solution for injection/infusion
	Pharmacotherapeutic Group of (API)	Anti-Biotics (Anti Bacterial)
	Reference to Finished product specifications	USP Specs
	Proposed Pack size	As per SRO **Innovator Product (MHRA) :** Pack sizes: 1 x 250 mg vial 10 x 250 mg vial Not all pack sizes may be marketed.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	**USFDA Approved** **(Primaxin Injection 500mg), Merck Inc USA.**
	For generic drugs (me-too status)	**Brand Name:** Cilapen 500mg Injection **Registration holder:** Bosh pharmaceuticals **Registration Number:** 048491
	Name and address of API manufacturer.	Sun Pharmaceutical Industries Limited, Industrial Area - 3 A.B. Road 455001 Madhya Pradesh , India GMP Certificate No. V/WHOGMP/Rev/Sun-17/2019
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{o}C \pm 2^{o}C$ / 75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{o}C \pm 2^{o}C$ / 65% ± 5% RH for 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.

	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been not been established/submitted.
	Analytical method validation/verification of product	Not Submitted.

STABILITY STUDY DATA			
Manufacturer of API	Sun Pharmaceutical Industries Limited, Industrial Area -3 A.B. Road 455001 Madhya Pradesh , India GMP Certificate No. V/WHOGMP/Rev/Sun-17/2019 valid till 02-10-2022		
API Lot No.	Imipenem Monohydrate & Cilastatin Sodium: API Lot No is AB06493		
Description of Pack (Container closure system)	**As per SRO**		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	004	005	006
Batch Size	700 vials	700 vials	700 vials
Manufacturing Date	11-2021	11-2021	11-2021
Date of Initiation	04-12-2021	04-12-2021	04-12-2021
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	• Not Submitted. • Firm has stated that Biogen is a new license facility and no such data is submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Sun Pharmaceutical Industries Limited, Industrial Area -3 A.B. Road 455001 Madhya Pradesh , India DML No. 24/24/83 in form no. 25 & 28/15/83 in form no.28
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**The invoice of relevant batch** AB06493 **used in Product Development is not provided.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not Submitted.**
6.	Record of Digital data logger for temperature and humidity monitoring of	**Not Submitted.**

	stability chambers (real time and accelerated)	

Evaluation by PEC:

1. Pack size of Drug Product is not submitted.
2. Provide the analytical method with complete detail as the submitted documents contain, missing/cutting along with test reports of API as performed by the Drug Substance manufacturer.
3. Provide the analytical method with complete detail along with test reports of API as performed by the Drug Product manufacturer.
4. The Manufacturing Protocol/Procedure for manufacture/Product Development are not submitted.
5. Batch detail along with BMR is not provided for manufacturing of Drug Product.
6. Stability data along with data sheets of three batches of API as performed by the API manufacturer needs to be submitted.
7. Documents for the procurement of API with approval from DRAP **of relevant batch** AB06493 **used in Product Development is not provided.**
8. Compliance Record of HPLC software 21CFR & audit trail reports on product testing is not Provided.
9. Submit microbial reports for the sterility testing of drug product along during stability studies.
10. Pharmaceutical Equivalence studies along with test reports of Drug Product with innovator Product are not submitted.
11. Provide supportive data i.e. attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
12. Detail of equipment/machinery needs to be submitted.
13. The chromatograms of HPLC submitted along with stability data sheets do not specify the analyte (whether standard , sample etc).

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

4. DEFFERED CASE:

62.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Pharmadic Laboratories (Pvt) Ltd, 16 KM, Multan Road, Lahore
	Name, address of Manufacturing site.	M/s Pharmadic Laboratories (Pvt) Ltd, 16 KM, Multan Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the drug product manufacturer	Firm has submitted copy of GMP certificate No. 93/2020-DRAP(AD-2003099-790) dated 09-06-2020
	Evidence of approval of manufacturing facility	Tablet General Section
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10710 dated 28-04-22
	Details of fee submitted	PKR30000 dated: 27.05.2022 bearing Deposit Slip No. 09713095356
	The proposed proprietary name / brand	Darvin Forte 75mg/650mg

	name	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tramadol HCL … 75mg Paracetamol ….. 650mg
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Opioid & Non-Opioid Analgesic
	Reference to Finished product specifications	**USP Specifications**
	Proposed Pack size	1x 10's (Alu-PVC Blisters)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	CLANDERON 75 mg / 650 mg , Aristo Pharma Iberia, Madrid Spain.
	For generic drugs (me-too status)	Tonoflex-P Forte (film coated) of M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi
	Name and address of API manufacturer.	**Paracetamol (USP/BP):** M/s Saakh Pharma (Pvt) Ltd, Karachi. **GMP Certificate No. 83/2020-DRAP(K) dated 23-06-2022** **Certificate No. ZJ20170049** **Tramadol HCL USP :** M/s S.L.R. Pharma (Pvt) Limited, Situated at Plot No. A-69, API Estate Settipalli Post, Tirupati, Chittor District, Andhra Pradesh, India. License Retention Certificate dated 05-12-2019.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module-III Drug Substance:	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time

		conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65% ± 5% RH for 24 months for both API's namely **Paracetamol & Tramadol HCL USP .**
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the Tonoflex-P Forte Tablet 75/650 mg by M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is Tonoflex-P Forte Tablet 75/650 mg by M/s Sami Pharmaceuticals (Pvt) Ltd, Karachi in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. **The F2 values are not found satisfactory.**
	Analytical method validation/verification of product	Firm has submitted report of validation studies of analytical method of drug substance. Firm has submitted report of verification of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	**Paracetamol (BP):** M/s Saakh Pharma (Pvt) Ltd, Karachi. **GMP Certificate No. 83/2020-DRAP(K) dated 23-06-2022** **Certificate No. ZJ20170049** **Tramadol HCL USP :** M/s S.L.R. Pharma (Pvt) Limited, Situated at Plot No. A-69, API Estate Settipalli Post, Tirupati, Chittor District, Andhra Pradesh, India. License Retention Certificate dated 05-12-2019.
API Lot No.	Paracetamol : ZPAR18-143 Tramadol HCL : TDH0480218
Description of Pack (Container closure system)	The proposed pack size of Darvin Forte Tablet is 1x10's in Alu—PVC Blister.
Stability Storage Condition	Real time : 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months Accelerated: 06 months

Frequency	Accelerated: 0, 3, 6(Months) Real Time: 0, 3, 6,9,12,18,24(Months)		
Batch No.	ACTD-TR001	ACTD-TR002	ACTD-TR003
Batch Size	1000 TABLETS	1000 TABLETS	1000 TABLETS
Manufacturing Date	10,2019	10,2019	10,2019
Date of Initiation	10-10-2019	10-10-2019	10-10-2019
No. of Batches	03		

DOCUMENTS / DATA TO BE PROVIDED ALONG WITH STABILITY STUDY DATA

1.	Reference of previous approval of applications with stability study data of the firm (if any)	• **Not Provided**
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Paracetamol (USP/BP):** M/s Saakh Pharma (Pvt) Ltd, Karachi. **GMP Certificate No. 83/2020-DRAP(K) dated 23-06-2022** **Certificate No. ZJ20170049** **Tramadol HCL USP :** M/s S.L.R. Pharma (Pvt) Limited, Situated at Plot No. A-69, API Estate Settipalli Post, Tirupati, Chittor District, Andhra Pradesh, India. License Retention Certificate dated 05-12-2019.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Paracetamol (BP):** Not Required **Tramadol HCL USP :** **Not Provided**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	**Not Provided.**

Evaluation by PEC:

1. Evidence of approval of applied formulation in reference regulatory authorities as defined by the registration Board shall be submitted. As the applied formulation in reference regulatory authorities is approved as "uncoated" tablets while the applicant has applied as film coated tablets

Decision: Since the applied product is approved as "uncoated tablet" in reference regulatory authorities while the applicant has applied for film coated tablet. Therefore, Registration Board decided to defer the case for evidence of approval of applied formulation in reference regulatory authorities/agencies a "film coated tablet" which were declared/approved by the Registration Board in its 275th meeting.

Reply of the firm :

1. Provide certificate of analysis of relevant batch(es) of Drug Substance(s) (Paracetamol & Tramadol HCL) used in product development (By both Drug Substance and Drug Product manufacturer.
2. The Pharmaceutical equivalence studies and comparative dissolution Profile studies are not conducted with the innovator Product.
3. Documents for the procurement of API with approval from DRAP (in case of import) of DS **Tramadol HCL USP :**
4. As per submitted data of comparative dissolution profile following points have been observed:
   - For Paracetamol:
     - Value of F2 factor is 46% in Buffer Acetate pH 4.5
     - Value of F2 factor is 38% in Phosphate Buffer pH 6.8
   - For Tramadol HCl:
     - value of F2 factor is 44% in 0.1N HCL
     - Value of F2 factor is 46% in Phosphate buffer pH 6.8

   Please justify scientifically.
5. Specificity testing in Analytical method validation has not been performed for the applied Product.
6. Analytical Method for related substances /impurities testing of DS Paracetamol (BP) the HPLC testing procedure/chromatographic conditions are different from the one as specified in BP.
7. DS manufacturer of Paracetamol has followed analytical method for testing(Assay) of API of BP while the Drug Product manufacturer has tested by USP Specs. (The analytical method by DS manufacturer is mentioned as BP but on COA of DS Assay is mentioned as USP)
8. The excipients being used are different from the ones used in Product Development of Innovator/Reference Product , therefore, provide compatibility studies protocol/method along with results.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

Item No. III: Agenda of Evaluator-XI (Dr. Farhadullah)

Case No. 01: Routine Cases for registration of Human Drugs on Form 5F (Local)

63.	Name, address of Applicant / Marketing Authorization Holder	M/s Shaigan Pharmaceuticals (Pvt.) Ltd., 14-Km Adyala Road, Post office Dahgal, Rawalpindi.
	Name, address of Manufacturing site.	M/s Shaigan Pharmaceuticals (Pvt.) Ltd., 14-Km Adyala Road, Post office Dahgal, Rawalpindi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33299 dated 09/12/2021
	Details of fee submitted	PKR 30,000/-: dated 26/11/2021 (Slip#6694987381)

	The proposed proprietary name / brand name	**Zedron oral solution**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Ondansetron…….. 4mg. (As Ondansetron Hydrochloride Dihydrate)
	Pharmaceutical form of applied drug	Oral solution
	Pharmacotherapeutic Group of (API)	Serotonin 5HT3 antagonist. (Anti-emetic)
	Reference to Finished product specifications	USP Specifications.
	Proposed Pack size	25ml & 50ml
	Proposed unit price	As per S.R.O
	The status in reference regulatory authorities	ZOFRAN (4mg/5ml) oral solution USFDA Approved
	For generic drugs (me-too status)	Onseron syrup by M/s Indus Pharma (Reg#058677)
	GMP status of the Finished product manufacturer	GMP certificate issued to the firm on 28-08-2020 based on inspection conducted on 25-09-2019.
	Name and address of API manufacturer.	CTX Lifesciences Pvt. Ltd., Block No: 251-252, Sachin- Magdalla Road GIDC, Sachin, Surat – 394 230 GUJARAT, INDIA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, analytical procedures verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. ***The real time stability data is conducted at 25°C ± 2°C / 60 ± 5% RH for 60 months.*** Batches; ON130001, ON130002, ON130003
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of

		analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Onseron 4mg/5ml syrup by M/s Indus Pharma (Pvt.) Ltd by performing quality tests (description, Identification, pH, Assay).
	Analytical method validation/verification of product	Firm have submitted Method verification studies including accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	CTX Lifesciences Pvt. Ltd., Block No: 251-252, Sachin- Magdalla Road GIDC, Sachin, Surat – 394 230 GUJARAT, INDIA		
API Lot No.	20ON00040		
Description of Pack (Container closure system)	Amber color Plastic Bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-0003
Batch Size	500 bottles	500 bottles	500 bottles
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	19-03-2021	22-03-2021	22-03-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of their product by the panel on the basis of which Registration Board in 297th meeting dated 12-15th January 2021 decided to approve registration of Emdagan 10mg & 25mg Tablets. Inspection date: 06-01-2021 The report shows that: • The HPLC software is 21CFR Compliant as per record of the firm. Audit trail was active Labsolutions version 6.86 SP 2 software of HPLC system used in the method validation and stability study. Individual user log in and IDs were available. • Audit trail reports were available and checked randomly. • Continuous power supply and monitoring are available for stability chambers supported by backup generators and robust alarm system.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm have submitted copy of GMP certificate #19061470 dated 02/07/2019 of M/s CTX Lifesciences Pvt. Ltd., Block No: 251/P, 252/P, 253 to 255, 256/P, 258/P, 276/P, 277, 278/P, 279 to 282, 283/P, 284/P,

		GIDC, City Sachin, District Surat GUJARAT STATE, INDIA issued by Food & Drugs Control Administration Gandhinagar, Gujrat India valid upto 01/07/2022. Firm has also submitted retention of Licence No; G/25/1723 in the name of M/s CTX Lifesciences Pvt. Ltd., Block No: 251/P, 252/P, 253 to 255, 256/P, 258/P, 276/P, 277, 278/P, 279 to 282, 283/P, 284/P, GIDC, City Sachin, District Surat GUJARAT STATE, INDIA that has been retained from 24/01/2021 to 2026
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted commercial invoice No. EI/30002100553 dated 12/12/2020 in the name of M/s Shaigan Pharmaceutical (Pvt.) Ltd. for import of 25Kg Ondansetron HCL (Batch No 20ON00040) from CTX Lifesciences Pvt. Ltd. India attested by AD (I&E) DRAP Islamabad on 29/12/2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, summary data sheets is submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.4	• Submit valid DML as the submitted DML expires on 06-01-2021	The firm has submitted valid DML
1.3.5	• Latest GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	The firm has submitted valid GMP inspection report issued on 28th December 2021 based on inspection conducted on 04-11-2021
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance manufacturer and Drug Product manufacturer is required.	Firm has submitted Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance manufacturer and Drug Product manufacturer.
3.2.S.7	• Submit readable copy of stability study of drug substance	The firm has submitted readable copy of stability study of drug substance. ***However stability study is not performed at per zone IV-A conditions***
3.2.P.2	• Justification is required since pharmaceutical equivalence have not been conducted against the innovator product.	Firm has submitted that pharmaceutical equivalence has been established on the basis of qualitative composition of Zofran oral solution (Innovator Product). Qualitative formulation of Zedron oral

		solution (test product) is in accordance with innovator product. As this product exists in USP pharmacopeia so both test and comparator product were tested as per parameters of innovator product for following tests according to monograph of Ondansetron Oral solution USP 43. Description, Identification, pH, Related compounds, Assay, Microbial enumeration test and test for specified microorganism. It is concluded that formulation and physicochemical test of product under test (Zedron Oral solution) is in accordance with formulation of Zofran oral solution (Innovator) and all tests are within limits as described by USP, so test product (Zedron Oral solution) is in pharmaceutical equivalence with innovator product Zofran oral solution (Innovator)
3.2.P.6	• COA of primary / secondary reference standard including source and lot number shall be provided.	Firm has submitted COA of working standard including source and lot number
3.2.P.8	• COA of all batches during the stability study at both real time and accelerated conditions at 3rd month and 6th month time point is not submitted	Firm has submitted COA of all batches during the stability study at both real time and accelerated conditions at 3rd month and 6th month time point.

Decision: Approved.

- **Firm will submit stability studies data of the drug substance as per the conditions of zone IV-A or otherwise provide degradation studies of the finished product for 6 months as per the decision of Registration Board before issuance of Registration letter**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

64.	Name, address of Applicant / Marketing Authorization Holder	M/s Caliph Pharmaceuticals (Pvt) Ltd. Plot No 17, Special Industrial Zone (EPZ), Risalpur
	Name, address of Manufacturing site.	M/s Caliph Pharmaceuticals (Pvt) Ltd. Plot No 17, Special Industrial Zone (EPZ), Risalpur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27283 dated 01/10/2021

	Details of fee submitted	PKR 30,000/-: dated 08/09/2021 (Slip#27580475902)
	The proposed proprietary name / brand name	CALSETRON 8mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ondansetron (as hydrochloride dihydrate)……8mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Serotonin (5HT3) antagonist
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zofran 8mg film coated tablet MHRA approved
	For generic drugs (me-too status)	Zofran 8mg Tablet by M/s Novartis Pharma Karachi (Pakistan) (Reg#084164)
	GMP status of the Finished product manufacturer	GMP certificate issued to the firm on 02-03-2021 based on inspection conducted on 02-03-2021.
	Name and address of API manufacturer.	M/s Anugraha Chemicals, No D-47, D-48, D-49, D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru, Dist: Bengaluru Rural-561203 India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, tests for impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (AOND-10003, AOND-10004, AOND-10005)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Zofran 8mg Tablet by Novartis Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Zofran 8mg Tablet by Novartis Pharma in 0.1 N HCl, 4.5 pH acetate buffer and 6.8pH phosphate buffer. Both the test and reference product show more than 85% release in 15 minutes.
	Analytical method validation/verification of product	Firm have submitted Method verification studies including accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Anugraha Chemicals, No D-47, D-48, D-49, D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru, Dist: Bengaluru Rural-561203 India		
API Lot No.	AOND-19010		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	07-01-2020	07-01-2020	07-01-2020
Date of Initiation	08-01-2020	08-01-2020	08-01-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of their product by the panel on the basis of which Registration Board in 308th meeting dated 21-22nd June 2021 decided to approve registration of Dexcal (Dexlansoprazole) 30mg & 60mg capsule. Inspection date: 01st June, 2021 (Morning) The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • The firm showed the audit trail reports on API and product testing • Continuous power supply and monitoring are available for stability chambers

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate #DCD/SPL.CL-1/CR-1510/2020-21 dated 06-02-2021 of M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru Rural District-561203 India issued by Drugs Control Department Government of Karnataka valid upto one year from the date of issue.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted commercial invoice No#ZHI-CI/3966/1119 dated 07/11/2019 in the name of M/s Caliph Pharmaceuticals Pvt. Ltd. for import of 1.00Kg Ondansetron HCL (Batch No AOND-19010) from Zeon-Health Industries India attested by AD (I&E) DRAP Peshawar on 20/11/2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, summary data sheets is submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.4	• Submit valid DML as the submitted DML expires on 12-08-2022	Firm has submitted copy of receiving letter applied for renewal of DML No. 000748 dated 10-08-2022
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer issued by relevant regulatory authority of country of origin is required	The firm has submitted copy of GMP certificate #DCD/SPL-1/CR-1733/2021-22 dated 31-01-2022 of M/s Anugraha Chemicals, No D-47 to D-50, and C-62, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru Rural District-561203 India issued by Drugs Control Department Government of Karnataka valid upto one year from the date of issue.
3.2.S.6	• Details of container closure system for ciprofloxacin HCl is provided instead of Ondansetron HCl	Details of container closure system for Ondansetron HCl is submitted
3.2.P.3	• Protocols for process validation is not submitted	Firm has submitted protocols for process validation
3.2.P.5	• Submit summary of analytical method verification studies for drug product	Report of analytical method verification studies of drug product is submitted
3.2.P.8	• Justification is required since you have mentioned Uniformity of dosage units (content uniformity test) as per USP monograph in batch analysis and drug product specifications, while you have performed weight variation test in stability study of all three batches at	• The firm submitted that we have included content uniformity test as per USP monograph in the drug product specification and also at batch release. However, during stability studies, we have not performed content uniformity test since it was not part of our stability

	both accelerated and real time conditions. • COA of all batches during the stability study at both real time and accelerated conditions at 3rd month and 6th month time point is not submitted • Submit UV spectra / absorbance of samples analysed in dissolution study. Furthermore, justify single absorbance value of sample and standard solution in dissolution studies. • Drug substance manufacturer as per section 3.2.S.2 is M/s Anugraha chemicals India while Drug substance is imported from M/s Zeon Health industries India as per submitted invoice, clarification is required • Compliance Record of HPLC software 21CFR & audit trail reports on product testing is required	specifications, instead we have performed weight variation test during stability studies as per our stability specifications. • The firm stated that we have submitted raw data sheets in the form of analytical report to provide results of assay and dissolution test along with calculations as per the guidelines of Registration Board. Analytical reports at each time point for all batches is again submitted. • The firm stated that our UV system display the absorbance results on its display screen and does not have the provision of printing the results. We note the results in form of absorbance values in QC registers and maintain all the records along with logs. • The firm stated that the UV absorbance values submitted in the analytical reports were average values. Now we are submitting the UV absorbance values for each analysis as well. • The firm submitted that M/s Zeon Health Industries India is supplier while the manufacturer of the API is M/s Anugraha Chemicals which is evident from the COA as well as Clearance certificate. The COA and clearance certificate is submitted. • The firm submitted that the stability studies for the instant product has been performed on HPLC system which is not 21 CFR compliant, hence audit trail reports are also not available.

Decision: Approved.

- **Registration Board directed the firm to include test of content uniformity as per USP monograph in drug product specifications for the commercial batches.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case No. 02; New application for registration of drugs with stability study data on Form 5-D on export facilitation

Assistant director PR-I/EFD vide letter No.F.1-6/2019-PR-I (EFD dated 06-10-2022 has informed that DRAP Authority in its 133rd meeting held on 13th April 2022, decided to grant registration on priority basis to the *pharmaceutical* i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year. In compliance to the aforementioned decision of the authority, the following firm have achieved the benchmark of more than **100,000 USD** during the **fiscal Year 2020-2021** and submitted their applications for priority consideration in lieu of export facilitation for Registration Board please.,

65.	Name and address of manufacturer / Applicant	M/s PharmEvo (Private) Limited., A-29, North Western Industrial Zone, Port Qasim Karachi
	Brand Name +Dosage Form + Strength	Empalin 10+5mg Tablet
	Composition	Each Tablet Contains: Empagliflozin…..……..10mg Linagliptin……..5mg
	Diary No. Date of R& I & fee	Dy. No. 778 dated 02-11-2015, Rs: 50,000/- dated 02-11-2015 ***Duplicate Dossier R&I verified***
	Pharmacological Group	Type 2 Diabetes mellitus
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	30's; As per SRO
	Approval status of product in Reference Regulator Authorities	GLYXAMBI® (empagliflozin;linagliptin) (10mg;5mg, 25mg;5mg) film coated tablets USFDA Approved
	Me-too status	NA
	GMP status	Not submitted
	Remarks of the Evaluator	

STABILITY STUDY DATA

Manufacturer of API	M/s Jiangsu Yungan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China		
API Lot No.	**Empagliflozin**: 4500-202006001 **Linagliptin:** 7700202005001		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Real Time: 0, 3, 6 (month) Accelerated: 0, 3, 6 (month)		
Batch No.	20PD-3443-01-T	20PD-3444-02-T	20PD-3445-03-T
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	19-12-2020	19-12-2020	19-12-2020
No. of Batches	03		
Date of Submission	09-11-2021 (30633)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of

		which Registration Board in 293rd meeting dated 6th-8th January, 2020 decided to approve registration of Erli Plus SR Tablets 5/1000mg, Erli Plus SR Tablets 10/1000mg, Erli Plus SR Tablets 12.5/1000mg, Erli Plus SR Tablets 25/1000mg. Inspection date: 05th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports are available. • The firm has 16 stability chambers, 02 for accelerated and 14 for real time stability testing. All chambers are properly qualified. All chambers are provided with continuous power supply and data loggers for continuous monitoring.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin**: Copy of COA (Batch#4500-202006001) of Empagliflozin from M/s Jiangsu Yungan Pharmaceutical CO., Ltd China and M/s PharmEvo (Private) Limited is submitted. **Linagliptin:** Copy of COA (Batch#7700202005001) of Linagliptin from M/s Jiangsu Yungan Pharmaceutical CO., Ltd China and M/s PharmEvo (Private) Limited is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer is provided by the firm.
4.	Stability study data of API from API manufacturer	**Linagliptin:** Firm has submitted stability study data of Empagliflozin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (20180201,20180202, 20180301) **Empagliflozin:** Firm has submitted stability study data of Empagliflozin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; *40°C ± 2°C / 75% ± 5%RH for 12 months* Batches: (130701, 130702, 130801)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate in the name of M/s Jiangsu Yungan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by***

<table>
<tr><td></td><td></td><td>Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu valid upto 14-01-2024.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Empagliflozin:
Firm has submitted copy of invoice No. ZY20072302G/W dated 23-07-2020 for import of 15kg of Empagliflozin (Batch#4500-202006001) in name of M/s PharmEvo (Private) Limited attested by AD (I&E) DRAP Karachi dated 30-07-2020.
Linagliptin:
Firm has also submitted copy of invoice No. ZY20060101G/W dated 01-07-2020 for import of 0.5kg of Linagliptin in name of M/s PharmEvo (Private) Limited attested by AD (I&E) DRAP Karachi dated 10-06-2020.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Submitted</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>The firm submitted that they used the same excipient as that of innovator</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted Batch Manufacturing record of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>20PD-3443-01-T</td><td>2500 tablets</td><td>11-2020</td></tr>
<tr><td>20PD-3444-02-T</td><td>2500 tablets</td><td>11-2020</td></tr>
<tr><td>20PD-3445-03-T</td><td>2500 tablets</td><td>11-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Comparative dissolution data of applied product was performed against innovator brand Glyxambi 10+5mg tablet by M/s Boehringer Ingelheim Pharmaceuticals, Inc. in dissolution medium pH 1.2, pH 4.5 and pH 6.8 buffer. The results of both product show more than 85% drug release of both the API within 15minutes in all three media hence F2 factor was not calculated</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of</td><td>Submitted</td></tr>
</table>

	stability chambers (real time and accelerated)	

REMARKS OF EVALUATOR [XI]

Deficiency/Observation	Response by Firm
• The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee	• The firm submitted that the product has been developed in accordance with innovator product as film coated tablets. The firm has revised label claim in form 5D along with submission of Rs 7500/- on deposit slip No. 847973002788. The revised label claim is as under: Each film coated Tablet Contains: Empagliflozin…..……..10mg Linagliptin……..5mg
• Submit GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	• The firm has submitted cGMP certificate issued on 22nd August 2022 based on inspection conducted on 23rd June 2022.
• Submit valid GMP certificate of API manufacturer issued by the relevant regulatory authority of country of origin	• Firm has again submitted copy of GMP certificate in the name of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. • The firm has also submitted DML # (Su 20160324) of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China valid upto December 06, 2025.
• Clarification is required since Chromatographic conditions i.e. Mobile phase and wavelength used for assay of empagliflozin by finished product manufacturer (buffer;acetonitrile 40;60, wavelength 210nm) is different than API manufacturer (methanol;water 68;32, wavelength 224nm,)	• The firm submitted the testing method of finished product i.e. Empalin 10+5mg tablet has been developed in accordance with the ICH Q14 than the validation of method has been performed accordingly. It may be noted that the testing method of API manufacturer has not been adopted while developing the testing method of finished product, therefore there is difference in wavelength of API and FP testing method.
• Clarification is required since Chromatographic conditions i.e. Mobile phase and column oven temperature used for assay of linagliptin by finished product manufacturer (acetonitrile:water 60;40, Temp 25ºC) is different than API manufacturer (Mobile phase-A Buffer:Methano 90;10 Mobile phase-B Acetonitril:water:methanol 700:150:150, Temp 45ºC). Furthermore, API manufacturer have used	• The firm submitted the testing method of finished product i.e. Empalin 10+5mg tablet has been developed in accordance with the ICH Q14 than the validation of method has been performed accordingly. It may be noted that the testing method of API manufacturer has not been adopted while developing the testing method of finished product, therefore there is difference in wavelength of API and FP testing method.

gradient elution while you have used isocratic method for analysis	
• Clarification is required since you have mentioned the use of 500ml of dissolution media in analytical method for analysis of finished product instead of 900ml as mentioned by innovator product review document/ USFDA drug database	• The firm submitted that in accordance with the clinical pharmacology and biopharmaceutics review, application number 206073Orig1s000, center for drug evaluation and research the recommended dissolution medium is 500ml, as under; 1. Dissolution method; Apparatus 2, ***100 rpm agitation rate, 500ml media*** volume, 37ºC, 50Mm potassium phosphate buffer, pH 6.8 2. Dissolution acceptance criteria; at 30 min • It is to mention that 500ml dissolution media is mentioned with 100rpm while firm has mentioned 50rpm and USFDA drug dissolution database recommends the use of ***900ml dissolution media with 50 rpm***

Decision: Approved with innovator's specifications with following label claim:
Each film coated tablet Contains:
Empagliflozin…..……..10mg
Linagliptin……..5mg

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided to verify fee challan as per decision of 285th meeting of Registration Board.**

66.	Name and address of manufacturer / Applicant	M/s PharmEvo (Private) Limited., A-29, North Western Industrial Zone, Port Qasim Karachi
	Brand Name +Dosage Form + Strength	Empalin 25+5mg Tablet
	Composition	Each Tablet Contains: Empagliflozin…..……..25mg Linagliptin……..5mg
	Diary No. Date of R& I & fee	Dy. No. 779 dated 02-11-2015, Rs: 50,000/- dated 02-11-2015 ***Duplicate Dossier R&I verified***
	Pharmacological Group	Type 2 Diabetes mellitus
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	30's; As per SRO
	Approval status of product in Reference Regulator Authorities	GLYXAMBI® (empagliflozin;linagliptin) (10mg;5mg, 25mg;5mg) film coated tablets USFDA Approved
	Me-too status	NA
	GMP status	Not submitted

	Remarks of the Evaluator	

STABILITY STUDY DATA			
Manufacturer of API	M/s Jiangsu Yungan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China		
API Lot No.	**Empagliflozin**: 4500-201909001 **Linagliptin:** 7700202005001		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Real Time: 0, 3, 6 (month) Accelerated: 0, 3, 6 (month)		
Batch No.	20PD-3396-02-T	20PD-3397-03-T	20PD-3398-04-T
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	11-2020	11-2020	11-2020
Date of Initiation	02-12-2020	02-12-2020	02-12-2020
No. of Batches	03		
Date of Submission	09-11-2021 (30634)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr. No.	**Documents to Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 293rd meeting dated 6th-8th January, 2020 decided to approve registration of Erli Plus SR Tablets 5/1000mg, Erli Plus SR Tablets 10/1000mg, Erli Plus SR Tablets 12.5/1000mg, Erli Plus SR Tablets 25/1000mg. Inspection date: 05th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports are available. • The firm has 16 stability chambers, 02 for accelerated and 14 for real time stability testing. All chambers are properly qualified. All chambers are provided with continuous power supply and data loggers for continuous monitoring.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin**: Copy of COA (Batch#4500-201909001) of Empagliflozin from M/s Jiangsu Yungan

		Pharmaceutical CO., Ltd China and M/s PharmEvo (Private) Limited is submitted. **Linagliptin:** Copy of COA (Batch#7700202005001) of Linagliptin from M/s Jiangsu Yungan Pharmaceutical CO., Ltd China and M/s PharmEvo (Private) Limited is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer is provided by the firm.
4.	Stability study data of API from API manufacturer	**Linagliptin:** Firm has submitted stability study data of Empagliflozin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (20180201,20180202, 20180301) **Empagliflozin:** Firm has submitted stability study data of Empagliflozin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; *40°C ± 2°C / 75% ± 5%RH for 12 months* Batches: (130701, 130702, 130801)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate in the name of M/s Jiangsu Yungan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin**: Firm has submitted copy of invoice No. ZY19101801G/W dated 18-10-2019 for import of 15kg of Empagliflozin in name of M/s PharmEvo (Private) Limited attested by AD (I&E) DRAP Karachi dated 22-10-2019. **Linagliptin:** Firm has submitted copy of invoice No. ZY20060101G/W dated 01-07-2020 for import of 0.5kg of Linagliptin in name of M/s PharmEvo (Private) Limited attested by AD (I&E) DRAP Karachi dated 10-06-2020.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted

9.	Drug-excipients compatibility studies (where applicable)	The firm submitted Formulation of applied drug product is qualitatively similar to that of innovator product Glyxambi 25mg/5mg tablet.
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted Batch Manufacturing record of following 03 Batches: **Batch No.** / **Batch Size** / **Mfg. Date** 20PD-3396-02-T / 2500 tablets / 11-2020 20PD-3397-03-T / 2500 tablets / 11-2020 20PD-3398-04-T / 2500 tablets / 11-2020
11.	Record of comparative dissolution data (where applicable)	Comparative dissolution data of applied product was performed against innovator brand Glyxambi 25+5mg tablet by M/s Boehringer Ingelheim Pharmaceuticals, Inc. in dissolution medium pH 1.2, pH 4.5 and pH 6.8 buffer. The results of both product show more than 85% drug release of both the API within 15minutes in all three media hence F2 factor was not calculated
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

REMARKS OF EVALUATOR [XI]

Deficiency/Observation	**Response by Firm**
• The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee	• The firm submitted that the product has been developed in accordance with innovator product as film coated tablets. The firm has revised label claim in form 5D along with submission of Rs 7500/- on deposit slip No. 18865905426. The revised label claim is as under: Each film coated Tablet Contains: Empagliflozin…..……..25mg Linagliptin……..5mg
• Submit GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	• The firm has submitted cGMP certificate issued on 22nd August 2022 based on inspection conducted on 23rd June 2022.
• Submit valid GMP certificate of API manufacturer issued by the relevant regulatory authority of country of origin	• Firm has again submitted copy of GMP certificate in the name of M/s Jiangsu Yungan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic

	Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. • The firm has also submitted DML # (Su 20160324) of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China valid upto December 06, 2025.
• Clarification is required since Chromatographic conditions i.e. Mobile phase and wavelength used for assay of empagliflozin by finished product manufacturer (buffer;acetonitrile 40;60, wavelength 210nm) is different than API manufacturer (methanol;water 68;32, wavelength 224nm,)	• The firm submitted the testing method of finished product i.e. Empalin 25+5mg tablet has been developed in accordance with the ICH Q14 than the validation of method has been performed accordingly. It may be noted that the testing method of API manufacturer has not been adopted while developing the testing method of finished product, therefore there is difference in wavelength of API and FP testing method.
• Clarification is required since Chromatographic conditions i.e. Mobile phase and column oven temperature used for assay of linagliptin by finished product manufacturer (acetonitrile:water 60;40, Temp 25ºC) is different than API manufacturer (Mobile phase-A Buffer:Methano 90;10 Mobile phase-B Acetonitril:water:methanol 700:150:150, Temp 45ºC). Furthermore, API manufacturer have used gradient elution while you have used isocratic method for analysis	• The firm submitted the testing method of finished product i.e. Empalin 10+5mg tablet has been developed in accordance with the ICH Q14 than the validation of method has been performed accordingly. It may be noted that the testing method of API manufacturer has not been adopted while developing the testing method of finished product, therefore there is difference in wavelength of API and FP testing method.
• Clarification is required since you have mentioned the use of 500ml of dissolution media in analytical method for analysis of finished product instead of 900ml as mentioned by innovator product review document/ USFDA drug database	• The firm submitted that in accordance with the clinical pharmacology and biopharmaceutics review, application number 206073Orig1s000, Center for Drug Evaluation and Research the recommended dissolution medium is 500ml, as under; 3. Dissolution method; Apparatus 2, ***100 rpm agitation rate, 500ml media*** volume, 37ºC, 50Mm potassium phosphate buffer, pH 6.8 4. Dissolution acceptance criteria; at 30 min • It is to mention that 500ml dissolution media is mentioned with 100rpm while firm has mentioned 50rpm and USFDA drug dissolution database recommends the use of ***900ml dissolution media with 50 rpm***

Decision: Approved with innovator's specifications and following label claim:
Each film coated Tablet contains:
Empagliflozin…..……..25mg
Linagliptin……..5mg

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided to verify fee challan as per decision of 285th meeting of Registration Board.**

67.	Name and address of manufacturer / Applicant	M/s Tabros Pharma (Pvt) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Klic-Quick Sachet 50mg/Sachet
	Composition	Each Sachet Contains: Diclofenac Potassium…..…….50mg
	Diary No. Date of R& I & fee	Dy. No. 582 dated 17-04-2015, Rs: 20,000/- dated 17-04-2015, Balance Fee Rs. 30,000/- dated 11-07-2017 ***Duplicate Dossier R&I verified***
	Pharmacological Group	NSAID
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulator Authorities	CAMBIA 50mg for oral solution USFDA Approved
	Me-too status	Diclovis-K 50mg Sachet by M/s Vision Pharmaceuticals (Reg#109783)
	GMP status	The firm was inspected on 25-03-2018 and conclusion of inspection was:
	Remarks of the Evaluator	

STABILITY STUDY DATA

Manufacturer of API	M/s Henan Dongtai Pharmacetical CO., Ltd., East Changhong Road, Tangyin County, Anyang City, China		
API Lot No.	303200720-5		
Description of Pack (Container closure system)	White to off white granular powder., packed in Aluminium paper foil laminated sachet		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Real Time: 0, 3, 6 (month) Accelerated: 0, 3, 6 (month)		
Batch No.	TR001-1/KIQ	TR002-1/KIQ	TR003-1/KIQ
Batch Size	1000 sachet	1000 sachet	1000 sachet
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	23-08-2021	23-08-2021	23-08-2021
No. of Batches	03		

Date of Submission	17-12-2021 (33099)	
DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr. No.	**Documents to Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm	Not provided
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Copy of COA (Batch#303200720-5) of Diclofenac potassium from M/s Henan Dongtai Pharm CO., Ltd China and M/s Tabros Pharma (Pvt) Ltd is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer is provided by the firm.
4.	Stability study data of API from API manufacturer	Firm has submitted stability study data of Diclofenac potassium as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 48 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (131118-5, 131118-6, 131119-5,)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. HA20170001 in the name of M/s Henan Dongtai Pharmacetical CO., Ltd., East Changhong Road, Tangyin County, Anyang City, China issued by Henan Province Food and Drug Administration valid upto 22-01-2022.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 6 for import of 350gm of Diclofenac Potassium from M/s Henan Dongtai Pharm Co., Ltd, China attested by AD (I&E) DRAP Karachi dated 07-06-2021. Firm has also submitted copy of invoice No. DT210505F dated 25-05-2021 for import of 350gm of Diclofenac Potassium in name of M/s Tabros Pharma (Pvt) Ltd., Karachi attested by AD (I&E) DRAP Karachi dated 07-06-2021.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted
9.	Drug-excipients compatibility studies (where applicable)	NA (Firm submitted that as same excipients used as used by the innovator so compatibility studies with excipient are not required).

10.	Complete batch manufacturing record of three stability batches.	The firm has submitted Batch Manufacturing record of following 03 Batches: **Batch No.** / **Batch Size** / **Mfg. Date** TR001-1/KIQ / 1000 sachet / 08-2021 TR002-1/KIQ / 1000 sachet / 08-2021 TR003-1/KIQ / 1000 sachet / 08-2021
11.	Record of comparative dissolution data (where applicable)	Comparative dissolution data of applied product was performed against Voltfast 50mg sachet by M/s Novartis Pharma in dissolution medium 0.1N HCl pH 1.2, Acetate Buffer pH 4.5, Phosphate Buffer pH 6.8 and Phosphate Buffer in 0.1N HCl pH 6.8 (QC Medium). The values of F2 factor was in acceptable range in all media
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

REMARKS OF EVALUATOR [XI]

Deficiency/Observation	**Response by Firm**
You have applied for manufacturer specification while the monograph for applied product is available in USP.	The firm submitted that Since the product was applied on "FORM 5D" at that time we have been searching this product in compendia monograph with the name Diclofenac potassium SACHET, the same name could not be found, Hence, mentioned manufacturer specification. After, we purchased the Innovator pack to perform the CDP, in innovator pack it is visibly mentioned that the product is POWDER FOR ORAL SOLUTION hence we have followed USP specification & performed analysis of stability samples as per USP monograph.
• Submit GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	• The firm has submitted cGMP certificate issued on 15th April 2022 based on inspection conducted on 07th April 2022
• Submit valid GMP certificate of API manufacturer issued by the relevant regulatory authority of country of origin	• Firm has submitted cGMP certificate No#HA20190077 of M/s Henan Dongtai Pharmaceutical Co., Ltd., No. 2, East Kangtai Road, Tangyin ounty, Anyang City China. Valid issued by Henan Province Drug Administration valid upto 05-11-2024

	• ***The firm further submitted undertaking from API manufacturer stating that our site address changed from East Changhong Road, Tangyin County, Anyang City, China to No. 2, East Kangtai Road, Tangyin, Anyang, Henan China***.
• Clarification is required since Chromatographic conditions i.e. Mobile phase composition, column oven temperature, column length, diluent composition and injection volume used for assay of diclofenac potassium sachet by finished product manufacturer (methanol; solution A (70;30), Temp Ambient, column length 250mm, injection volume 30ul) is different than that recommended by USP. (Acetonitrile and Solution A (40:60), Temp 40ºC, column length 150mm, injection volume 20ul)	• The firm submitted that for the determination of Assay and Impurities SIM method was developed • We acquired the USP diclofenac potassium method of drug substance under the heading of organic impurities, Mobile phase composition, column oven temperature, column length, diluent composition and injection volume are all followed same as USP organic impurities method along with chromatographic conditions.

INDICATIONS AND USAGE

CAMBIA is indicated for the acute treatment of migraine attacks with or without aura in adults (18 years of age or older).

Limitations of Use

- CAMBIA is not indicated for the prophylactic therapy of migraine.
- The safety and effectiveness of CAMBIA have not been established for cluster headache, which is present in an older, predominantly male population.

DOSAGE AND ADMINISTRATION

Acute Treatment of Migraine

Administer one packet (50 mg) of CAMBIA for the acute treatment of migraine. Empty the contents of one packet into a cup containing 1 to 2 ounces or 2 to 4 tablespoons (30 to 60 mL) of water, mix well and drink immediately.

Do not use liquids other than water.

Taking CAMBIA with food may cause a reduction in effectiveness compared to taking CAMBIA on an empty stomach. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

The safety and effectiveness of a second dose have not been established.

Decision: Approved with USP specifications.

- **Registration Board directed the firm to perform analysis of finished product as per USP monograph on next time point of long term stability study and submit data before issuance of registration letter**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021**
- **Registration Board further decided to verify fee challan as per decision of 285th meeting of Registration Board.**

68.	Name and address of manufacturer / Applicant	M/s Macter International Limited F-216, S.I.T.E Karachi
	Brand Name +Dosage Form + Strength	Empozin-L 10mg+5mg Tablet

	Composition	Each Film Coated Tablet Contains: Empagliflozin…..……..10mg Linagliptin……..5mg
	Diary No. Date of R& I & fee	Dy. No. 14722 dated 07-03-2019, Rs: 50,000/- dated 06-03-2019
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	14's, 28's; As per SRO
	Approval status of product in Reference Regulator Authorities	GLYXAMBI® (empagliflozin;linagliptin) (10mg;5mg, 25mg;5mg) film coated tablets USFDA Approved
	Me-too status	NA
	GMP status	The firm was inspected on 25-03-2018 and conclusion of inspection was: The firm is found to be complying at a good level of GMP compliance at the time of inspection. Continuous improvements for procedures shall be followed in letter and spirit as per the Drug Act 1976, DRAP Act 2012 and rules framed there under.
	Remarks of the Evaluator	

STABILITY STUDY DATA			
Manufacturer of API	M/s Fuxin Long Rui Pharmaceutical CO., Ltd., Fluoride Industrial Park, Fuxin City, Liaoning Province-123000, China		
API Lot No.	**Empagliflozin**: E-20190920-D02-E06-01 **Linagliptin:** L-20190305-D01-L09-08		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 9 months Accelerated: 6 months		
Frequency	Real Time: 0, 1, 3, 6, 9 (month) Accelerated: 0, 1, 3, 6 (month)		
Batch No.	20SB-212-002	20SB-213-003	20SB-214-004
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	06-2020	06-2020	06-2020
No. of Batches	03		
Date of Submission	12-04-2021 (11125)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr. No.	**Documents to Be Provided**	**Status**

1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 296th meeting dated 8th, 9th & 10th September, 2020 decided to approve registration of Vireof-N 25mg Tablets. Inspection date: 18th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports on Tenofovir Alafenamide Fumarate API and Vireof-N tablets 25mg is available. • The firm has adequate monitoring and control system for stability chambers.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin**: Copy of COA (Batch#E-20190920-D02-E06-01) of Empagliflozin from M/s Fuxin Long Rui Pharmaceutical CO., Ltd China and M/s Macter International Ltd is submitted. **Linagliptin:** Copy of COA (Batch#L-20190305-D01-L09-08) of Linagliptin from M/s Fuxin Long Rui Pharmaceutical CO., Ltd China and M/s Macter International Ltd is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer is provided by the firm.
4.	Stability study data of API from API manufacturer	**Linagliptin:** Firm has submitted stability study data of Linagliptin. Stability study is conducted at Real time conditions***; 25°C ± 2°C / 60% ± 5%RH for 12 month***s and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (L-20170429-D01-L9-01, L-20170604-D01-L9-02, L-20170604-D01-L9-03) **Empagliflozin:** Firm has submitted stability study data of Empagliflozin. Stability study is conducted at Real time conditions***; 25°C ± 2°C / 60% ± 5%RH for 36 months*** and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20160606, 20161017, 20161219)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate in the name of M/s Fuxin Long Rui Pharmaceutical CO., Ltd., Fluoride Industrial Park, Fuxin City, Liaoning Province-123000, China ***issued by Liaoning Fuxin***

<table>
<tr><td></td><td></td><td>Management Committee for Fluoride Industrial Development Zone valid upto 23-08-2023.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Empagliflozin:
Firm has submitted copy of invoice No. HN19122501-H dated 25-12-2019 for import of 05kg of Empagliflozin (Batch No. E-20190920-D02-E06-01) in name of M/s Macter International Limited attested by AD (I&E) DRAP Karachi dated 31-12-2019.
Linagliptin:
Firm has submitted copy of Form 6 for import of 1.5kg of Linagliptin from M/s Fuxin Long Rui Pharmaceutical CO., Ltd China attested by AD (I&E) DRAP Karachi.
Firm has also submitted copy of invoice No. HN/200304-U dated 04-03-2020 for import of 1.5kg of Linagliptin (Batch No. L20190305-D01-L09-08) in name of M/s Macter International Limited attested by AD (I&E) DRAP Karachi dated 17-03-2020.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Submitted</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA
(Formulation of applied drug product is qualitatively similar to that of innovator product Glyxambi 10mg/5mg tablet).</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted Batch Manufacturing record of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>20SB-212-002</td><td>5000 tablets</td><td>06-2020</td></tr>
<tr><td>20SB-213-003</td><td>5000 tablets</td><td>06-2020</td></tr>
<tr><td>20SB-214-004</td><td>5000 tablets</td><td>06-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Not submitted</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Not Submitted</td></tr>
</table>

REMARKS OF EVALUATOR [XI]

Deficiency/Observation	Response by Firm
Submit valid GMP certificate of API manufacturer issued by the relevant regulatory authority of country of origin	• Firm has again submitted copy of GMP certificate in the name of M/s Fuxin Long Rui Pharmaceutical CO., Ltd., Fluoride Industrial Park, Fuxin City, Liaoning Province-123000, China ***issued by Liaoning Fuxin Management Committee for Fluoride Industrial Development Zone*** valid upto 23-08-2023. • Firm has submitted copy of DML (Certificate# Liao20150233) in the name of M/s Fuxin Long Rui Pharmaceutical CO., Ltd., issued by Liaoning Provincial Drug Administration, valid upto 20-12-2022.
Submit latest GMP inspection report conducted within last three years	Firm has submitted cGMP certificate issued on 05th August 2022 based on inspection conducted on 04th August 2022.
In COA of empagliflozin working standard is written. Clarification is required whether it is COA of API or working standard.	Firm has submitted separate COA of Empagliflozin API and working standard.
Submit stability study data of Linagliptin and Empagliflozin API as per zone IV-A.	• The firm submitted that HVAC system is installed to control the environment to keep raw material properly in store room (below 25ºC & 45%RH) and we have given finish good stability data at zone IV-A. • The firm has not submitted stability study data of Linagliptin and Empagliflozin API as per zone IV-A conditions.
CDP studies for the applied product is not submitted	• The firm submitted that due to similar formulation CDP performed on its higher strength which is Empozin-L 25mg+5mg tablet but we have also performed CDP for lower strength (Empozin-L 10mg+5mg tablet) against Glyxambi 10mg+5mg tablets in Potassium Phosphate buffer pH 6.8. • However, it is to submit that as per WHO guidelines CDP studies should be performed in at least three media covering the physiological range, including pH 1.2 hydrochloric acid, pH 4.5 buffer and pH 6.8 buffer and the firm has not performed CDP as per WHO guidelines
Justification is required as you have not included test for content uniformity in drug product specification for the applied drug product	The firm submitted that content uniformity of core tablets are mentioned.
Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Firm shall submit following before issuance of registration letter:

- **Fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**
- **Stability studies data of both the drug substances as per the conditions of zone IV-A or otherwise provision of degradation studies of the finished product for 6 months as per the decision of Registration Board before issuance of Registration letter.**
- **CDP studies for applied formulation in three buffers of pH 1.2, 4.5 and 6.8.**

69.	Name and address of manufacturer / Applicant	M/s Macter International Limited F-216, S.I.T.E Karachi
	Brand Name +Dosage Form + Strength	Empozin-L 25mg+5mg Tablet
	Composition	Each Film Coated Tablet Contains: Empagliflozin…..……..25mg Linagliptin……..5mg
	Diary No. Date of R& I & fee	Dy. No. 14721 dated 07-03-2019, Rs: 50,000/- dated 06-03-2019
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	14's, 28's; As per SRO
	Approval status of product in Reference Regulator Authorities	GLYXAMBI® (empagliflozin;linagliptin) (10mg;5mg, 25mg;5mg) film coated tablets USFDA Approved
	Me-too status	NA
	GMP status	The firm was inspected on 25-03-2018 and conclusion of inspection was: The firm is found to be complying at a good level of GMP compliance at the time of inspection. Continuous improvements for procedures shall be followed in letter and spirit as per the Drug Act 1976, DRAP Act 2012 and rules framed there under.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Manufacturer of API	M/s Fuxin Long Rui Pharmaceutical CO., Ltd., Fluoride Industrial Park, Fuxin City, Liaoning Province-123000, China
API Lot No.	**Empagliflozin**: E-20190920-D02-E06-01 **Linagliptin:** L-20190305-D01-L09-08
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%

Time Period	Real time: 9 months Accelerated: 6 months		
Frequency	Real Time: 0, 1, 3, 6, 9 (month) Accelerated: 0, 1, 3, 6 (month)		
Batch No.	20SB-191-005	20SB-192-006	20SB-193-007
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	06-2020	06-2020	06-2020
No. of Batches	03		
Date of Submission	12-04-2021 (11124)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	**Documents to be provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 296th meeting dated 8th, 9th & 10th September, 2020 decided to approve registration of Vireof-N 25mg Tablets. Inspection date: 18th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports on Tenofovir Alafenamide Fumarate API and Vireof-N tablets 25mg is available. • The firm has adequate monitoring and control system for stability chambers.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Empagliflozin**: Copy of COA (Batch#E-20190920-D02-E06-01) of Empagliflozin from M/s Fuxin Long Rui Pharmaceutical CO., Ltd China and M/s Macter International Ltd is submitted. **Linagliptin:** Copy of COA (Batch#L-20190305-D01-L09-08) of Linagliptin from M/s Fuxin Long Rui Pharmaceutical CO., Ltd China and M/s Macter International Ltd is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer is provided by the firm.
4.	Stability study data of API from API manufacturer	**Linagliptin:** Firm has submitted stability study data of Linagliptin. Stability study is conducted at Real time conditions; 25°C ± 2°C / 60% ± 5%RH for 12 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 6 months

		Batches: (L-20170429-D01-L9-01, L-20170604-D01-L9-02, L-20170604-D01-L9-03) **Empagliflozin:** Firm has submitted stability study data of Empagliflozin. Stability study is conducted at Real time conditions; 25°C ± 2°C / 60% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20160606, 20161017, 20161219)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate in the name of M/s Fuxin Long Rui Pharmaceutical CO., Ltd., Fluoride Industrial Park, Fuxin City, Liaoning Province-123000, China ***issued by Liaoning Fuxin Management Committee for Flouride Industrial Development Zone*** valid upto 23-08-2023.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin**: Firm has submitted copy of invoice No. HN19122501-H dated 25-12-2019 from exporter M/s Beijing Sino Hanson Import and Export Co., Ltd China for import of 05kg of Empagliflozin (Batch No. E-20190920-D02-E06-01) in name of M/s Macter International Limited attested by AD (I&E) DRAP Karachi dated 31-12-2019. **Linagliptin:** Firm has submitted copy of Form 6 for import of 1.5kg of Linagliptin from M/s Fuxin Long Rui Pharmaceutical CO., Ltd China attested by AD (I&E) DRAP Karachi. Firm has also submitted copy of invoice No. HN/200304-U dated 04-03-2020 from exporter M/s Beijing Sino Hanson Import and Export Co., Ltd China for import of 1.5kg of Linagliptin (Batch No. L20190305-D01-L09-08) in name of M/s Macter International Limited attested by AD (I&E) DRAP Karachi dated 17-03-2020.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted
9.	Drug-excipients compatibility studies (where applicable)	NA (Formulation of applied drug product is qualitatively similar to that of innovator product Glyxambi 25mg/5mg tablet).

<table>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted Batch Manufacturing record of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>20SB-191-005</td><td>5000 tablets</td><td>06-2020</td></tr>
<tr><td>20SB-192-006</td><td>5000 tablets</td><td>06-2020</td></tr>
<tr><td>20SB-193-007</td><td>5000 tablets</td><td>06-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Not submitted</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Not Submitted</td></tr>
</table>

REMARKS OF EVALUATOR [XI]

Deficiency/Observation	Response by Firm
Submit valid GMP certificate of API manufacturer issued by the relevant regulatory authority of country of origin	• Firm has again submitted copy of GMP certificate in the name of M/s Fuxin Long Rui Pharmaceutical CO., Ltd., Fluoride Industrial Park, Fuxin City, Liaoning Province-123000, China ***issued by Liaoning Fuxin Management Committee for Fluoride Industrial Development Zone*** valid upto 23-08-2023. • Firm has submitted copy of DML (Certificate# Liao20150233) in the name of M/s Fuxin Long Rui Pharmaceutical CO., Ltd., issued by Liaoning Provincial Drug Administration, valid upto 20-12-2022.
Submit latest GMP inspection report conducted within last three years	Firm has submitted cGMP certificate issued on 05th August 2022 based on inspection conducted on 04th August 2022.
In COA of empagliflozin working standard is written. Clarification is required whether it is COA of API or working standard.	Firm has submitted separate COA of Empagliflozin API and working standard.
Submit stability study data of Linagliptin and Empagliflozin API as per zone IV-A.	• The firm submitted that HVAC system is installed to control the environment to keep raw material properly in store room (below 25ºC & 45%RH) and we have given finish good stability data at zone IV-A. • The firm has not submitted stability study data of Linagliptin and Empagliflozin API as per zone IV-A conditions.

CDP studies for the applied product is not submitted	Comparative dissolution studies of applied product was performed against innovator brand Glyxambi 25+5mg tablet in dissolution medium pH 1.2, pH 4.5 and pH 6.8 buffer. The value of F2 factor are in acceptable range
Justification is required as you have not included test for content uniformity in drug product specification for the applied drug product	The firm submitted that content uniformity of core tablets are mentioned.
Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Firm shall submit following before issuance of registration letter:

- **Fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**
- **Stability studies data of both the drug substances as per the conditions of zone IV-A or otherwise provision of degradation studies of the finished product for 6 months as per the decision of Registration Board before issuance of Registration letter.**

70.	Name and address of manufacturer / Applicant	M/s Macter International Limited F-216, S.I.T.E Karachi
	Brand Name +Dosage Form + Strength	Obet 5mg Tablet
	Composition	Each Tablet Contains: Obeticholic Acid…….5mg
	Diary No. Date of R& I & fee	Dy. No. 2324 dated 17-01-2018, Rs: 50,000/- dated 16-01-2018
	Pharmacological Group	Modified bile acid and farnesoid X receptor (FXR) agonist
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulator Authorities	OCALIVA (5mg, 10mg) film coated tablets USFDA Approved
	Me-too status	Obliva Tablet 5mg by M/s Hilton Pharma (Reg#108921)
	GMP status	The firm was inspected on 25-03-2018 and conclusion of inspection was: The firm is found to be complying at a good level of GMP compliance at the time of inspection. Continuous improvements for procedures shall be followed in letter and spirit as per the Drug Act 1976, DRAP Act 2012 and rules framed there under.

	Remarks of the Evaluator	

STABILITY STUDY DATA			
Manufacturer of API	M/s Virupaksha Organics Limited India Sy No-10 Gaddapotharam, Gaddapotharam (V), Jinnaram (M), Sangareddy (Dist.) 502319 India		
API Lot No.	AOBTC0118002		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 9 months Accelerated: 6 months		
Frequency	Real Time: 0, 1, 3, 6, 9 (month) Accelerated: 0, 1, 3, 6 (month)		
Batch No.	20SB-142-001	20SB-143-002	20SB-144-003
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	05-2020	05-2020	05-2020
Date of Initiation	06-2020	06-2020	06-2020
No. of Batches	03		
Date of Submission	30-06-2021 (18372)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr. No.	**Documents to Be Provided**	**Status**
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 296th meeting dated 8th, 9th & 10th September, 2020 decided to approve registration of Vireof-N 25mg Tablets. Inspection date: 18th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports on Tenofovir Alafenamide Fumarate API and Vireof-N tablets 25mg is available. • The firm has adequate monitoring and control system for stability chambers.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Copy of COA (Batch#AOBTC0118002) of API from M/s Virupaksha Organics Limited India and M/s Macter International Ltd is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer is provided by the firm.
4.	Stability study data of API from API manufacturer	Firm has submitted stability study data of API as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ±

<table>
<tr><td></td><td></td><td>5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 6 months
Batches:(AOBTC0217001, AOBTC0217002, AOBTC0217003)</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Firm has submitted copy of GMP certificate No; 44139/TS/2020 dated 05-10-2020 in the name of M/s Virupaksha Organics Limited India Sy No-10 Gaddapotharam, Gaddapotharam (V), Jinnaram (M), Sangareddy (Dist.) 502319 India issued by Drugs Control Administration Telangana state India valid upto 05-10-2021.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Firm has submitted copy of Form 6 for import of 250gm of Obeticholic Acid from M/s Virupaksha Organics Limited India attested by AD (I&E) DRAP Karachi.
Firm has also submitted copy of invoice No. AEX/100/2019-20 dated 11-02-2020 for import of 250gm of Obeticholic Acid (Batch No. AOBTC0118002) in name of M/s Macter International Limited attested by AD (I&E) DRAP Karachi dated 24-02-2020.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Submitted</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA
(Formulation of applied drug product is qualitatively similar to that of innovator product Ocaliva 5mg tablet).</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted Batch Manufacturing record of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>20SB-142-001</td><td>5000 tablets</td><td>05-2020</td></tr>
<tr><td>20SB-143-002</td><td>5000 tablets</td><td>05-2020</td></tr>
<tr><td>20SB-144-003</td><td>5000 tablets</td><td>05-2020</td></tr>
</table>
</td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Comparative dissolution was performed against Ocaliva 5mg tablet in dissolution medium pH 1.2, pH 4.5, pH 6.8 buffer and FDA dissolution medium (0.05mM Sodium Phosphate Buffer, pH 6.8 in 0.08% tween 80).</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
</table>

13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

REMARKS OF EVALUATOR [XI]

Deficiency/Observation	**Response by Firm**
• The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee	• The firm stated that we have submitted all technical documents on film coated tablets and also revised the label claim along with submission of Rs. 7500/- on deposit slip# 946567667. The revised label claim is as under: Each film coated Tablet Contains: Obeticholic Acid…….5mg
• Submit valid GMP certificate of API manufacturer issued by the relevant regulatory authority of country of origin	• Firm has submitted copy of GMP certificate No; 70109/TS/2021 dated 27-10-2021 in the name of M/s Virupaksha Organics Limited India Sy No-10 Gaddapotharam, Gaddapotharam (V), Jinnaram (M), Sangareddy (Dist.) 502319 India issued by Drugs Control Administration Telangana state India valid upto 26-10-2022.
• Submit latest GMP inspection report conducted within last three years	• Firm has submitted cGMP certificate issued on 05th August 2022 based on inspection conducted on 04th August 2022.
• The European public assessment report has specified the conditions for real time and accelerated stability studies as 5°C ± 3°C and 25 °C/60% RH, respectively. The drug substance manufacturer has provided the data as per Zone IV-A. Justification is required about the stability of the drug substance in Zone IV-A as compared to 5°C ± 3°C	• We have various storage facilities in our raw material store., i.e. 2-8ºC, below 15ºC, below 25ºC, below -40ºC and -80ºC. Subject raw material will store as per require conditions. • The stability in our dossier provided is of manufacturer and it's part of DMF.
• Clarification is required since the dissolution media mentioned in the submitted application is different from that of the innovator product given in FDA dissolution database (0.08% polysorbate 80 in 50mM sodium phosphate dibasic buffer, pH 6.8) Applied / used (0.050mM sodium phosphate buffer, pH 6.8 in 0.08% tween 80)	• The firm submitted that similar dissolution media used in submitted application (i.e. 0.08% Polysorbate 80 in 50 mM Sodium phosphate dibasic buffer, pH 6.8). According to the calculation (for 50mM 7.09g sodium phosphate dibasic is required and we also used 7.09g sodium phosphate dibasic but it considered as typing error 0.05mM, its actually 0.05M i.e. equal to 50mM.
• Submit details of manufacturer of Ocaliva 5mg tablet against which CDP study is conducted	• The firm submitted details of manufacturer of Ocaliva 5mg tablet. M/s Intercept Pharma International Ltd., 31-36 Ormond Quay Upper Dublin 7, Ireland.
• The limits of assay test mentioned in specifications is 95-105% while the limits	• The firm submitted that our stability study data results of accelerated and long term are

mentioned in stability summary sheets is 90-110%, clarification is required	stable within limits 95-105%. We have corrected specifications and revised specification is submitted
• Justification is required as you have not included test for content uniformity in drug product specification for the applied drug product	• The firm submitted that content uniformity of core tablets are mentioned in our application, as our product has non-functional coating so we didn't perform CU on coated tablets.
• Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.	• The firm has submitted compliance Record of HPLC software 21CFR & audit trail reports on product testing.
• Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• The firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

INDICATIONS AND USAGE:

Ocaliva is indicated for the treatment of adult patients with primary biliary cholangitis (PBC)

- without cirrhosis or
- with compensated cirrhosis who do not have evidence of portal hypertension,

either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA.

WARNING: HEPATIC DECOMPENSATION AND FAILURE IN PRIMARY BILIARY CHOLANGITIS PATIENTS WITH CIRRHOSIS

- Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in primary biliary cholangitis (PBC) patients with either compensated or decompensated cirrhosis.
- OCALIVA is contraindicated in PBC patients with decompensated cirrhosis, a prior decompensation event, or with compensated cirrhosis who have evidence of portal hypertension.
- Permanently discontinue OCALIVA in patients who develop laboratory or clinical evidence of hepatic decompensation; have compensated cirrhosis and develop evidence of portal hypertension; or experience clinically significant hepatic adverse reactions while on treatment

Decision: Approved with innovator's specifications and following label claim:

Each film coated Tablet Contains:

Obeticholic Acid…….5mg

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

71.	Name and address of manufacturer / Applicant	M/s Macter International Limited F-216, S.I.T.E Karachi
	Brand Name +Dosage Form + Strength	Obet 10mg Tablet
	Composition	Each Tablet Contains: Obeticholic Acid…….10mg
	Diary No. Date of R& I & fee	Dy. No. 2325 dated 17-01-2018, Rs: 50,000/- dated 16-01-2018
	Pharmacological Group	Modified bile acid and farnesoid X receptor (FXR) agonist
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer specifications

	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulator Authorities	OCALIVA (5mg, 10mg) film coated tablets USFDA Approved
	Me-too status	Obliva Tablet 10mg by M/s Hilton Pharma (Reg#108922)
	GMP status	The firm was inspected on 25-03-2018 and conclusion of inspection was: The firm is found to be complying at a good level of GMP compliance at the time of inspection. Continuous improvements for procedures shall be followed in letter and spirit as per the Drug Act 1976, DRAP Act 2012 and rules framed there under.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Manufacturer of API	M/s Virupaksha Organics Limited India Sy No-10 Gaddapotharam, Gaddapotharam (V), Jinnaram (M), Sangareddy (Dist.) 502319 India		
API Lot No.	AOBTC0118002		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40 °C ± 2 °C / 75% ± 5%		
Time Period	Real time: 9 months Accelerated: 6 months		
Frequency	Real Time: 0, 1, 3, 6, 9 (month) Accelerated: 0, 1, 3, 6 (month)		
Batch No.	20SB-150-001	20SB-151-002	20SB-152-003
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	05-2020	05-2020	05-2020
Date of Initiation	06-2020	06-2020	06-2020
No. of Batches	03		
Date of Submission	30-06-2021 (18371)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 296th meeting dated 8th, 9th & 10th September, 2020 decided to approve registration of Vireof-N 25mg Tablets. Inspection date: 18th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm.

		• Audit Trail on the testing reports on Tenofovir Alafenamide Fumarate API and Vireof-N tablets 25mg is available. • The firm has adequate monitoring and control system for stability chambers.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Copy of COA (Batch#AOBTC0118002) of API from M/s Virupaksha Organics Limited India and M/s Macter International Ltd is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer is provided by the firm.
4.	Stability study data of API from API manufacturer	Firm has submitted stability study data of API as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(AOBTC0217001, AOBTC0217002, AOBTC0217003)
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No; 44139/TS/2020 dated 05-10-2020 in the name of M/s Virupaksha Organics Limited India Sy No-10 Gaddapotharam, Gaddapotharam (V), Jinnaram (M), Sangareddy (Dist.) 502319 India issued by Drugs Control Administration Telangana state India valid upto 05-10-2021.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 6 for import of 250gm of Obeticholic Acid from M/s Virupaksha Organics Limited India attested by AD (I&E) DRAP Karachi. Firm has also submitted copy of invoice No. AEX/100/2019-20 dated 11-02-2020 for import of 250gm of Obeticholic Acid (Batch No. AOBTC0118002) in name of M/s Macter International Limited attested by AD (I&E) DRAP Karachi dated 24-02-2020.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted
9.	Drug-excipients compatibility studies (where applicable)	NA (Formulation of applied drug product is qualitatively similar to that of innovator product Ocaliva 10mg tablet).

<table>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted Batch Manufacturing record of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>20SB-150-001</td><td>5000 tablets</td><td>05-2020</td></tr>
<tr><td>20SB-151-002</td><td>5000 tablets</td><td>05-2020</td></tr>
<tr><td>20SB-152-003</td><td>5000 tablets</td><td>05-2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Comparative dissolution was performed against Ocaliva 10mg tablet in dissolution medium pH 1.2, pH 4.5, pH 6.8 buffer and FDA dissolution medium (0.05mM Sodium Phosphate Buffer, pH 6.8 in 0.08% tween 80).</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Not Submitted</td></tr>
<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Not Submitted</td></tr>
</table>

REMARKS OF EVALUATOR [XI]

Deficiency/Observation	Response by Firm
• The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee	• The firm stated that we have submitted all technical documents on film coated tablets and also revised the label claim along with submission of Rs. 7500/- on deposit slip# 392056704846. The revised label claim is as under: Each film coated Tablet Contains: Obeticholic Acid…….10mg
• Submit valid GMP certificate of API manufacturer issued by the relevant regulatory authority of country of origin	• Firm has submitted copy of GMP certificate No; 70109/TS/2021 dated 27-10-2021 in the name of M/s Virupaksha Organics Limited India Sy No-10 Gaddapotharam, Gaddapotharam (V), Jinnaram (M), Sangareddy (Dist.) 502319 India issued by Drugs Control Administration Telangana state India valid upto 26-10-2022.
• Submit latest GMP inspection report conducted within last three years	• Firm has submitted cGMP certificate issued on 05th August 2022 based on inspection conducted on 04th August 2022.
• The European public assessment report has specified the conditions for real time and accelerated stability studies as 5°C ± 3°C and 25	• The firm submitted that we have various storage facilities in our raw material store., i.e. 2-8ºC, below 15ºC, below 25ºC, below

°C/60% RH, respectively. The drug substance manufacturer has provided the data as per Zone IV-A. Justification is required about the stability of the drug substance in Zone IV-A as compared to 5°C ± 3°C	-40ºC and -80ºC. Subject raw material will store as per require conditions. • The stability in our dossier provided is of manufacturer and it's part of DMF.
• Clarification is required since the dissolution media mentioned in the submitted application is different from that of the innovator product given in FDA dissolution database (0.08% polysorbate 80 in 50mM sodium phosphate dibasic buffer, pH 6.8) Applied / used (0.050mM sodium phosphate buffer, pH 6.8 in 0.08% tween 80)	• The firm submitted that similar dissolution media used in submitted application (i.e. 0.08% Polysorbate 80 in 50 mM Sodium phosphate dibasic buffer, pH 6.8). According to the calculation (for 50mM 7.09g sodium phosphate dibasic is required and we also used 7.09g sodium phosphate dibasic but it considered as typing error 0.05mM, its actually 0.05M i.e. equal to 50mM.
• Submit details of manufacturer of Ocaliva 10mg tablet against which CDP study is conducted	• The firm submitted details of manufacturer of Ocaliva 10mg tablet. M/s Intercept Pharma International Ltd., 31-36 Ormond Quay Upper Dublin 7, Ireland.
• The limits of assay test mentioned in specifications is 95-105% while the limits mentioned in stability summary sheets is 90-110%, clarification is required	• The firm submitted that our stability study data results of accelerated and long term are stable within limits 95-105%. We have corrected specifications and revised specification is submitted
• Justification is required as you have not included test for content uniformity in drug product specification for the applied drug product	• The firm submitted that content uniformity of core tablets are mentioned in our application, as our product has non-functional coating so we didn't perform CU on coated tablets.
• Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.	• The firm has submitted compliance Record of HPLC software 21CFR & audit trail reports on product testing.
• Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• The firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

INDICATIONS AND USAGE:

Ocaliva is indicated for the treatment of adult patients with primary biliary cholangitis (PBC)

- without cirrhosis or
- with compensated cirrhosis who do not have evidence of portal hypertension,

either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA.

WARNING: HEPATIC DECOMPENSATION AND FAILURE IN PRIMARY BILIARY CHOLANGITIS PATIENTS WITH CIRRHOSIS

- Hepatic decompensation and failure, sometimes fatal or resulting in liver transplant, have been reported with OCALIVA treatment in primary biliary cholangitis (PBC) patients with either compensated or decompensated cirrhosis.
- OCALIVA is contraindicated in PBC patients with decompensated cirrhosis, a prior decompensation event, or with compensated cirrhosis who have evidence of portal hypertension.
- Permanently discontinue OCALIVA in patients who develop laboratory or clinical evidence of hepatic decompensation; have compensated cirrhosis and develop evidence of portal hypertension; or experience clinically significant hepatic adverse reactions while on treatment

Decision: Approved with innovator's specifications and following label claim:
Each film coated Tablet Contains:
Obeticholic Acid…….10mg

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case No. 03; New application for registration of drugs on Form 5-F on export facilitation

72.	Name, address of Applicant / Marketing Authorization Holder	M/s PharmEvo (Pvt) Ltd., Plot No. A-29, North Western Industrial Zone, Port Qasim Karachi
	Name, address of Manufacturing site.	M/s PharmEvo (Pvt) Ltd., Plot No. A-29, North Western Industrial Zone, Port Qasim Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8312 dated 30/03/2022
	Details of fee submitted	PKR 75,000/-: dated 28/02/2022 (Deposit slip#3477572439)
	The proposed proprietary name / brand name	Trilin XR 25+5+1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin …… 25mg Linagliptin ……. 5mg Metformin HCl as extended release …. 1000mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-Diabetic (Type II)
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	As per SRO
	Proposed unit price	7's, 10's, 14's, 20's, 21's, 28's, 30's, 56's, 84's, 100's, 122's
	The status in reference regulatory authorities	TRIJARDY XR (5mg;2.5mg;1gm/ 10mg;5mg;1gm/ 12.5mg;2.5mg;1gm/ 25mg;5mg;1gm) film coated tablet by

		M/s Boehringer Ingelheim Pharmaceuticals, USFDA Approved.
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	GMP certificate issued 17th September, 2020 based on inspection conducted on 16th September 2020.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Linagliptin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Metformin HCl:** *M/s Shouguang Fukang Pharmaceutical Co., Ltd., North-East of Dongwaihuan Road, Dongcheng Industrial Area, China*
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin:** Firm has submitted stability study data of Empagliflozin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; ***40°C ± 2°C / 75% ± 5%RH for 12 months***

		Batches: (130701, 130702, 130801) **Linagliptin:** Firm has submitted stability study data of Linagliptin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (20180201,20180202, 20180301) **Metformin HCl:** Firm has submitted stability study data of Metformin HCl as per zone IV-A. Stability study is conducted at *Real time conditions; 30°C ± 2°C / 75% ± 5%RH for 60 months* and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: *(A-72611405016, A-72611405017, A-72611405018)*
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator that is TRIJARDY XR 25+5+1000mg Tablet by M/s Boehringer Ingelheim Pharmaceutical Inc. by performing quality tests (Identification, Assay, Dissolution, content uniformity). CDP has been performed against the same brand that is Trijardy XR 25+5+1000mg Tablet by M/s Boehringer Ingelheim Pharmaceutical Inc. in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted method validation studies including linearity, range, accuracy, precision, repeatability, robustness.
STABILITY STUDY DATA		
Manufacturer of API		**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China

		Linagliptin: M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Metformin HCl:** *M/s Shouguang Fukang Pharmaceutical Co., Ltd., North-East of Dongwaihuan Road, Dongcheng Industrial Area, China*		
API Lot No.		Empagliflozin: 4500-202006001 Linagliptin: 7700-20200501 *Metformin HCl: A-15212005110*		
Description of Pack (Container closure system)		Alu-Alu blister packed in unit carton		
Stability Storage Condition		Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		21PD-3549-03-T	21PD-3550-04-T	21PD-3551-05-T
Batch Size		2500 tab	2500 tab	2500 tab
Manufacturing Date		02-2021	02-2021	02-2021
Date of Initiation		12-03-2021	12-03-2021	12-03-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 293rd meeting dated 6th-8th January, 2020 decided to approve registration of Empagin XR Tablets 5/1000mg, Empagin XR Tablets 10/1000mg, Empagin XR Tablets 12.5/1000mg, Empagin XR Tablets 25/1000mg. Inspection date: 05th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports are available. The firm has 16 stability chambers, 02 for accelerated and 14 for real time stability testing. All chambers are properly		

		qualified. All chambers are provided with continuous power supply and data loggers for continuous monitoring.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin and Linagliptin:** Firm has submitted copy of GMP certificate in the name of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. **Metformin HCl:** *Firm has submitted copy of GMP certificate in the name of M/s Shouguang Fukang Pharmaceutical Co., Ltd., North-East of Dongwaihuan Road, Dongcheng Industrial Area, Shandong Province China issued by Shandong Food and Drug Administration valid upto 12-03-2024.*
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin**: Firm has submitted copy of invoice No. ZY20072302G/W dated 23-07-2020 for import of 15kg of Empagliflozin in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 30-07-2020. **Linagliptin:** Firm has submitted copy of invoice No. ZY20060101G/W dated 01-06-2020 for import of 0.5kg of Linagliptin in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 10-06-2020. **Metformin HCl:** *Firm has submitted copy of invoice No. 20FK04Z4133B dated 10-08-2020 for import of 10000kg of Metformin HCl in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 26-08-2020.*
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Fir has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted

Remarks of Evaluator [XI]:

- The firm submitted that 10 % excess is included in the drug substances (Empagliflozin & Linagliptin) to compensate process loss during active coating
- The firm submitted that Seal coting and film coating materials contain 25% excess to compensate process loss

Section	Observations	Response
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer for empagliflozin and Linagliptin issued by relevant regulatory authority of country of origin is required	• Firm has again submitted copy of GMP certificate in the name of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. • The firm has also submitted DML # (Su 20160324) of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China valid upto December 06, 2025.
2.3.R.1	• Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	Firm has submitted copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is performed.
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance Empagliflozin, Linagliptin and Metformin HCl by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Empagliflozin, Linagliptin and Metformin HCl shall be submitted.	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug Substance Metformin HCl, Empagliflozin & Linaglitpin by drug product manufacturer is submitted. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Empagliflozin, Linagliptin and Metformin HCl is submitted.

<table>
<tr><td>3.2S.7</td><td>• Submit stability study data for metformin HCl drug substance as per zone-IV-A conditions</td><td>Firm has submitted stability study data of Metformin HCl. Stability study is conducted at Real time conditions; 30˚C ± 2˚C / 75% ± 5%RH for 36 months and at Accelerated conditions; 40˚C ± 2˚C / 75% ± 5%RH for 06 months
Batches: (A-71411711073, A-71411711074, A-71411711075)</td></tr>
<tr><td>3.2.P.2.2.1</td><td>• Justify why the pharmaceutical equivalence study does not include complete testing of the drug product and the innovator/comparator product including the tests recommended by innovator product. (arginine content, water content)</td><td>Firm submitted that complete testing has been done while performing Pharmaceutical Equivalence test includes Appearance, Identification, Average weight, Assay, Dissolution, Content Uniformity and impurities. Furthermore, Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and supporting data is submitted</td></tr>
<tr><td>3.2.P.5</td><td>• Justification is required for not including test for arginine content in specification as recommended by innovator product review document
• In dissolution method only 2hr, 4hr and 12 are considered for dissolution of metformin HCl instead of 1, 2, 4, 6, 8, 10 and 12 hours as recommended by USFDA dissolution data base
• Specificity test is not performed in method validation studies
• Justification is required for not performing test for arginine content in batch analysis as recommended by innovator product review document</td><td>• The firm submitted that Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and submitted revised specifications and analytical record for determination of arginine content.
• In accordance with the chemistry review, application number 212614Orig1s000, Center for Drug Evaluation and Research recommended the acceptable criteria for metformin HCl are as 2 hour, 4 hour, and 12 hours.
Please refer below details:
<table>
<tr><td colspan="2">Review Summary:</td></tr>
<tr><td>Approved dissolution acceptance criteria</td><td>Empagliflozin
Q= in 45 minutes
Linagliptin
Q= in 30 minutes
Metformin HCl
2 hours:
4 hours:
12 hours: NLT</td></tr>
</table>
• The firm submitted that specificity test has been performed in validation studies covered under accuracy test in method validation.</td></tr>
</table>

		• The firm submitted that Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and submitted revised specifications and analytical record for determination of arginine content.
3.2.P.8	• Clarification is required since stability study is performed as per given dates 09-03-2021 (initial time point), 28-06-2021 (03 months), 05-10-2021 (07 months) which is different from that recommended by ICH guidelines.	Registration Board was apprised that delay of one month in drug product testing from the due tine point of stability studies is permissible as stated in the FAQs published on DRAP's website

Decision: Approved with innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

73.	Name, address of Applicant / Marketing Authorization Holder	M/s PharmEvo (Pvt) Ltd., Plot No. A-29, North Western Industrial Zone, Port Qasim Karachi
	Name, address of Manufacturing site.	M/s PharmEvo (Pvt) Ltd., Plot No. A-29, North Western Industrial Zone, Port Qasim Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10391 dated 23/04/2022
	Details of fee submitted	PKR 75,000/-: dated 28/02/2022 (Deposit slip#998387544595)
	The proposed proprietary name / brand name	Trilin XR 5+2.5+1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin …… 5mg Linagliptin ……. 2.5mg Metformin HCl as extended release …. 1000mg
	Pharmaceutical form of applied drug	Film coated tablet

	Pharmacotherapeutic Group of (API)	Anti-Diabetic (Type II)
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	As per SRO
	Proposed unit price	7's, 10's, 14's, 20's, 21's, 28's, 30's, 56's, 84's, 100's, 122's
	The status in reference regulatory authorities	TRIJARDY XR (5mg;2.5mg;1gm/ 10mg;5mg;1gm/ 12.5mg;2.5mg;1gm/ 25mg;5mg;1gm) film coated tablet by M/s Boehringer Ingelheim Pharmaceuticals, USFDA Approved.
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	GMP certificate issued 17th September, 2020 based on inspection conducted on 16th September 2020.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Linagliptin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Metformin HCl:** M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.

	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin:** Firm has submitted stability study data of Empagliflozin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 12 months Batches: (130701, 130702, 130801) **Linagliptin:** Firm has submitted stability study data of Linagliptin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (20180201,20180202, 20180301) **Metformin HCl:** Firm has submitted stability study data of Metformin HCl as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 60 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (MFH-352/04, MFH-353/04, MFH-354/04,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator that is TRIJARDY XR 5+2.5+1000mg Tablet by M/s Boehringer Ingelheim Pharmaceutical Inc. by performing quality tests (Identification, Assay, Dissolution, content uniformity). CDP has been performed against the same brand that is Trijardy XR 5+2.5+1000mg Tablet by M/s Boehringer Ingelheim Pharmaceutical Inc. in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted method validation studies including linearity, range, accuracy, precision, repeatability, robustness.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Linagliptin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Metformin HCl:** M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India		
API Lot No.	Empagliflozin: 4500-202006001 Linagliptin: 7700-20200501 Metformin HCl: MET-0105/21		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21PD-3681-02-T	21PD-3682-03-T	21PD-3683-04-T
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	04-2021	04-2021	04-2021

Date of Initiation	16-05-2021	16-05-2021	16-05-2021
No. of Batches	03		
Administrative Portion			
7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 293rd meeting dated 6th-8th January, 2020 decided to approve registration of Empagin XR Tablets 5/1000mg, Empagin XR Tablets 10/1000mg, Empagin XR Tablets 12.5/1000mg, Empagin XR Tablets 25/1000mg. Inspection date: 05th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports are available. The firm has 16 stability chambers, 02 for accelerated and 14 for real time stability testing. All chambers are properly qualified. All chambers are provided with continuous power supply and data loggers for continuous monitoring.	
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin and Linagliptin:** Firm has submitted copy of GMP certificate in the name of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. **Metformin HCl:** Firm has submitted copy of GMP certificate in the name of M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India issued by Commissioner Food and Drug	

		Administration, Maharashtra State India valid upto 13th November 2022.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin**: Firm has submitted copy of invoice No. ZY20072302G/W dated 23-07-2020 for import of 15kg of Empagliflozin in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 30-07-2020. **Linagliptin:** Firm has submitted copy of invoice No. ZY20060101G/W dated 01-06-2020 for import of 0.5kg of Linagliptin in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 10-06-2020. **Metformin HCl:** Firm has submitted copy of invoice No. E-144 dated 15-02-2021 for import of 10000kg of Metformin HCl in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 08-03-2021.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Fir has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted

Remarks of Evaluator [XI]:

- The firm submitted that 10 % excess is included in the drug substances (Empagliflozin & Linagliptin) to compensate process loss during active coating
- The firm submitted that Seal coting and film coating materials contain 25% excess to compensate process loss

Section	Observations	Response
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer for	• Firm has again submitted copy of GMP certificate in the name of M/s Jiangsu

	empagliflozin and Linagliptin issued by relevant regulatory authority of country of origin is required	Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. • The firm has also submitted DML # (Su 20160324) of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China valid upto December 06, 2025.
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance Empagliflozin, Linagliptin and Metformin HCl by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Empagliflozin, Linagliptin and Metformin HCl shall be submitted. • Clarification is required as the drug substance manufacturer has performed assay of drug substance Metformin HCl in batch analysis by potentiometric method and drug product manufacturer has performed assay of drug substance Metformin HCl in batch analysis by titrometric method instead of HPLC method as recommended by USP. • COA of primary / secondary reference standard including source and lot number for metformin HCl shall be provided.	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug Substance Metformin HCl, Empagliflozin & Linaglitpin by drug product manufacturer is submitted. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Empagliflozin, Linagliptin and Metformin HCl is submitted. • The firm submitted that previously, USP-42 described the potentiometric titration method for metformin. The same method was used for analysis, but in USP-43, the HPLC method is given. Consequently, the potentiometric method is switched to the HPLC method. Verification studies for the HPLC method are submitted • Firm has submitted COA of primary / secondary reference standard including source and lot number for metformin HCl
3.2.P.2.2.1	• Justify why the pharmaceutical equivalence study does not include complete testing of the drug product and the innovator/comparator product including the tests recommended by innovator product. (arginine content, water content)	Firm submitted that complete testing has been done while performing Pharmaceutical Equivalence test includes Appearance, Identification, Average weight, Assay, Dissolution, Content Uniformity and impurities. Furthermore, Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product,

<table>
<tr><td></td><td></td><td>we have now performed arginine content, and supporting data is submitted</td></tr>
<tr><td>3.2.P.5</td><td>• Justification is required for not including test for arginine content in specification as recommended by innovator product review document
• In dissolution method only 2hr, 4hr and 12 are considered for dissolution of metformin HCl instead of 1, 2, 4, 6, 8, 10 and 12 hours as recommended by USFDA dissolution data base
• Specificity test is not performed in method validation studies
• Justification is required for not performing test for arginine content in batch analysis as recommended by innovator product review document</td><td>• The firm submitted that Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and submitted revised specifications and analytical record for determination of arginine content.
• In accordance with the chemistry review, application number 212614Orig1s000, Center for Drug Evaluation and Research recommended the acceptable criteria for metformin HCl are as 2 hour, 4 hour, and 12 hours.
Please refer below details:
<table><tr><th colspan="2">Review Summary:</th></tr><tr><td>Approved dissolution acceptance criteria</td><td>Empagliflozin
Q= in 45 minutes
Linagliptin
Q= in 30 minutes
Metformin HCl
2 hours:
4 hours:
12 hours: NLT</td></tr></table>• The firm submitted that specificity test has been performed in validation studies covered under accuracy test in method validation.
• The firm submitted that Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and submitted revised specifications and analytical record for determination of arginine content.</td></tr>
<tr><td>3.2.P.8</td><td>• Clarification is required since stability study is performed as per given dates 07-05-2021 (initial time point), 10-10-2021 (05 months), 20-12-2021 (07 months) which is different from that recommended by ICH guidelines.</td><td>The firm submitted that after completing the initial study, product stability was charged on 07-05-2021. As per the defined interval, samples have to be tested within one month according to SOP, but due to different gradient programming in the method, there were different tests that needed to be performed according to the method and the compilation of data, which caused delays in the completion of testing of stability batches.</td></tr>
</table>

		Furthermore, the stability study results at both conditions, long term and accelerated, are well within specification, showing that the product was properly stored and no effect observed due to this delay in time period of stability testing. Moreover, we assure that all testing of stability batches will be tested on time as per the recommendation of the ICH guideline. Registration Board was apprised that delay of one month in drug product testing from the due tine point of stability studies is permissible as stated in the FAQs published on DRAP website

Decision: Approved with innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

74.	Name, address of Applicant / Marketing Authorization Holder	M/s PharmEvo (Pvt) Ltd., Plot No. A-29, North Western Industrial Zone, Port Qasim Karachi
	Name, address of Manufacturing site.	M/s PharmEvo (Pvt) Ltd., Plot No. A-29, North Western Industrial Zone, Port Qasim Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8630 dated 04/04/2022
	Details of fee submitted	PKR 75,000/-: dated 28/02/2022 (Deposit slip#339271157400)
	The proposed proprietary name / brand name	Trilin XR 10+5+1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin …… 10mg Linagliptin ……. 5mg Metformin HCl as extended release …. 1000mg
	Pharmaceutical form of applied drug	Film coated tablet

	Pharmacotherapeutic Group of (API)	Anti-Diabetic (Type II)
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	As per SRO
	Proposed unit price	7's, 10's, 14's, 20's, 21's, 28's, 30's, 56's, 84's, 100's, 122's
	The status in reference regulatory authorities	TRIJARDY XR (5mg;2.5mg;1gm/ 10mg;5mg;1gm/ 12.5mg;2.5mg;1gm/ 25mg;5mg;1gm) film coated tablet by M/s Boehringer Ingelheim Pharmaceuticals, USFDA Approved.
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	GMP certificate issued 17th September, 2020 based on inspection conducted on 16th September 2020.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Linagliptin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Metformin HCl:** M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug substance
	Stability studies	**Empagliflozin:** Firm has submitted stability study data of Empagliflozin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 12 months Batches: (130701, 130702, 130801) **Linagliptin:** Firm has submitted stability study data of Linagliptin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (20180201,20180202, 20180301) **Metformin HCl:** Firm has submitted stability study data of Metformin HCl as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 60 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (MFH-352/04, MFH-353/04, MFH-354/04,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator that is TRIJARDY XR 10+5+1000mg Tablet by M/s Boehringer Ingelheim Pharmaceutical Inc. by performing quality tests (Identification, Assay, Dissolution, content uniformity). CDP has been performed against the same brand that is Trijardy XR 10+5+1000mg Tablet by M/s Boehringer Ingelheim Pharmaceutical Inc. in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.

	Analytical method validation/verification of product	Firm has submitted method validation studies including linearity, range, accuracy, precision, repeatability, robustness.

STABILITY STUDY DATA			
Manufacturer of API	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Linagliptin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Metformin HCl:** M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India		
API Lot No.	Empagliflozin: 4500-202006001 Linagliptin: 7700-20200501 Metformin HCl: MET-0105/21		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21PD-3742-02-T	21PD-3743-03-T	21PD-3744-04-T
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	28-07-2021	28-07-2021	28-07-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 293rd meeting dated 6th-8th January, 2020 decided to approve registration of Empagin XR Tablets 5/1000mg, Empagin XR Tablets 10/1000mg, Empagin XR Tablets 12.5/1000mg, Empagin XR Tablets 25/1000mg. Inspection date: 05th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm.

		• Audit Trail on the testing reports are available. The firm has 16 stability chambers, 02 for accelerated and 14 for real time stability testing. All chambers are properly qualified. All chambers are provided with continuous power supply and data loggers for continuous monitoring.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin and Linagliptin:** Firm has submitted copy of GMP certificate in the name of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. **Metformin HCl:** Firm has submitted copy of GMP certificate in the name of M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India issued by Commissioner Food and Drug Administration, Maharashtra State India valid upto 13th November 2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin**: Firm has submitted copy of invoice No. ZY20072302G/W dated 23-07-2020 for import of 15kg of Empagliflozin in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 30-07-2020. **Linagliptin:** Firm has submitted copy of invoice No. ZY20060101G/W dated 01-06-2020 for import of 0.5kg of Linagliptin in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 10-06-2020. **Metformin HCl:** Firm has submitted copy of invoice No. E-144 dated 15-02-2021 for import of 10000kg of Metformin HCl in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 08-03-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Fir has submitted data of stability batches supported by attested respective documents like chromatograms, Raw

		data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted

Remarks of Evaluator [XI]:

- The firm submitted that 10 % excess is included in the drug substances (Empagliflozin & Linagliptin) to compensate process loss during active coating
- The firm submitted that Seal coting and film coating materials contain 25% excess to compensate process loss

Section	Observations	Response
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer for empagliflozin and Linagliptin issued by relevant regulatory authority of country of origin is required	• Firm has again submitted copy of GMP certificate in the name of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. • The firm has also submitted DML # (Su 20160324) of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China valid upto December 06, 2025.
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance Empagliflozin, Linagliptin and Metformin HCl by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Empagliflozin, Linagliptin and Metformin HCl shall be submitted. • Clarification is required as the drug substance manufacturer has performed assay of drug substance Metformin HCl in batch analysis by	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug Substance Metformin HCl, Empagliflozin & Linaglitpin by drug product manufacturer is submitted. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Empagliflozin, Linagliptin and Metformin HCl is submitted. • The firm submitted that previously, USP-42 described the potentiometric titration method for metformin. The same method was used for analysis, but in USP-43, the HPLC method is given. Consequently, the potentiometric method is switched to the HPLC method. Verification studies for the HPLC method are submitted • Firm has submitted COA of primary / secondary reference standard including source and lot number for metformin HCl

<table>
<tr><td></td><td>potentiometric method and drug product manufacturer has performed assay of drug substance Metformin HCl in batch analysis by titrometric method instead of HPLC method as recommended by USP.
• COA of primary / secondary reference standard including source and lot number for metformin HCl shall be provided.</td><td></td></tr>
<tr><td>3.2.P.2.2.1</td><td>• Justify why the pharmaceutical equivalence study does not include complete testing of the drug product and the innovator/comparator product including the tests recommended by innovator product. (arginine content, water content)</td><td>Firm submitted that complete testing has been done while performing Pharmaceutical Equivalence test includes Appearance, Identification, Average weight, Assay, Dissolution, Content Uniformity and impurities. Furthermore, Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and supporting data is submitted</td></tr>
<tr><td>3.2.P.5</td><td>• Justification is required for not including test for arginine content in specification as recommended by innovator product review document
• In dissolution method only 2hr, 4hr and 12 are considered for dissolution of metformin HCl instead of 1, 2, 4, 6, 8, 10 and 12 hours as recommended by USFDA dissolution data base
• Specificity test is not performed in method validation studies
• Justification is required for not performing test for not performing test for arginine content in batch analysis as recommended by innovator product review document</td><td>• The firm submitted that Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and submitted revised specifications and analytical record for determination of arginine content.
• In accordance with the chemistry review, application number 212614Orig1s000, Center for Drug Evaluation and Research recommended the acceptable criteria for metformin HCl are as 2 hour, 4 hour, and 12 hours.
Please refer below details:
<table><tr><td colspan="2">Review Summary:</td></tr><tr><td>Approved dissolution acceptance criteria</td><td>Empagliflozin
Q= in 45 minutes
Linagliptin
Q= in 30 minutes
Metformin HCl
2 hours:
4 hours:
12 hours: NLT</td></tr></table>
• The firm submitted that specificity test has been performed in validation studies covered under accuracy test in method validation.</td></tr>
</table>

		• The firm submitted that Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and submitted revised specifications and analytical record for determination of arginine content.
3.2.P.8	• Clarification is required since stability study is performed as per given dates 05-07-2021 (initial time point), 20-12-2021 (05 months), 03-02-2022 (07 months) which is different from that recommended by ICH guidelines.	The firm submitted that after completing the initial study, product stability was charged on 05-07-2021. As per the defined interval, samples have to be tested within one month according to SOP, but due to different gradient programming in the method, there were different tests that needed to be performed according to the method and the compilation of data, which caused delays in the completion of testing of stability batches. Furthermore, the stability study results at both conditions, long term and accelerated, are well within specification, showing that the product was properly stored and no effect observed due to this delay in time period of stability testing. Moreover, we assure that all testing of stability batches will be tested on time as per the recommendation of the ICH guideline.

Decision: Approved with innovator's specifications.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**
- **Registration Board directed the firm to optimize the formulation to minimise the overage of "Active coating solution of Empagliflozin & Linagliptin" during commercial production.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

75.	Name, address of Applicant / Marketing Authorization Holder	M/s PharmEvo (Pvt) Ltd., Plot No. A-29, North Western Industrial Zone, Port Qasim Karachi
	Name, address of Manufacturing site.	M/s PharmEvo (Pvt) Ltd., Plot No. A-29, North Western Industrial Zone, Port Qasim Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale

		☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11087 dated 07/05/2022
	Details of fee submitted	PKR 75,000/-: dated 28/02/2022 (Deposit slip#3490848609)
	The proposed proprietary name / brand name	Trilin XR 12.5+2.5+1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin …… 12.5mg Linagliptin ……. 2.5mg Metformin HCl as extended release …. 1000mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-Diabetic (Type II)
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	As per SRO
	Proposed unit price	7's, 10's, 14's, 20's, 21's, 28's, 30's, 56's, 84's, 100's, 122's
	The status in reference regulatory authorities	TRIJARDY XR (5mg;2.5mg;1gm/ 10mg;5mg;1gm/ 12.5mg;2.5mg;1gm/ 25mg;5mg;1gm) film coated tablet by M/s Boehringer Ingelheim Pharmaceuticals, USFDA Approved.
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	GMP certificate issued 17th September, 2020 based on inspection conducted on 16th September 2020.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Linagliptin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Metformin HCl:** M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification,

		batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin:** Firm has submitted stability study data of Empagliflozin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; ***40°C ± 2°C / 75% ± 5%RH for 12 months*** Batches: (130701, 130702, 130801) **Linagliptin:** Firm has submitted stability study data of Linagliptin as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 36 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (20180201,20180202, 20180301) **Metformin HCl:** Firm has submitted stability study data of Metformin HCl as per zone IV-A. Stability study is conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 60 months and at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (MFH-352/04, MFH-353/04, MFH-354/04,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator that is TRIJARDY XR 12.5+2.5+1000mg Tablet by M/s Boehringer Ingelheim Pharmaceutical Inc. by performing quality tests (Identification, Assay, Dissolution, content uniformity). CDP has been performed against the same brand that is Trijardy XR 12.5+2.5+1000mg Tablet by M/s Boehringer Ingelheim Pharmaceutical Inc. in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted method validation studies including linearity, range, accuracy, precision, repeatability, robustness.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Linagliptin:** M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China **Metformin HCl:** M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India		
API Lot No.	Empagliflozin: 4500-202006001 Linagliptin: 7700-20200501 Metformin HCl: MET-0105/21		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	21PD-3745-04-T	21PD-3746-05-T	21PD-3747-06-T
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	07-2021	07-2021	07-2021

Date of Initiation		10-08-2021	10-08-2021	10-08-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 293rd meeting dated 6th-8th January, 2020 decided to approve registration of Empagin XR Tablets 5/1000mg, Empagin XR Tablets 10/1000mg, Empagin XR Tablets 12.5/1000mg, Empagin XR Tablets 25/1000mg. Inspection date: 05th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports are available. The firm has 16 stability chambers, 02 for accelerated and 14 for real time stability testing. All chambers are properly qualified. All chambers are provided with continuous power supply and data loggers for continuous monitoring.	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin and Linagliptin:** Firm has submitted copy of GMP certificate in the name of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. **Metformin HCl:** Firm has submitted copy of GMP certificate in the name of M/s Smruthi Organics Limited., Plot No. A-27, M.I.D.C., Chincholi, Taluka: Mohol, Solapur, Maharashtra, India issued by Commissioner Food and Drug Administration, Maharashtra State India valid upto 13th November 2022.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin**: Firm has submitted copy of invoice No. ZY20072302G/W dated 23-07-2020 for		

		import of 15kg of Empagliflozin in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 30-07-2020. **Linagliptin:** Firm has submitted copy of invoice No. ZY20060101G/W dated 01-06-2020 for import of 0.5kg of Linagliptin in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 10-06-2020. **Metformin HCl:** Firm has submitted copy of invoice No. E-144 dated 15-02-2021 for import of 10000kg of Metformin HCl in name of M/s PharmEvo (Pvt) Ltd attested by AD (I&E) DRAP Karachi dated 08-03-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Fir has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted

Remarks of Evaluator [XI]:

- The firm submitted that 10 % excess is included in the drug substances (Empagliflozin & Linagliptin) to compensate process loss during active coating
- The firm submitted that Seal coting and film coating materials contain 25% excess to compensate process loss

Section	Observations	Response
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer for empagliflozin and Linagliptin issued by relevant regulatory authority of country of origin is required	• Firm has again submitted copy of GMP certificate in the name of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China ***issued by Huaian Pharmaceutical Industry Association No. 168, West Chaoyang Road, Qingpu Industrial Park, Huaian, Jiangsu*** valid upto 14-01-2024. • The firm has also submitted DML # (Su 20160324) of M/s Jiangsu Yongan Pharmaceutical CO., Ltd., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu China valid upto December 06, 2025.

3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance Empagliflozin, Linagliptin and Metformin HCl by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Empagliflozin, Linagliptin and Metformin HCl shall be submitted. • Clarification is required as the drug substance manufacturer has performed assay of drug substance Metformin HCl in batch analysis by potentiometric method and drug product manufacturer has performed assay of drug substance Metformin HCl in batch analysis by titrometric method instead of HPLC method as recommended by USP. • COA of primary / secondary reference standard including source and lot number for metformin HCl shall be provided.	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug Substance Metformin HCl, Empagliflozin & Linaglitpin by drug product manufacturer is submitted. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) Empagliflozin, Linagliptin and Metformin HCl is submitted. • The firm submitted that previously, USP-42 described the potentiometric titration method for metformin. The same method was used for analysis, but in USP-43, the HPLC method is given. Consequently, the potentiometric method is switched to the HPLC method. Verification studies for the HPLC method are submitted • Firm has submitted COA of primary / secondary reference standard including source and lot number for metformin HCl
3.2.P.2.2.1	• Justify why the pharmaceutical equivalence study does not include complete testing of the drug product and the innovator/comparator product including the tests recommended by innovator product. (arginine content, water content)	Firm submitted that complete testing has been done while performing Pharmaceutical Equivalence test includes Appearance, Identification, Average weight, Assay, Dissolution, Content Uniformity and impurities. Furthermore, Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and supporting data is submitted
3.2.P.5	• Justification is required for not including test for arginine content in specification as recommended by innovator product review document • In dissolution method only 2hr, 4hr and 12 are considered for dissolution of metformin HCl instead of 1, 2, 4, 6, 8, 10 and 12	• The firm submitted that Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and submitted revised specifications and analytical record for determination of arginine content. • In accordance with the chemistry review, application number **212614Orig1s000**, Center for Drug Evaluation and Research

<table>
<tr>
<td></td>
<td>hours as recommended by USFDA dissolution data base
• Specificity test is not performed in method validation studies
• Justification is required for not performing test for arginine content in batch analysis as recommended by innovator product review document</td>
<td>recommended the acceptable criteria for metformin HCl are as 2 hour, 4 hour, and 12 hours.
Please refer below details:
<table><tr><td colspan="2">Review Summary:</td></tr><tr><td>Approved dissolution acceptance criteria</td><td>Empagliflozin
Q= in 45 minutes
Linagliptin
Q= in 30 minutes
Metformin HCl
2 hours:
4 hours:
12 hours: NLT</td></tr></table>
• The firm submitted that specificity test has been performed in validation studies covered under accuracy test in method validation.

• The firm submitted that Arginine used in formulation was considered as an excipient previously. In accordance with the innovator product, we have now performed arginine content, and submitted revised specifications and analytical record for determination of arginine content.</td>
</tr>
<tr>
<td>3.2.P.8</td>
<td>• Clarification is required since stability study is performed as per given dates 04-08-2021 (initial time point), 20-12-2021 (04 months), 06-03-2022 (07 months) submitted which is different from that recommended by ICH guidelines.</td>
<td>The firm submitted that after completing the initial study, product stability was charged on 04-08-2021. As per the defined interval, samples have to be tested within one month according to SOP, but due to different gradient programming in the method, there were different tests that needed to be performed according to the method and the compilation of data, which caused delays in the completion of testing of stability batches. Furthermore, the stability study results at both conditions, long term and accelerated, are well within specification, showing that the product was properly stored and no effect observed due to this delay in time period of stability testing. Moreover, we assure that all testing of stability batches will be tested on time as per the recommendation of the ICH guideline.</td>
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<td colspan="3">Decision: Approved with innovator’s specifications.
• Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.
• The Registration Board directed the firm to optimize the formulation to minimise the overage of “Active coating solution of Empagliflozin & Linagliptin” during commercial production.</td>
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</table>

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
76.	Name, address of Applicant / Marketing Authorization Holder	M/s Macter International Limited., F-216, S.I.T.E Karachi
	Name, address of Manufacturing site.	M/s Macter International Limited., F-216, S.I.T.E Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 18584 dated 27-06-2022
	Details of fee submitted	Rs.50,000/- dated 17-03-2021 & Rs.25,000/- dated 13-07-2021
	The proposed proprietary name / brand name	Ticago 90mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Ticagrelor……90mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Platelet aggregation inhibitors excl. heparin
	Reference to Finished product specifications	N/A
	Proposed Pack size	As per SRO
	Proposed unit price	10's, 14's, 28's
	The status in reference regulatory authorities	BRILINTA (90mg, 60mgelor) film coated tablet USFDA Approved.
	For generic drugs (me-too status)	Briltiga 90mg Tablet by M/s Global Pharmaceuticals (Reg#111631)
	GMP status of the Finished product manufacturer	GMP certificate issued to firm date 13th August, 2020 based on inspection conducted on 10th October 2019.
	Name and address of API manufacturer.	**Manufacturer:** M/s Nantong Chanyoo Pharmatech CO., Ltd., No.2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangso Province 226407, P.R. China **DMF Holder/Headquarter:**

		Changzhou Pharmaceutical Factory., No. 518 Laodong East Road, Changzhou, Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Firm has submitted stability study data of Ticagrelor. Stability study is conducted at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (140901, 141001, 141101) Stability study data conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 24 months is submitted for following batches. Batches: RD-TG-201806261, RD-TG-201808021, RD-TG-201810081 ***Stability study data of different batches at real time and accelerated conditions is submitted*
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator that is Brilinta 90mg Tablet by M/s AstraZeneca Pharma Sweden by

		performing quality tests (Identification, Assay, Dissolution, average weight of tablet). CDP has been performed against the same brand that is Brilinta 90mg Tablet by M/s AstraZeneca Pharma Sweden in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8) and 0.2% Tween 80 in water. The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted method validation studies including accuracy, linearity, precision (i.e. repeatability and intermediate precision), specificity, robustness and solution stability.

STABILITY STUDY DATA			
Manufacturer of API	**Manufacturer:** M/s Nantong Chanyoo Pharmatech CO., Ltd., No.2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangso Province 226407, P.R. China **DMF Holder/Headquarter:** Changzhou Pharmaceutical Factory., No. 518 Laodong East Road, Changzhou, Province, China		
API Lot No.	RD-TG-201911261		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 9 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 3, 6 (Months) Real Time: 0, 1, 3, 6, 9 (Months)		
Batch No.	20TB-042-001	20TB-043-002	20TB-044-003
Batch Size	5000 tab	5000 tab	5000 tab
Manufacturing Date	20-03-2020	31-03-2020	31-03-2020
Date of Initiation	12-04-2020	12-04-2020	12-04-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 296th meeting dated 8th, 9th &

		10th September, 2020 decided to approve registration of Vireof-N 25mg Tablets. Inspection date: 18th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports on Tenofovir Alafenamide Fumarate API and Vireof-N tablets 25mg is available. The firm has adequate monitoring and control system for stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate in the name of M/s Nantong Chanyoo Pharmatech CO., Ltd., No.2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, P.R. China ***issued by Nantong Chemical & Medical Industry Association China*** valid upto 05-05-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 6 dated 04-03-2020 for import of 02kg of Ticagrelor in name of M/s Macter International Ltd., attested by AD (I&E) DRAP Karachi dated 04-03-2020. Firm has submitted copy of invoice No. CY120039 dated 25-02-2020 for import of 02kg of Ticagrelor in name of M/s Macter International Ltd., attested by AD (I&E) DRAP Karachi dated 04-03-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Fir has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.5	• Latest GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	Firm has submitted cGMP certificate issued on 05th August 2022 based on inspection conducted on 04th August 2022.
1.5.6	• You have not mentioned any specifications in this section while the official monograph is available in	The firm submitted that we have performed /develop and submitted its data in 2020 at that time this molecule was not

	BP. Revise your specification as per BP monograph along with submission of applicable fee	available in BP. It is now available in BP2022 and revised details in this section are submitted. The firm has also submitted Rs. 7500/- on deposit slip No# 9101119948 for revision of specifications
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer issued by relevant regulatory authority of country of origin is required	• Firm has submitted copy of GMP certificate in the name of M/s Nantong Chanyoo Pharmatech CO., Ltd., No.2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, P.R. China ***issued by Nantong Chemical & Medical Industry Association China*** valid upto 21-02-2026. • Firm has submitted copy of DML (No. Su 20160512) in the name of M/s Nantong Chanyoo Pharmatech CO., Ltd., China issued by Jiangsu Provincial Drug Administration China valid upto 02-12-2025.
3.2.S.4	• Manufacturer specification are claimed for the drug substance by drug substance manufacturer while the official monograph is available in BP. Justification shall be submitted. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	• The firm submitted that at the time of development 2020, the product was not included in any official monograph that's why manufacturer provided data on manufacturer specification. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance by Drug Product manufacturer is not submitted • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance is not submitted.
3.2.P.5.1	• This section has mentioned in-house specifications while the official monograph of the applied formulation is available in BP. Revise your specifications and analytical procedure as per BP monograph. • Justification is required since the limits of submitted dissolution specification and assay specification for shelf life provided by the drug product manufacturer (NLT 75% Q in 30 minutes, 90-110%) are different from official BP monograph (Q = 70% after 45 minutes, 95-105%).	• The firm has submitted revised specifications and analytical procedure as BP monograph • The firm submitted that for limits of dissolution and assay specifications, testing method is revised along with the limits of assay and dissolution. • Method verification studies for applied product as per BP method is not submitted

	• Submit method verification studies for applied product as per BP monograph	
3.2.P.6	• COA of primary / secondary reference standard including source and lot number shall be provided.	• COA of primary / secondary reference standard including source and lot number is submitted
3.2.P.8	• Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• The firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Decision: Approved with BP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of following:**
  - **Specifications, analytical procedures and analytical method verification studies for both drug substance and drug product as per BP monograph of Ticagrelor and Ticagrelor Tablet respectively, from M/s Macter International Limited**
  - **Fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

77.	Name, address of Applicant / Marketing Authorization Holder	M/s Macter International Limited., F-216, S.I.T.E Karachi
	Name, address of Manufacturing site.	M/s Macter International Limited., F-216, S.I.T.E Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 18583 dated 27-06-2022
	Details of fee submitted	Rs.50,000/- dated 05-03-2021 & Rs.25,000/- dated 13-07-2021
	The proposed proprietary name / brand name	Ticago 60mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet Contains: Ticagrelor……60mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Platelet aggregation inhibitors excl. heparin
	Reference to Finished product specifications	N/A
	Proposed Pack size	As per SRO
	Proposed unit price	10’s, 14’s, 28’s

	The status in reference regulatory authorities	BRILINTA (90mg, 60mgelor) film coated tablet USFDA Approved.
	For generic drugs (me-too status)	Briltiga 60mg Tablet by M/s Global Pharmaceuticals (Reg#111630)
	GMP status of the Finished product manufacturer	GMP certificate issued to firm date 13th August, 2020 based on inspection conducted on 10th October 2019.
	Name and address of API manufacturer.	**Manufacturer:** M/s Nantong Chanyoo Pharmatech CO., Ltd., No.2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangso Province 226407, P.R. China **DMF Holder/Headquarter:** Changzhou Pharmaceutical Factory., No. 518 Laodong East Road, Changzhou, Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Firm has submitted stability study data of Ticagrelor. Stability study is conducted at Accelerated conditions; 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (140901, 141001, 141101) Stability study data conducted at Real time conditions; 30°C ± 2°C / 65% ± 5%RH for 24 months is submitted for following batches.

		Batches: RD-TG-201806261, RD-TG-201808021, RD-TG-201810081 ***Stability study data of different batches at real time and accelerated conditions is submitted*
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator that is Brilinta 60mg Tablet by M/s AstraZeneca Pharma Canada by performing quality tests (Identification, Assay, Dissolution, average weight of tablet). CDP has been performed against the same brand that is Brilinta 60mg Tablet by M/s AstraZeneca Pharma Canada in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8) and 0.2% Tween 80 in water. The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted method validation studies including accuracy, linearity, precision (i.e. repeatability and intermediate precision), specificity, robustness and solution stability.

STABILITY STUDY DATA	
Manufacturer of API	**Manufacturer:** M/s Nantong Chanyoo Pharmatech CO., Ltd., No.2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangso Province 226407, P.R. China **DMF Holder/Headquarter:** Changzhou Pharmaceutical Factory., No. 518 Laodong East Road, Changzhou, Province, China
API Lot No.	RD-TG-201911261
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 9 months Accelerated: 6 months
Frequency	Accelerated: 0, 1, 3, 6 (Months) Real Time: 0, 1, 3, 6, 9 (Months)

Batch No.		20TB-031-001	20TB-032-002	20TB-033-003
Batch Size		5000 tab	5000 tab	5000 tab
Manufacturing Date		20-03-2020	31-03-2020	31-03-2020
Date of Initiation		10-04-2020	10-04-2020	10-04-2020
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of their product conducted by the panel on the basis of which Registration Board in 296th meeting dated 8th, 9th & 10th September, 2020 decided to approve registration of Vireof-N 25mg Tablets. Inspection date: 18th December, 2019 The report shows that: • The HPLC software is 21 CFR compliant as per record available with the firm. • Audit Trail on the testing reports on Tenofovir Alafenamide Fumarate API and Vireof-N tablets 25mg is available. The firm has adequate monitoring and control system for stability chambers.	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	• Firm has submitted copy of GMP certificate in the name of M/s Nantong Chanyoo Pharmatech CO., Ltd., No.2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, P.R. China ***issued by Nantong Chemical & Medical Industry Association China*** valid upto 05-05-2022. • Firm has submitted copy of DML (No. Su 20160512) in the name of M/s Nantong Chanyoo Pharmatech CO., Ltd., China issued by Jiangsu Provincial Drug Administration China valid upto 02-12-2025.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 6 dated 04-03-2020 for import of 02kg of Ticagrelor in name of M/s Macter International Ltd., attested by AD (I&E) DRAP Karachi dated 04-03-2020. Firm has submitted copy of invoice No. CY120039 dated 25-02-2020 for import of 02kg of Ticagrelor in name of M/s		

		Macter International Ltd., attested by AD (I&E) DRAP Karachi dated 04-03-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Fir has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.5	• Latest GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	Firm has submitted cGMP certificate issued on 05th August 2022 based on inspection conducted on 04th August 2022.
1.5.6	• You have not mentioned any specifications in this section while the official monograph is available in BP. Revise your specification as per BP monograph along with submission of applicable fee	The firm submitted that we have performed /develop and submitted its data in 2020 at that time this molecule was not available in BP. It is now available in BP2022 and revised details in this section are submitted. The firm has also submitted Rs. 7500/- on deposit slip No# 97804485326 for revision of specifications
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer issued by relevant regulatory authority of country of origin is required	Firm has submitted copy of GMP certificate in the name of M/s Nantong Chanyoo Pharmatech CO., Ltd., No.2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, P.R. China ***issued by Nantong Chemical & Medical Industry Association China*** valid upto 21-02-2026.
3.2.S.4	• Manufacturer specification are claimed for the drug substance by drug substance manufacturer while the official monograph is available in BP. Justification shall be submitted. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy	• The firm submitted that at the time of development 2020, the product was not included in any official monograph that's why manufacturer provided data on manufacturer specification. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance by Drug Product manufacturer is not submitted • Analytical Method Verification studies including specificity,

	and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance is not submitted.
3.2.P.5.1	• This section has mentioned in-house specifications while the official monograph of the applied formulation is available in BP. Revise your specifications and analytical procedure as per BP monograph. • Justification is required since the limits of submitted dissolution specification and assay specification for shelf life provided by the drug product manufacturer (NLT 75% Q in 30 minutes, 90-110%) are different from official BP monograph (Q = 70% after 45 minutes, 95-105%). • Submit method verification studies for applied product as per BP monograph	• The firm has submitted revised specifications and analytical procedure as BP monograph • The firm submitted that for limits of dissolution and assay specifications, testing method is revised along with the limits of assay and dissolution. • Method verification studies for applied product as per BP method is not submitted
3.2.P.6	• COA of primary / secondary reference standard including source and lot number shall be provided.	• COA of primary / secondary reference standard including source and lot number is submitted
3.2.P.8	• Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• The firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Decision: Approved with BP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration leter will be issued upon submission of following:**
  - **Specifications, analytical procedures and analytical method verification studies for both drug substance and drug product as per BP monograph of Ticagrelor and Ticagrelor Tablet respectively, from M/s Macter International Limited**
  - **Fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

Case No. 04: Deferred cases of Human Drugs on form 5F (Local)

78.	Name, address of Applicant / Marketing Authorization Holder	M/s Axis Pharmaceuticals., 3-B Value Addition City, 1.5 Km Khurrianwala – Sahianwala Road, Faisalabad – Pakistan
	Name, address of Manufacturing site.	M/s Axis Pharmaceuticals., 3-B Value Addition City, 1.5 Km Khurrianwala – Sahianwala Road, Faisalabad – Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25932 dated: 17-09-2021
	Details of fee submitted	PKR 30,000/-: 02-09-2021 (deposit slip # 977318003814)
	The proposed proprietary name / brand name	**Monticel Sachet 4mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each sachet contains: Montelukast (as Sodium)……4mg
	Pharmaceutical form of applied drug	Powder for Oral use
	Pharmacotherapeutic Group of (API)	Leukotriene receptor antagonist
	Reference to Finished product specifications	BP specification
	Proposed Pack size	14's and 28's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Singulair (4mg) oral granules USFDA Approved
	For generic drugs (me-too status)	Myteka 4mg Sachet by M/s Hilton Pharma (Reg#039695)
	GMP status of the Finished product manufacturer	Firm has submitted GMP certificate issued on 06-07-2020, based on inspection conducted on 09-06-2020
	Name and address of API manufacturer.	Zhejiang Tianyu Pharmaceutical Co., Ltd., No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China 317016
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Stability studies	Firm has submitted stability study data of 3 batches of API as per zone IV-A conditions Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (11001-161001, 11001-161002, 11001-161003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence and comparative dissolution study against the comparator product i.e. Myteka Sachet 4mg by M/s Hilton Pharma. Pharmaceutical Equivalence have been conducted by performing quality tests (Assay, Dissolution and Uniformity of dosage form). Results of CDP studies have been submitted against the same brand in Pharmacopoeial Media (0.5% SLS) only. Release of both the test and reference product is more than 85% in hence no calculation of f2 factor is required.
	Analytical method validation/verification of product	Firm has submitted report of verification of analytical method for the drug product including specificity, accuracy, and precision.

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Tianyu Pharmaceutical Co., Ltd., No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China 317016		
API Lot No.	11001-201005		
Description of Pack (Container closure system)	Alu – Foil Sachet, packed in carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	T-002	T-003	T-004
Batch Size	300 Sachet	500 Sachet	500 Sachet
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	15-04-2021	20-04-2021	20-04-2021

No. of Batches	03

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate of M/s Zhejiang Tianyu Pharmaceutical Co., Ltd., issued by China Food and Drug Administration valid till 14-03-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of commercial invoice No#TYI21009 dated 29-12-2020 for import of 60kg of Montelukast Sodium attested by AD (I&E) DRAP Lahore.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail reports on product testing
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time)

Remarks of Evaluator [XI]:

Section	Observations	Response
3.2.S.4	• Drug substance manufacturer has stated USP specifications while drug product manufacturer has stated USP/BP specifications, clarify? • Analytical procedure of drug substance by drug substance manufacturer shall be submitted • You have mentioned the use of Montelukast sodium working standard in analytical procedure during preparation of standard solution while pharmacopeia states the use of montelukast dicyclohexylamine reference standard, clarify?	• Analytical method and specifications of montelukast sodium in both pharmacopeia (BP/USP) are same, therefore both standards are mentioned on COA. Evidence is submitted. • Firm has submitted analytical procedure of drug substance by provided drug substance manufacturer • ***The firm submitted that montelukast sodium is readily available as raw material and used as working standard in routine testing after standardization against montelukast dicyclohexylamine (reference standard).***
3.2.S.5	Reference standard is montelukast dicyclohexylamine while working standard is montelukast sodium, clarify?	***Montelukast sodium (working standard) is used in routine testing, which is standardized against montelukast dicyclohexylamine (reference standard).***
3.2.P.2.1	• Clarification is required since the innovator product contain magnesium stearate in addition to other excipients while the applied product does not contain magnesium stearate.	• The firm submitted that magnesium stearate is routinely used as lubricant in oral solid dosage form to improve flow characteristics of the product. ***The drug product is fine granular powder having satisfactory flow characteristics without***

	• Justify why Pharmaceutical equivalence of the applied product has not been performed against the innovator product? • The results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 shall be submitted and discussed	***the use of magnesium stearate. Moreover, addition of magnesium stearate causes haziness in solution prepared after reconstitution as observed in product development phase. That is why, the said excipient was not used.*** • Firm submitted that Pharmaceutical equivalence of the applied product has been performed against comparator product as per DRAP's guidance document (FAQs about form 5F) dated 28-01-21. • The firm submitted that comparative dissolution profile has been conducted in three BCS media (pH 1.2, 4.5 &6.8) and already submitted pharmacopeial method (0.5% SLS) & already submitted. ***Montelukast sodium did not show any response in the stated BCS media across physiological range (pH 1.2, 4.5 & 6.8) therefore it was not applicable to calculate similarity factor in those media (firm has submitted a few chromatograms for evidence). However, in pharmacopeial method both products showed more than 85% dissolution, therefore no calculation was required.***
3.2.P.3.2	The reference formulation states granules for oral suspension for applied formulation. Clarification is required in manufacturing process and process control whether granules will be prepared in-house or otherwise.	The firm submitted that the applied formulation is free flowing granular powder and is completely soluble after reconstitution for use. API is geometrically mixed with other excipients.
3.2.P.5	• You have mentioned the use of Montelukast sodium working standard in analytical procedure during preparation of standard solution while pharmacopeia states the use of montelukast dicyclohexylamine reference standard, clarify?	***The firm submitted that montelukast sodium is readily available as raw material and used as working standard in routine testing after standardization against montelukast dicyclohexylamine (reference standard).***
3.2.P.6	Reference standard is montelukast dicyclohexylamine while working standard is montelukast sodium, clarify?	***Montelukast sodium (working standard) is used in routine testing, which is standardized against montelukast dicyclohexylamine (reference standard).***
3.2.P.8	• Submit 6th month stability study data at both real time and accelerated conditions • Submit readable copy of commercial invoice • Compliance Record of HPLC software 21CFR shall be submitted	• Firm has submitted 6th month stability study data at both real time and accelerated conditions • Firm has submitted readable copy of commercial invoice • The firm has submitted Compliance Record of HPLC software 21CFR

	• Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated conditions)	• Firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated conditions)

Previous Decision (321-DRB): Deferred for Scientific justification for use of Montelukast sodium as reference standard in analytical procedures instead of Montelukast dicyclohexylamine specified by BP monograph.

Evaluation by PEC:

The firm submitted that Montelukast sodium (working standard) is used in routine testing, which is standardized against Montelukast Dicyclohexylamine (reference standard) and submitted Evidence of standardization.

Furthermore, analytical testing of the subjected drug product was performed at 18-month testing using both standards i.e. Montelukast Sodium as well as Montelukast dicyclohexylamine to provide a comparative examination. Analytical Testing Sheet attached herewith.

Result of the assay of all three stability trial batches (T-002, T-003 & T-004) are similar w.r.t. to both standards and are summarized below;

Standard	**Weight Taken**	**Average Area**	**% RSD**	**Retention Time**	**Tailing Factor**
Montelukast Sodium (WS)	20.8 mg (eq. to 20.0 mg Montelukast)	1746539.2	0.44 %	5.8	0.96
Montelukast Dicyclohexylamine (RS)	26.2 mg (eq. to 20.0 mg Montelukast)	1751716.6	0.10 %	5.8	1.04

Trial	**Weight Taken**	**Average Area**	**Assay**	
			w.r.t. Mont. Sodium	**w.r.t. Mont. DCHA**
T-002	500.2 mg	1799961.5	102.45 %	102.48 %
T-003	500.5 mg	1791612.5	101.88 %	101.91 %
T-004	500.4 mg	1805250.5	102.81 %	102.84 %

It can be clearly seen that irrespective of the standard used for analytical testing, the impact on the results is negligible to none. Therefore, it is requested to you to kindly accept the stability data results w.r.t. to montelukast sodium standard and approve registration of our drug product. Moreover, we will assure to use Montelukast Dicyclohexylamine standard when commercialized.

Firm has submitted following details for procurmenet of USP reference standard of Montelukast Dicyclohexylamine:

- Commercial invoice no. 34182376 from USP in name of M/s Axis Pharmaceuticals for Montelukast Dicyclohexylamine (Catalogue# 1446815).
- Airway Bill

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

79.	Name, address of Applicant /	ATCO Laboratories Limited., B-18, S.I.T.E., Karachi

	Marketing Authorization Holder	-7500, Pakistan
	Name, address of Manufacturing site.	ATCO Laboratories Limited., B-18, S.I.T.E., Karachi -7500, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28455 Dated 15/ 10/ 2021
	Details of fee submitted	PKR 30,000/-: Dated 04/10/2021 (Deposit Slip#03634033378)
	The proposed proprietary name / brand name	Ondansetron Tablet 8mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ondansetron……..8mg (as Ondansetron Hydrochloride Dihydrate BP)
	Pharmaceutical form of applied drug	Film coated Tablet
	Pharmacotherapeutic Group of (API)	Antiemetics and antinauseants, Serotonin (5-HT3) antagonists.
	Reference to Finished product specifications	USP
	Proposed Pack size	7's, 10's, 14's, 20's, 28's, 30's.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zofran 8mg film coated tablet MHRA approved
	For generic drugs (me-too status)	Ongene 8mg Tablet by M/s High-Q Pharmaceuticals (Reg#091207)
	GMP status of the Finished product manufacturer	The firm was inspected on 22-03-2022 & 05-04-2022 by the panel for renewal of DML, regularization of section as per layout plan and additional sections and decision of panel is: Keeping in view the good facilities provided for manufacturing and quality control of pharmaceutical products registered in the name of firm being produced at the site and overall good maintenance of plan and the required documentation and SOPs, the panel recommended the grand of DML of the firm as well as regularization of sections as per layout plan and approval of additional sections
	Name and address of API manufacturer.	M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru Rural District-561203 India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD

		template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time:30°C±2°C/75% ± 5%RH Accelerated:40°C±2°C/75%±5%RH Stability of all three batches at accelerated conditions (AOND-17002, AOND-17003, AOND-17004) conducted for 06 months Real time stability study of two batches AOND-17002, AOND-17003, conducted for 36 months while real time stability study of one batch AOND-17004 conducted for 24 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Zofran 8mg Tablet by **GlaxoSmithKline Research Triangle Park, NC 27709** **Marketed by: Novartis Pharmaceuticals UK Limited** performing quality tests (Identification, Assay, Dissolution, disintegration). CDP of ondansetron 8mg tablets has been performed against the zofran 8mg tablets in Acid media (pH 1.2), acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted method verification studies including range, accuracy, precision, specificity and robustness.

STABILITY STUDY DATA	
Manufacturer of API	M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bangaluru Rural District-561203 India
API Lot No.	AOND-20013
Description of Pack (Container closure	ALU-ALU Blister pack packed in unit carton

system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MA089C	MA090C	MA091C
Batch Size	5000 Tablets	5000 Tablets	5000 Tablets
Manufacturing Date	03/2021	03/2021	03/2021
Date of Initiation	25/03/2021	25/03/2021	25/03/2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of Rofl 500mcg tablet on the basis of which Registration Board in its 277th meeting dated 27-29 December, 2017 decided to approve registration of Rofl 500mcg tablet. Inspection date: 10-10-2017 The report shows that: The HPLC software is 21 CFR compliant. Adequate monitoring and control are available for stability chambers
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm have submitted copy of GMP certificate #DCD/SPL.CL-1/CR-1510/2020-21 dated 06-02-2021 of M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru Rural District-561203 India valid upto one year from the date of issue. The firm has submitted copy of DML #DCD/MFG/Applicant Id-240 dated 26/06/2020 of M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bangaluru Rural District-561203 India valid upto 13/02/2025
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice # OND1200 dated 10-11-2020 for import of 300gm of Ondansetron HCl Dihydrate Batch #AOND-20014, AOND-20012 and AOND-20013 in the name of M/s Atco Laboratories Ltd Karachi from M/s Anugraha Chemical India. ***However, the invoice is not attested by AD (I&E) DRAP field office***
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator [XI]:

<table>
<tr><th>Section</th><th>Observations</th><th>Response</th></tr>
<tr><td>1.6.5</td><td>Valid GMP certificate issued by the relevant regulatory authority of country of origin of drug substance manufacturer shall be submitted</td><td>The firm has submitted valid copy of GMP certificate #DCD/SPL-1/CR-1733/2021-22 dated 31-01-2022 of M/s Anugraha Chemicals, D-47, D-48, D-49, D-50 and C-62, KSSIDC, Industrial Estate, Doddaballapur, India valid upto one year from the date of issue.</td></tr>
<tr><td>3.2.S.4</td><td>• Copies of the analytical procedures used for routine testing of the Drug substance / Active Pharmaceutical ingredient by Drug Product manufacturer is required.
• Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.</td><td>• Firm has submitted copy of BP Monograph mentioning the test used for routine testing of the Drug substance / Active Pharmaceutical ingredient by Drug Product manufacturer.
• Firm has submitted analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance.</td></tr>
<tr><td>3.2.P.2</td><td>• Submit compatibility study as the qualitative composition of the applied formulation is not similar to innovator / reference product.
<table>
<tr><td>Applied product</td><td>Zofran 8mg tab</td></tr>
<tr><td>Lactose anhydrous</td><td>Lactose</td></tr>
<tr><td>Sodium starch glycolate</td><td>Microcrystalline Cellulose</td></tr>
<tr><td>Crospovidone</td><td>Pregelatinized maize starch</td></tr>
<tr><td>Magnesium stearate</td><td>Magnesium Stearate,</td></tr>
<tr><td>Opadry white</td><td>Methyl hydroxypropyl cellulose</td></tr>
<tr><td>Purified water</td><td>Titanium dioxide (E171)</td></tr>
<tr><td></td><td>Iron oxide (E172)</td></tr>
</table></td><td>Firm has submitted drug excipient compatibility study and the results show that insignificant variation occurs during compatibility studies. Hence it is concluded that drug is compatible with excipients.</td></tr>
<tr><td>3.2.P.5.1</td><td>Justification for finished product specifications of USP is required as the drug substance has been analysed as per BP specifications by M/s Atco Laboratories.</td><td>The firm submitted that initially at the time of development, we have started the material and product development according to British pharmacopeia monograph. During the development of</td></tr>
</table>

	(drug substance manufacturer given both BP & USP specifications)	product, we found that the drug release of both test and reference sample is greater than 85% within 15 minutes in comparison studies while the time limit mentioned in BP was 45 minutes. We switched to more stringent specification for our products and complies with USP specifications which states that "NLT 80% (Q) of the labeled amount of $C_{18}H_{19}N_3O$ is dissolved in 15 minutes".
3.2.P.8	Submit documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice No. EXP-018 dated 17-08-2021 from M/s Anugraha Chemicals India in the Name of Atco Laboratories Ltd for import of 180gm of Ondansetron Hydrochloride dihydrate batch No AOND-21007 attested by AD (I&E) DRAP Karachi dated 05-09-2021. ***The batch No. of API is different from that submitted in batch analysis of drug substance and stability summary sheets. Furthermore the date of manufacturing of API mentioned in invoice is June 2021 and attestation date of AD (I&E) DRAP Karachi is 5/09/2021 while manufacturing of finished product is 03/2021.***

Previous Decision (321-DRB): Deferred for clarification since batch No. of API mentioned in invoice attested by AD (I&E) DRAP is different from that mentioned in batch analysis of drug substance, BMR and stability summary sheets of drug product

Response by the firm: The firm stated that We would like to submit some pertinent facts as follows, which may supportive for respected Registration Board as well as you to understand the reason of above observation.

- For product development purpose, initially ATCO has arranged Ondansetron drug substance form M/s Anugrha Chemicals, India via our UAE based indenter Pan Golf Sourcing and Trading International on 10-11-2020. This sample was imported by our indenter in Sharja, UAE and then supplied us complementary through courier service. Due to direct courier of material on ATCO premises from Sharja, material was not hold at port for clearance and we forgot to attest the invoice with DRAP ADC.
- We have used this material for product development and further put the 03 development batches for stability studies up to 6 months on accelerated and real time conditions as per requirement of Zone IV-B (each for tablet and syrup). Same stability data as well as material arrangement documents with ADC non-attested invoice were initially submitted with dossier in DRAP. After pre-screening, dossiers were accepted by DRAP and log for further evaluation.
- At the time of dossier compilation before the submission in DRAP, we have already gauged that non-attested ADC invoice issue can be identified during dossier evaluation. Therefore, we have immediately arranged another lot of Ondansetron drug substance from the same manufacturer i.e. M/s Anugrha Chemicals, India with attested ADC invoice.
- We have manufactured another 03 development batches with this material and also re-conducted the stability studies up to 6 months on accelerated and real time conditions as per Zone (IV-B) requirement. (Both for Tablet and Syrup)
- At the time of dossier evaluation, Evaluator has advised us to submit the attested ADC invoice and we have submitted the ADC attested invoice of second supply mentioned Ondansetron Batch#AOND-21007. But the BMR and Stability report which was produced with first supply of Ondansetron Batch#

AOND-20013 were not replaced in dossier. This is the reason for difference in Batch No. of API between the material invoice and product development documents.

- All tracking record for import of first material (API) dated 10-11-2020 which was imported by our UAE based indenter Pan Golf Sourcing and Trading International form M/s Anugrha Chemicals, India has been arranged from indenter and attached along with CoA and un-attested sale invoice for your kind perusal.

The firm submitted that keeping in view the of above facts, you may consider that we have tried our level best to meet all quality requirements for the development and stability studies of ondansetron tablet and syrup. And executed more development work to meet the compliance requirement.

The firm also stated that we would like to share one more point with you that as per current policy of Registration Board, API use for development can be arranged through direct import or may be arranged as a loan / borrow by any other means having all record related to arrangement tracking as well as quality verification.

The firm requested to consider these submissions for further approval of ondansetron tablet and syrup. We assure you that we will be more vigilant in future to meet the compliance as per requirement.

Decision: Approved.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

80.	Name, address of Applicant / Marketing Authorization Holder	ATCO Laboratories Limited., B-18, S.I.T.E., Karachi -7500, Pakistan
	Name, address of Manufacturing site.	ATCO Laboratories Limited., B-18, S.I.T.E., Karachi -7500, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 30933 Dated 11/ 11/ 2021
	Details of fee submitted	PKR 30,000/-: Dated 04/10/2021 (Deposit Slip#65306391198)
	The proposed proprietary name / brand name	Ondansetron Syrup 4mg/5ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Ondansetron……..4mg (as Ondansetron Hydrochloride Dihydrate BP)
	Pharmaceutical form of applied drug	Syrup
	Pharmacotherapeutic Group of (API)	Antiemetics and antinauseants, Serotonin (5-HT3) antagonists.
	Reference to Finished product	USP

	specifications	
	Proposed Pack size	5ml, 15ml, 25ml, 50ml, 60ml, 100ml, 120ml.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zofran Syrup 4 mg/5 ml MHRA approved
	For generic drugs (me-too status)	Dysit 4mg/5ml Syrup by M/s Wimits Pharmaceuticals (Reg#096447)
	GMP status of the Finished product manufacturer	The firm was inspected on 22-03-2022 & 05-04-2022 by the panel for renewal of DML, regularization of section as per layout plan and additional sections and decision of panel is: Keeping in view the good facilities provided for manufacturing and quality control of pharmaceutical products registered in the name of firm being produced at the site and overall good maintenance of plan and the required documentation and SOPs, the panel recommended the grand of DML of the firm as well as regularization of sections as per layout plan and approval of additional sections
	Name and address of API manufacturer.	M/s Anugraha Chemicals, No D-47 to D-50, and C-62 to C-63, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru Rural District-561203 India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time:30°C±2°C/75% ± 5%RH Accelerated:40°C±2°C/75%±5%RH Stability of all three batches at accelerated conditions (AOND-17002, AOND-17003, AOND-17004) conducted for 06 months Real time stability study of two batches AOND-17002, AOND-17003, conducted for 36 months while real time stability study of one batch AOND-17004 conducted for 24 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its

		verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Onseron 4mg/5ml syrup by M/s Indus Pharma (Pvt.) Ltd by performing quality tests (description, Identification, pH, Assay).
	Analytical method validation/verification of product	Firm has submitted method verification studies including range, accuracy, precision, specificity and robustness.

STABILITY STUDY DATA

Manufacturer of API	M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bangaluru Rural District-561203 India		
API Lot No.	AOND-20013		
Description of Pack (Container closure system)	Amber glass bottle packed in printed carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	FE074C	MA077C	MA088C
Batch Size	2000ml	2000ml	2000ml
Manufacturing Date	05/03/2021	05/03/2021	05/03/2021
Date of Initiation	17/03/2021	17/03/2021	17/03/2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of Rofl 500mcg tablet on the basis of which Registration Board in its 277th meeting dated 27-29 December, 2017 decided to approve registration of Rofl 500mcg tablet. Inspection date: 10-10-2017 The report shows that: The HPLC software is 21 CFR compliant. Adequate monitoring and control are available for stability chambers
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm have submitted copy of GMP certificate #DCD/SPL.CL-1/CR-1510/2020-21 dated 06-02-2021 of M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru Rural District-561203 India valid upto one year from the date of issue. The firm has submitted copy of DML #DCD/MFG/Applicant Id-240 dated 26/06/2020 of M/s Anugraha Chemicals, No D-47 to D-50, C-62 and

		C-63, KSSIDC, Industrial Estate, Doddaballapur, Bangaluru Rural District-561203 India valid upto 13/02/2025
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice # OND1200 dated 10-11-2020 for import of 300gm of Ondansetron HCl Dihydrate Batch #AOND-20014, AOND-20012 and AOND-20013 in the name of M/s Atco Laboratories Ltd Karachi from M/s Anugraha Chemical India. ***However, the invoice is not attested by AD (I&E) DRAP field office***
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator [XI]:

Section	Observations	Response
1.6.5	Valid GMP certificate issued by the relevant regulatory authority of country of origin of drug substance manufacturer shall be submitted	The firm has submitted valid copy of GMP certificate #DCD/SPL-1/CR-1733/2021-22 dated 31-01-2022 of M/s Anugraha Chemicals, D-47, D-48, D-49, D-50 and C-62, KSSIDC, Industrial Estate, Doddaballapur, India valid upto one year from the date of issue.
3.2.S.4	• Copies of the analytical procedures used for routine testing of the Drug substance / Active Pharmaceutical ingredient by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	• Firm has submitted copy of BP Monograph mentioning the test used for routine testing of the Drug substance / Active Pharmaceutical ingredient by Drug Product manufacturer. • Firm has submitted analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance.
3.2.P.2	• Submit compatibility study as the qualitative composition of the applied formulation is not similar to innovator / reference product. Applied product: Zofran 4mg/5ml syrup Citric acid monohydrate: Citric acid Sodium citrate dihydrate: Sodium citrate dihydrate	• Firm has submitted drug excipient compatibility study and the results show that insignificant variation occurs during compatibility studies. Hence it is concluded that drug is compatible with excipients. • Firm submitted that Pharmaceutical equivalence studies of test formulation against locally available approved formulation has been performed due to

	<table><tr><td>Sodium benzoate</td><td>Sodium benzoate</td></tr><tr><td>Liquid Sorbitol</td><td>Sorbitol solution</td></tr><tr><td>Sodium Saccharin</td><td>------</td></tr><tr><td>Liquid Glucose</td><td>--------</td></tr><tr><td>Banana Flavour</td><td>Strawberry flavour (contains ethanol*)</td></tr><tr><td>Purified water</td><td>Purified water</td></tr></table> • Justification is required since pharmaceutical equivalence have not been conducted against the innovator product.	unavailability of innovator product in Pakistan with reference to "Decision of 307th and 308th meeting of Drug Registration Board"
3.2.P.5.1	Justification for finished product specifications of USP is required as the drug substance has been analysed as per BP specifications by M/s Atco Laboratories. ***(drug substance manufacturer given both BP & USP specifications)***	The firm submitted that initially at the time of development, we have started the material and product development for tablet dosage form according to British pharmacopeia monograph. Once the material has been established as per BP Specification, parallel development of syrup dosage form started. The syrup formulation is only available in United States Pharmacopeia so we have to develop the specifications of Ondansetron Syrup 4mg/5mL as per USP monograph.
3.2.P.8	Submit documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice No. EXP-018 dated 17-08-2021 from M/s Anugraha Chemicals India in the Name of Atco Laboratories Ltd for import of 180gm of Ondansetron Hydrochloride dihydrate batch No AOND-21007 attested by AD (I&E) DRAP Karachi dated 05-09-2021. ***The batch No. of API is different from that submitted in batch analysis of drug substance and stability summary sheets. Furthermore the date of manufacturing of API mentioned in invoice is June 2021 and attestation date of AD (I&E) DRAP Karachi is 5/09/2021 while manufacturing of finished product is 03/2021.***

Previous Decision (321-DRB): Deferred for clarification since batch No. of API mentioned in invoice attested by AD (I&E) DRAP is different from that mentioned in batch analysis of drug substance, BMR and stability summary sheets of drug product

Response by the firm: The firm stated that We would like to submit some pertinent facts as follows, which may supportive for respected Registration Board as well as you to understand the reason of above observation.

- For product development purpose, initially ATCO has arranged Ondansetron drug substance form M/s Anugrha Chemicals, India via our UAE based indenter Pan Golf Sourcing and Trading International

on 10-11-2020. This sample was imported by our indenter in Sharja, UAE and then supplied us complementary through courier service. Due to direct courier of material on ATCO premises from Sharja, material was not hold at port for clearance and we forgot to attest the invoice with DRAP ADC.

- We have used this material for product development and further put the 03 development batches for stability studies up to 6 months on accelerated and real time conditions as per requirement of Zone IV-B (each for tablet and syrup). Same stability data as well as material arrangement documents with ADC non-attested invoice were initially submitted with dossier in DRAP. After pre-screening, dossiers were accepted by DRAP and log for further evaluation.
- At the time of dossier compilation before the submission in DRAP, we have already gauged that non-attested ADC invoice issue can be identified during dossier evaluation. Therefore, we have immediately arranged another lot of Ondansetron drug substance from the same manufacturer i.e. M/s Anugrha Chemicals, India with attested ADC invoice.
- We have manufactured another 03 development batches with this material and also re-conducted the stability studies up to 6 months on accelerated and real time conditions as per Zone (IV-B) requirement. (Both for Tablet and Syrup)
- At the time of dossier evaluation, Evaluator has advised us to submit the attested ADC invoice and we have submitted the ADC attested invoice of second supply mentioned Ondansetron Batch#AOND-21007. But the BMR and Stability report which was produced with first supply of Ondansetron Batch# AOND-20013 were not replaced in dossier. This is the reason for difference in Batch No. of API between the material invoice and product development documents.
- All tracking record for import of first material (API) dated 10-11-2020 which was imported by our UAE based indenter Pan Golf Sourcing and Trading International form M/s Anugrha Chemicals, India has been arranged from indenter and attached along with CoA and un-attested sale invoice for your kind perusal.

The firm submitted that keeping in view the of above facts, you may consider that we have tried our level best to meet all quality requirements for the development and stability studies of ondansetron tablet and syrup. And executed more development work to meet the compliance requirement.

The firm also stated that we would like to share one more point with you that as per current policy of Registration Board, API use for development can be arranged through direct import or may be arranged as a loan / borrow by any other means having all record related to arrangement tracking as well as quality verification.

The firm requested to consider these submissions for further approval of ondansetron tablet and syrup. We assure you that we will be more vigilant in future to meet the compliance as per requirement.

Decision: Approved.

- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case No. 05: Deferred cases of Human Drugs on form 5F import

81.	Name, address of Applicant / Importer	M/s AMB HK ENTERPRISES (PVT) LTD., 2nd Floor, Plaza 60, Commercial, Block-K, Phase 1 DHA Lahore
	Details of Drug Sale License of importer	**License No:** 05-352-0058-066904D **Address:** 2nd Floor, Plaza 60, Commercial Block-K, Phase 1 DHA Lahore **Address of Godown:** NA **Validity:** 24-02-2023.

		Status: License to sell drugs as distributor **Renewal:** NA
	Name and address of marketing authorization holder (abroad)	Hainan Brilliant Pharmaceutical Co., Ltd., 4 Medicine Valley, No. 1 Road, Haikou National High-tech Development Zone, Haikou City, China.
	Name, address of manufacturer(s)	Hainan Brilliant Pharmaceutical Co., Ltd., No. 4 Fist Road of Yaogu, Haikou National High-tech Industrial Development Zone, Haikou City, Hainan Province, China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original legalized CoPP certificate (No. 20210060) dated 16-04-2021 issued by Hainan Provincial Medical Products Administration China for azithromycin for injection 0.5g. The CoPP confirms that the product strength is not in market of exporting country as well as GMP status of the manufacturing site through periodic inspection every year. The name of importing country on CoPP is mentioned as Pakistan. Furthermore, the CoPP was valid till 15-04-2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted notarized copy of agency agreement from M/s Hainan Brilliant Pharmaceutical Co., Ltd. The letter species that the manufacturer appoints **M/s AMB HK ENTERPRISES Pvt Ltd, Lahore** to register their products in Pakistan. The authorization letter is valid till 22-10-2024. The letter issued for azithromycin for injection 500mg.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 26416: 23-09-2021
	Details of fee submitted	PKR 150,000/-: 29-06-2021 (Slip#306286776760)
	The proposed proprietary name / brand name	**ZITHROBAR INJECTION 500mg**

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Active ingredient Name; Azithromycin Strength; 500mg
	Pharmaceutical form of applied drug	Powder for injection (Lyophillized)
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, Macrolides
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	Rs 215/-
	The status in reference regulatory authorities	ZITHROMAX 500mg for injection USFDA Approved.
	For generic drugs (me-too status)	Azineu 500mg Injection by M/s Neutro Pharma (Reg# 097656)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Zhejiang Goubang Pharmaceutical Co., Ltd., No.6, Weiwu Road, Hangzhou Gulf Shangyu Economic & Technological Development Zone, Zhejiang China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 30 ºC ± 2ºC / 75 ± 5% RH for 24 months while accelerated stability study is conducted at 40 ºC ± 2ºC / 75 ± 5% RH for 06 months. Batch No# (103-180306-11, 103-180307-11, 103-180308-11)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of

		excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence against the innovator product Zithromax 500mg Inj by performing quality test (pH, Water Content, Bacterial Endotoxin, Sterility, Visible particle, Assay).
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Injection Vial made of Middle Borosilicate Glass tubing (10ml) with brominated rubber stopper and caps made of aluminium-polypropylene combinations
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH. ***The real time stability study data is submitted for 18 months only.***

Batch No.	**Mfg. date**	**Batch size**
1905051	05.05.2019	5000 vials
1905091	09.05.2019	5000 vials
1905131	13.05.2019	5000 vials

Remarks of Evaluator [XI]:

Section	**Observations**	**Response**
1.3.3	The submitted CoPP confirms that the product strength is not in market of exporting country, clarify?	The firm submitted clarification from Director Quality Department, Hainan Brilliant Pharmaceutical Co., Ltd and stated that the azithromycin for injection 0.5g has been marketed in China (Exporting Country). The person responsible for the application of CoPP misunderstood he exporting country was referring to Pakistan thus ticked wrong column in CoPP.
1.5.2	Strength of Active ingredient shall be stated clearly. In case API is in the form of salt / hydrate, specify the equivalent strength of the base e.g., AAA sodium 50 mg (equivalent to AAA) etc.	The firm have submitted the label claim as: Each vial contains: Azithromycin as dihydrate…….500mg
1.5.15-1.5.20	Commitments must be submitted by applicant (marketing authorization Holder) instead of manufacturer	The firm has submitted commitments as per guidance document
1.6.5	Valid GMP certificate / DML of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin is required	The firm has submitted GMP certificate No. ZJ20190170 in the name of M/s Zhejiang Goubang Pharmaceutical Co., Ltd., No.6, Weiwu Road, Hangzhou Gulf

		Shangyu Economic & Technological Development Zone, Zhejiang China valid upto 29/11/2024
3.2.S.4	• Copies of the analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer and drug product manufacturer is required • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	• Copies of the analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer and drug product manufacturer is submitted. • Analytical Method Verification studies including specificity, linearity range, precision, accuracy, solution stability and robustness performed by the Drug Product manufacturer for drug substance(s) is submitted.
3.2.P.5	• You have applied for USP specifications. However, the limits for assay test given in specifications is not according to USP monograph, clarify? ***Release specifications; (103%-113%)*** ***Shelf life specifications; (101%-115%)*** ***Monograph: (90%-110%)*** • Test for uniformity of dosage units is not included in specifications recommended by USP • The chromatographic conditions of the analytical method are different from the USP monograph (mobile phase, injection volume, lambda,	The firm submitted that specification applied for azithromycin for injection 0.5g is in-house specification rather than USP, so there is difference in specification, test items and chromatographic conditions compared to USP.
3.2.P.8	• Submit stability study data of drug product till the claimed shelf life	The firm have submitted stability study data of three batches. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 65% ± 5% RH for 24 months

Previous Decision (321-DRB): Deferred for following points:

- clarification for not complying USP specifications of finished drug product as USP specifications are more stringent to in-house specifications.
- Whether manufacturing has been done via lyophilization or dry powder filling and relevant manufacturing facility thereof.

Evaluation by PEC:

- The firm has submitted USP specifications for the applied product. The firm has also submitted commitment to provide product according to USP specifications.
- The firm submitted that manufacturing has been done by method of lyophilisation and submitted inspection report for relevant section of manufacturer. The firm has also submitted cGMP certificate No#HI20190027 in name of M/s Hainan Brilliant Pharmaceutical Co., Ltd., 4 Medicine Valley, No. 1 Road, Haikou National High-tech Development Zone, Haikou City, China for lyophilized powder for injection valid upto 28-05-2024

Decision: Deferred for following:

- **Clarification since the Chinese Pharmacopeia doesnot include the test for quantification of impurity E as recommended by USP monograph**

• **Clarification since the limits of assay test given in Chinese Pharmcoapeia i.e. 101-115% is different than that recommended by USP i.e. 90-110%.**		
82.	Name, address of Applicant / Importer	M/s AMB HK ENTERPRISES (PVT) LTD., 2nd Floor, Plaza 60, Commercial, Block-K, Phase 1 DHA Lahore
	Details of Drug Sale License of importer	**License No:** 05-352-0058-066904D **Address:** 2nd Floor, Plaza 60, Commercial Block-K, Phase 1 DHA Lahore **Address of Godown:** NA **Validity:** 24-02-2023. **Status:** License to sell drugs as distributor **Renewal:** NA
	Name and address of marketing authorization holder (abroad)	JARI Pharmaceutical Co., Ltd., 18 Zhenhua Road, Lianyungang City, Jiangsu P.R China, 222006
	Name, address of manufacturer(s)	JARI Pharmaceutical Co., Ltd., 18 Zhenhua Road, Lianyungang City, Jiangsu P.R China, 222006
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized CoPP certificate (No. JS20210117) dated 04-02-2021 issued by Jiangsu drug Administration China for oxaliplatin for injection 50mg. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. The name of importing country on CoPP is mentioned as Pakistan. Furthermore, the CoPP is valid till 03-02-2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted notarized copy of foreign agency agreement dated February 02, 2021 in which M/s JARI Pharmaceutical Co., Ltd., referred to as the manufacturer grants M/s Liaoning Hongyan Pharmaceutical Co., Ltd exclusive right to export and sell all product (Ten (10) in number) including oxaliplatin for injection 50mg in Pakistan. M/s Liaoning Hongyan Pharmaceutical Co., Ltd referred to as exporter grants **M/s AMB HK ENTERPRISES Pvt Ltd, Pakistan** exclusive rights to sell and distribute the products from M/s Liaoning Hongyan Pharmaceutical Co., Ltd in Pakistan which has an understanding with M/s JARI Pharmaceutical Co., Ltd., The agreement shall be effective from date of execution and shall remain in force for five (05) years.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	***☐ Domestic sale*** ***☐ Export sale*** ***☒ Domestic and Export sales***
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 24847: 08-09-2021
	Details of fee submitted	PKR 150,000/-: 26-05-2021 (Slip#076513194992)
	The proposed proprietary name / brand name	Runplatin Injection 50mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Active ingredient Name: Oxaliplatin Strength; 50mg
	Pharmaceutical form of applied drug	Lyophilized powder for Injection
	Pharmacotherapeutic Group of (API)	Not applicable
	Reference to Finished product specifications	Chinese Pharmacopeia
	Proposed Pack size	20 ml
	Proposed unit price	PKR 7700/-
	The status in reference regulatory authorities	GN-OXALIPLATIN oxaliplatin 50 mg powder for injection vial TGA Approved.
	For generic drugs (me-too status)	Oxaliplatino Varifarma Lyophilized Powder for Injection 50mg by M/s Medinet Pharmaceuticals (Reg# '095884)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Kunming Guiyan Pharmaceutical Co., Ltd., Room 706, Integrated Business Building in Jinding Science & technology zone, 690#, Xuefu Road, Kuming, Yunnan, China, 650033
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions.

		The real time stability data is conducted at 25 ºC ± 2ºC / 60 ± 5% RH for 36 months of following batches. Batch No# (L20150613, L20161010, L20161106) Accelerated stability study is conducted at 40 ºC ± 2ºC / 75 ± 5% RH for 06 months of following batches. Batch No# (L20090107, L20090108, L20090109)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability study of drug product.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Not submitted
	Analytical method validation/verification of product	Not submitted
	Container closure system of the drug product	Medium boron silicon glass tube-type vial (20ml), pharmaceutical bromobutyl rubber stopper and caps made of aluminium plastic combination
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40ºC ±2ºC / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30ºC ±2ºC / 75% ± 5% RH. The real time stability study data is submitted for 36 months only.

Batch No.	**Mfg. date**	**Date of initiation**
17101817	02-2017	03-2017
17102517	02-2017	03-2017
18051217	02-2017	03-2017

Remarks of Evaluator [XI]:

Section	**Observations**	**Response**
1.4.1	Applicant needs to clarify whether the applied product (drug product) is intended for sale in domestic market or both for domestic and export market. There is no column for overseas sale	The firm have submitted that applied product is intended both for domestic and export sale
1.5.2	Strength of Active ingredient shall be stated clearly. In case API is in the form of salt / hydrate, specify the equivalent strength of the base e.g., AAA sodium 50 mg (equivalent to AAA) etc.	Each vial contains: Oxaliplatin …….50mg
1.5.5	Indicate Pharmacological class of the API (drug substance) with proper reference. Also, state the WHO ATC	Firm have indicated Pharmacological class of the API (drug substance). Third generation platinum anticancer drug

	code for each distinct therapeutic indication.	ATC Code; L01XA03
1.5.15-1.5.20	Commitments must be submitted by applicant (marketing authorization Holder) instead of manufacturer	Firm have submitted commitment as per guidance document
1.6.5	• The drug substance manufacturer as per section 3.2.S.2 is Kunming Guiyan Pharmaceutical Co., Ltd., Room 706, Integrated Business Building in Jinding Science & technology zone, 690#, Xuefu Road, Kuming, Yunnan, China, 650033 while you have written JARI Pharmaceutical Co., Ltd., 18 Zhenhua Road, Lianyungang City, Jiangsu P.R China, 222006 China in this section, clarify? • Submit GMP certificate of drug substance manufacturer	• The firm submitted that drug substance manufacturer is Kunming Guiyan Pharmaceutical Co., Ltd., Room 706, Integrated Business Building in Jinding Science & technology zone, 690#, Xuefu Road, Kuming, Yunnan, China, 650033 and it was a mistake at their end by writing wrong name of manufacturer • The firm has submitted copy of GMP certificate No. YN20170040 in the name of M/s Kunming Guiyan Pharmaceutical Co., Ltd., Inside Kunming Precious Metals Research Institute, No. 988, Keji Road, High-tech Development Zone, Kunming City China valid upto 24/12/202
3.2.S.4	• Test for content of platinum is not included in specifications although recommended by USP • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both drug substance manufacturer and Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted. • Test results of Batch analysis are submitted as per USP specifications. However, the specifications of applied product are given according to EP, clarify?	• We refer to EP, content of platinum is not included in EP specifications • Firm have submitted copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient Drug Product manufacturer. ***Copies of Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is not submitted*** • ***Analytical Method Verification studies is not submitted as per requirement*** • The firm submitted batch analysis of drug substance as per EP.
3.2.S.8	Justify why stability study data of different batches of drug substance conducted at accelerated and real time conditions is submitted.	Firm have submitted long term stability study data at 25 ºC ± 2ºC / 60 ± 5% RH for 36 months of same batches for which stability study data at accelerated conditions is submitted. Batch No# (L20090107, L20090108, L20090109)
3.2.P.2	• Reference product has used lactose monohydrate while you have use lactose in composition of applied product, clarify?	• The firm submitted that through conversion lactose content is consistent with reference product

	• Submit Pharmaceutical equivalence of the applied product against the innovator product	• ***The firm submitted pharmaceutical equivalence of applied product with product of Jiangsu Hengrui Pharmaceutical Co., Ltd***
3.2.P.5	• Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug product shall be submitted.	Firm have submitted Analytical Method Verification studies including specificity, and repeatability (method precision). ***However, results of accuracy test is still not submitted***
The firm has applied for Chinese pharmacopeia specifications while the monograph for the applied product is available in USP and the limits of tests of applied product are in line with USP specifications.		

Previous Decision (321-DRB): Deferred for following:

- Submission of Pharmaceutical equivalence studies against the innovator product.
- Submission of Copies of Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer.
- Submission of Analytical Method Verification studies for drug substance
- Submission of results of accuracy test in method verification studies for drug product

Evaluation by PEC:

- The firm has submitted pharmaceutical equivalence of applied product against innovator product Eloxatin Injection Batch No. 1802956 manufactured by M/s Sanofi-Aventis U.S. LLC, Bridgewater, NJ 08807, A SANOFI COMPANY 2020 sanofi-aventis U.S. LLC.
- Firm has submitted Copies of Drug substance specifications and analytical procedures used for routine testing of the Drug substance by Drug substance manufacturer.
- Firm has submitted Analytical Method Verification studies for drug substance
- Firm has submitted results of accuracy test in method verification studies for drug product

Decision: Approved with USP specifications and with following label claim.
Each vial contains:
Oxaliplatin …….50mg

- **Approval is as per Policy for inspection of Manufacturer abroad and verification of local storage facility.**
- **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

Deferred Cases of Paracetamol containing formulations

DRAP Authority in its 147th meeting decided as under:

"In order to ensure the smooth and continuous supply of paracetamol tablets across Pakistan under prevailing circumstances, the Authority, as one-time exercise, approved incentivization to the manufacturers in the form of out-of-queue consideration of applications of registration of:

iii) 01 generic (me-too) molecule on manufacturing and immediate distribution of at least 15,000 packs of paracetamol tablets with pack size of 200 tablets.

iv) *All dosage forms of paracetamol & its combination products with the condition of immediate manufacturing and distribution.*

83.	Name, address of Applicant / Marketing Authorization Holder	M/s Bosch Pharmaceuticals (Pvt.) Ltd., Plot No. 209, Sector 23, Korangi Industrial Area, Karachi
	Name, address of Manufacturing site.	M/s Bosch Pharmaceuticals (Pvt.) Ltd., Plot No. 209, Sector 23, Korangi Industrial Area, Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12642 dated 24/05/2022
	Details of fee submitted	PKR 50,000/-: dated 26/04/2021 PKR 25000/- dated 14/03/2022 (Slip#446590164659)
	The proposed proprietary name / brand name	Bofalgan Plus 1gm / 300mg infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml vial contains: Paracetamol……..……..1000mg. Ibuprofen (as sodium dihydrate)…….300mg
	Pharmaceutical form of applied drug	Infusion
	Pharmacotherapeutic Group of (API)	Other Analgesics and Antipyretics
	Reference to Finished product specifications	Innovator's Specifications.
	Proposed Pack size	1's
	Proposed unit price	As per S.R.O
	The status in reference regulatory authorities	MAXIGESIC IV paracetamol 1000mg and ibuprofen (as sodium dihydrate) 300mg in 100mL solution for infusion vial TGA Approved Combogesic IV 10mg/ml + 3mg/ml [1000mg / 300mg in 100ml] solution for infusion MHRA Approved Combogesic 10 mg/ml Paracetamol + 3 mg/ml Ibuprofen solution for infusion Ireland Approved
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	GMP certificate issued to the firm on 17-07-2020 based on inspection conducted on 26-06-2019.
	Name and address of API manufacturer.	**Paracetamol:** Mallinckrodt Inc. Raleigh Pharmaceutical Plant 8801 Capital Boulevard Raleigh, North Carolina 27616 **Ibuprofen:** **Manufacturing Facility I:** Solara Active Pharma Sciences Limited., Mathur Road, periyakalapet Puducherry 605014, India **Manufacturing Facility II:** Solara Active Pharma Sciences Limited., AI/B, SIPCOT Industrial Complex, Kudikadu Village, Cuddalore 607005 Tamil Nadu India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, impurities, specifications, analytical procedures and its

		verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	**Paracetamol:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months of following batches: Batches; 6088907C189, 0057907C398, 4814907C222 The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for following batches; 005712B026 for 02 years, 7637511C029 for 03years, 554210C126 for 04 years. **Ibuprofen:** Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. ***The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 18months at manufacturing facility I;*** Batches; 3ISH180001, 3ISH180002, 3ISH180003 Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. ***The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 09months at manufacturing facility II;*** Batches; CIBD19001V, CIBD19002V, CIBD19003V,
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that ***is Maxigesic IV Solution for Infusion by M/s AFT Pharmaceuticals New Zealand*** by performing quality tests (description, filled volume, particulate matter, Assay).

	Analytical method validation/verification of product	Firm have submitted analytical method validation studies including accuracy, precision, specificity, linearity and robustness.		
STABILITY STUDY DATA				
Manufacturer of API		**Paracetamol:** Mallinckrodt Inc. Raleigh Pharmaceutical Plant 8801 Capital Boulevard Raleigh, North Carolina 27616 **Ibuprofen:** **Manufacturing Facility I:** Solara Active Pharma Sciences Limited., Mathur Road, periyakalapet Puducherry 605014, India **Manufacturing Facility II:** Solara Active Pharma Sciences Limited., AI/B, SIPCOT Industrial Complex, Kudikadu Village, Cuddalore 607005 Tamil Nadu India		
API Lot No.		Paracetamol; 784520M020 Ibuprofen Sodium dihydrate; CISH210013		
Description of Pack (Container closure system)		Clear Transparent glass vial (100ml) with rubber stopper and dark blue aluminum seal with Bosch logo		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		TR-BFP-02	TR-BFP-03	TR-BFP-04
Batch Size		250 Vials	250 Vials	250 Vials
Manufacturing Date		07-2021	07-2021	07-2021
Date of Initiation		07-2021	07-2021	07-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	No details of previous inspection submitted the firm		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm have submitted copy of CoPP certificate #01-0028-2016-02-ES dated 28/01/2016 of M/s Mallinckrodt Inc. Raleigh Pharmaceutical Plant 8801 Capital Boulevard Raleigh, North Carolina 27616 for Acetaminophen USP / Paracetamol Fine Powder issued by USFDA indicating the GMP compliant status of the manufacturer. The firm have submitted copy of GMP certificate #WC-0126 dated 26/07/2019 of M/s Solara Active Pharma Sciences Limited., R.S.No. 33& 34, Mathur Road, periyakalapet, Puducherry-605014, India ***(for Ibuprofen Sodium Dihydrate)*** issued by Central Drugs Standard Control Organization Ministry of Health and		

		Family welfare India valid upto three years from date of issue. ***This certificate is being issued subject to condition that the firm shall obtain NOC from competent authority, case to case basis, to manufacturer the above mentioned active substance for purpose of export only, as above mentioned active substance are not approved for manufacturer for sale in India***
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice No. 19075278 dated 17/02/2021 in the name of M/s Bosch Pharmaceuticals (Pvt.) Ltd., for import of 1500Kg Paracetamol Fine powder (Batch No 784520M020) from M/s Mallinckrodt Chemical Limited attested by AD (I&E) DRAP Karachi on 22/02/2021. Firm has submitted copy of commercial invoice No. 1107300837 dated 16/04/2021 in the name of M/s Bosch Pharmaceuticals (Pvt.) Ltd., for import of 05Kg Ibuprofen Sodium (Batch No CISH210013) from M/s Solara Active Pharma Sciences Limited manufacturing site II attested by AD (I&E) DRAP Karachi on 29/04/2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets is submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.1	• Submit original fee deposit slip of PKR 25000/-	
1.3.5	• Submit GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years	
1.6.5	• Mention Name and address of API manufacturer (Both paracetamol and Ibuprofen) in this section • Submit Valid GMP certificate / DML of the Drug Substance manufacturer (for ibuprofen) issued by relevant regulatory authority of country of origin. • GMP certificate of manufacturing site I is submitted while API is imported from manufacturing site II	
3.2.S.4	• Copies of specifications and analytical procedure used for routine testing of drug	

	substance paracetamol by drug product manufacturer is required • Analytical method verification studies for paracetamol drug substance by drug product manufacturer is required • Submit Certificate of Analysis (CoA) of the relevant batch used during product development and stability studies from Drug Substance manufacturer. • Copies of specifications and analytical procedure used for routine testing of drug substance Ibuprofen by drug product manufacturer is required • Analytical method validation studies for ibuprofen drug substance by drug product manufacturer is required • Some analytical procedure for ibuprofen drug substance given by drug substace manufacturer is from M/s Shasun chemicals and drugs, clarify? • Submit Certificate of Analysis (CoA) of the relevant batch used during product development and stability studies from Drug Substance manufacturer.	
3.2.S.6	• Reference standard of Ibuprofen drug substance if provided from M/s Shasun chemicals and drugs while Solara Active Pharma Sciences Limited is manufacturer of Ibuprofen, clarify?	
3.2.S.7	• Stability data of paracetamol of different batches at real time and accelerated conditions is submitted clarify?	
3.2.P.1	• Justification is required for not preforming pH test and sterility test in pharmaceutical equivalence as per submitted specification of drug product	
3.2.P.6	• Reference standard of Ibuprofen drug substance if provided from M/s Shasun chemicals and drugs while Solara Active Pharma Sciences Limited is manufacturer of Ibuprofen, clarify?	
3.2.P.8	• Submit 6th month stability study data at both real time and accelerated conditions • Initial page of stability summary sheet containing batch No. of FPP, API, storage conditions, date of manufacturing, date of initiation of stability study is not submitted • Stability data of different batches at real time conditions (TR-BFP-02, TR-BFP-03, TR-BFP-04) and Accelerated conditions (TR-BOINJ-02, TR-BOINJ-04, TR-BOINJ-03) is submitted clarify	

	• Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Decision of 321st meeting of Registration Board:
The Board deferred the case for clarification of the above mentioned points.

Evaluation by PEC:

Section	Observations	Response
1.1	• Submit original fee deposit slip of PKR 25000/-	The firm has submitted original fee challan # 446590164659 of Rs. 25000/- for applied product
1.3.5	• Submit GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years	The firm has submitted cGMP certificate issued on 13th June, 2022 based on inspection conducted on 13-06-2022
1.6.5	• Mention Name and address of API manufacturer (Both paracetamol and Ibuprofen) in this section • Submit Valid GMP certificate / DML of the Drug Substance manufacturer (for ibuprofen) issued by relevant regulatory authority of country of origin. • GMP certificate of manufacturing site I is submitted while API is imported from manufacturing site II	• The firm has mentioned Mention Name and address of API manufacturer (Both paracetamol and Ibuprofen) in this section • The firm have submitted copy of GMP certificate No: K. Dis. No: 12632/D1/4/2020 dated 17-02-2021 of manufacturing sit II of M/s Solara Active Pharma Sciences Limited., AI/B, SIPCOT Industrial Complex, Kudikadu Village, Cuddalore 607005 India issued by Directir of Drugs Control Tamil Nadu India valid upto 31-12-2023.
3.2.S.4	• Copies of specifications and analytical procedure used for routine testing of drug substance paracetamol by drug product manufacturer is required • Analytical method verification studies for paracetamol drug substance by drug product manufacturer is required • Submit Certificate of Analysis (CoA) of the relevant batch used during product development and stability studies from Drug Substance manufacturer. • Copies of specifications and analytical procedure used for routine testing of drug substance Ibuprofen by drug product manufacturer is required • Analytical method validation studies for ibuprofen drug substance by drug product manufacturer is required • Some analytical procedure for ibuprofen drug substance given by drug substance manufacturer is from M/s Shasun chemicals and drugs, clarify?	• Copies of specifications and analytical procedure used for routine testing of drug substance paracetamol by drug product manufacturer is submitted • Analytical method verification studies for paracetamol drug substance by drug product manufacturer is submitted. ***However, results of repeatability (method) precision is not submitted*** • Firm has submitted Certificate of Analysis (CoA) of the relevant batch of paracetamol drug substance used during product development and stability studies from Drug Substance manufacturer. • Copies of specifications and analytical procedure used for routine testing of drug substance Ibuprofen by drug product manufacturer is submitted

	• Submit Certificate of Analysis (CoA) of the relevant batch used during product development and stability studies from Drug Substance manufacturer.	• Analytical method validation studies (including linearity, range, accuracy, precision, specificity, and robustness) for ibuprofen drug substance by drug product manufacturer is submitted • The firm submitted that Shasun Chemical / Solara Active Pharma science is same company as Solara Active Pharma Science are new name of merged entity. The firm has also submitted relevant details from manufacturer. The firm further stated that name change donot have any impact on the manufacturing process, facility, specification and testing method employed for product. • Firm has submitted Certificate of Analysis (CoA) of the relevant batch of Ibuprofen Sodium dihydrate drug substance used during product development and stability studies from Drug Substance manufacturer.
3.2.S.6	• Reference standard of Ibuprofen drug substance is provided from M/s Shasun chemicals and drugs while Solara Active Pharma Sciences Limited is manufacturer of Ibuprofen, clarify?	Firm has submitted Reference standard of Ibuprofen sodium dihydrate drug substance from manufacturer Solara Active Pharma Sciences Limited
3.2.S.7	• Stability data of paracetamol of different batches at real time and accelerated conditions is submitted clarify?	Firm has submitted stability study data of 3 batches of drug substance paracetamol at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months and The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH. Batches; 005712B026, 737511C029, 016713H864. Real time stability study of batch 005712B026 is conducted for 2 years, of batch 737511C029 for three years, of batch 016713H864 for 18 months
3.2.P.1	• Justification is required for not preforming pH test and sterility test in pharmaceutical equivalence as per submitted specification of drug product	The firm submitted that pharmaceutical equivalence is performed as per specifications (Description, filled volume, particulate matter, assay) and stated that they also performed pH and sterility simultaneously and now have incorporated required information in

		pharmaceutical equivalence protocol and record.
3.2.P.6	• Reference standard of Ibuprofen drug substance if provided from M/s Shasun chemicals and drugs while Solara Active Pharma Sciences Limited is manufacturer of Ibuprofen, clarify?	Firm has submitted Reference standard of Ibuprofen sodium dihydrate drug substance from manufacturer Solara Active Pharma Sciences Limited
3.2.P.8	• Submit 6th month stability study data at both real time and accelerated conditions • Initial page of stability summary sheet containing batch No. of FPP, API, storage conditions, date of manufacturing, date of initiation of stability study is not submitted • Stability data of different batches at real time conditions (TR-BFP-02, TR-BFP-03, TR-BFP-04) and Accelerated conditions (TR-BOINJ-02, TR-BOINJ-04, TR-BOINJ-03) is submitted clarify • Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• Firm has submitted 6th month stability study data at both real time and accelerated conditions • Firm has submitted Initial page of stability summary sheet containing batch No. of FPP, API, storage conditions, date of manufacturing, date of initiation of stability study • The firm submitted that we regret for typographical error on accelerated condition stability summary sheet batch No has been corrected as real time conditions (TR-BFP-02, TR-BFP-03, TR-BFP-04). • Firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Therapeutic indications

Maxigesic® IV is indicated in adults for the relief of mild to moderate pain and the reduction of fever, where an intravenous route of administration is considered clinically necessary.

Dose and method of administration

Administer one vial (100 mL) Maxigesic® IV as a 15-minute infusion every 6 hours, as necessary. Do not exceed a total daily dose of 4000 mg (4 g) paracetamol.

Decision: Approved.

- **Registration Board directed the firm to submit results of repeatability (method precision) test for drug substance paracetamol and submit data before issuance of registration letter.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Deferred case of New Section:

M/s Invictus Pharmaceuticals Plot No. 21 & 26, Street No. NS-2, RCCI, Industrial Estate, Rawat".

The Central Licensing Board in its 273rd meeting held on 15th January, 2020 has considered and approved the following three (03) sections of "M/s Invictus Pharmaceuticals Plot No. 21 & 26, Street No. NS-2, RCCI, Industrial Estate, Rawat" under Drug Manufacturing License No. 000892 (Formulation) vide approval letter No. F. 1-37/2016-Lic (Vol-I) dated 18th February 2020.

S No.	Section
1.	Dry Powder Injection Section (Cephalosporine)
2.	Dry Powder for suspension Section (Cephalosporine))

3.	Capsule Section (Cephalosporine)

Following applications have been submitted for registration by the firm.

84.	Name, address of Applicant / Marketing Authorization Holder	Invictus Pharmaceuticals., NS2, Rawalpindi, Rawat Industrial Estate, Islamabad, Rawalpindi, Islamabad Capital Territory
	Name, address of Manufacturing site.	Invictus Pharmaceuticals., NS2, Rawalpindi, Rawat Industrial Estate, Islamabad, Rawalpindi, Islamabad Capital Territory
	Status of the applicant	☒ Manufacturer ☐ Importer ☐Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23341 dated 26-08-2021
	Details of fee submitted	PKR 30,000/-: dated 26-07-2021
	The proposed proprietary name / brand name	Cef-Vic 400mg capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Cefixime as Trihydrate…….400mg
	Pharmaceutical form of applied drug	White to off white powder filled in Size “0” Shell and packed in Alu-Alu pack of 5’s.
	Pharmacotherapeutic Group of (API)	Cephalosporin Antibiotic
	Reference to Finished product specifications	Innovator specifications
	Proposed Pack size	Alu/Alu of Pack size of 5’s.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cefixime 400mg Capsule by M/s Alkem Labs Ltd USFDA approved
	For generic drugs (me-too status)	Cebosh 400mg Capsule by M/s Bosch Pharmaceuticals (Reg# 027160)
	GMP status of the Finished product manufacturer	New section
	Name and address of API manufacturer.	Pharmagen Limited., Kot Nabi Bukshwala, 34 Km Ferozepur Road, Lahore. Tel: +92 (042) 5935261-68 Fax: +92 (042) 5935269 E-mail: pblbd@hotmail.com Web: www.pharmagen.com.pk
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form,

		manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 36 months.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence and comparative dissolution profile against the product Cefspan Capsule 400mg by M/s Barrett Hodgson (Pvt) Ltd
	Analytical method validation/verification of product	Not submitted

STABILITY STUDY DATA	
Manufacturer of API manufacturer	Pharmagen Limited., Kot Nabi Bukshwala, 34 Km Ferozepur Road, Lahore. Tel: +92 (042) 5935261-68 Fax: +92 (042) 5935269 E-mail: pblbd@hotmail.com Web: www.pharmagen.com.pk
API Lot No.	00243/078/2020
Description of Pack (Container closure system)	The granular dry powder for capsule will be filled in a Size "0" Empty Hard Gelatin Shell and blistered in Alu/Alu of Pack size of 5's.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	Tc-001	Tc-002	Tc-003
Batch Size	2500	2500	2500
Manufacturing Date	05-20	05-20	05-20
Date of Initiation	13-05-20	13-05-20	13-05-20
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s Pharmagen Limited issued on 11.01.2019 based on inspection conducted on 08.01.2019
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not Applicable
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC [XI]:

Section	Observations	Response
1.3.3	Specify the status of applicant as you have submitted that applicant "Is involved in none of the above (contract giver)" in module 1 of form 5F	The firm have submitted revised form 5-F and specified the status of applicant as "manufacturer"
1.3.1.-1.3.2	The address mentioned in submitted application is different from the address mentioned on DML, clarify?	The firm have submitted revised form 5-F and corrected the address as per DML
1.5.6	In Form 5F you have mentioned innovator's specifications for the product under section 1.5.6. while the monograph of applied product is available in JP, clarify?	***The firm have revised the specifications to JP specifications***
2.3.	Submit module 2 as per WHO QOS-PD template without referring to any annexure of Module III.	Firm have submitted module 2 as per WHO QOS-PD template

<table>
<tr><td>3.2.S.4.1.</td><td>As per the drug substance specifications of the drug substance manufacturer i.e. M/s Pharmagen Limited, the firm submitted that material complies BP, USP and in-house specifications, justification is required as how the drug substance follow all the specifications</td><td>The firm have submitted certificate of analysis of drug substance in which the drug substance follows USP specifications</td></tr>
<tr><td>3.2.S.4.1. - 3.2.S.4.2</td><td>Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required.</td><td>Drug substance specification and analytical procedure of Invictus Pharmaceuticals is provided. However, the analytical procedure does not contain procedure for identification test (IR), pH, water content and specific rotation as recommended by USP and contain only procedure for assay test.</td></tr>
<tr><td>3.2.S.4.3</td><td>Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer drug substance(s) shall be submitted.</td><td>No reply submitted</td></tr>
<tr><td>3.2.S.4.4</td><td>The Batch No. mentioned in batch analysis by drug substance manufacturer is 00243/078/2020 while the Batch No. mentioned in batch analysis by drug product manufacturer 00243/264/2020, clarify?
Furthermore, COA submitted by the drug substance manufacturer and drug product manufacturer shows that micronized cefixime was used in formulation of cefixime capsule, clarify?</td><td>The firm submitted that batch No. of the drug substance cefixime used is 00243/078/2020 and submitted COA of drug substance from drug substance manufacturer and drug product manufacturer. The firm further stated that compacted cefixime is used in formulation of cefixime capsule as depicted in COA. However, COA of same batch number of API was submitted for micronized form of cefixime previously.</td></tr>
<tr><td>3.2.P.1</td><td>• The composition of applied product is not as per innovator’s product, clarify
<table>
<tr><td>Applied product</td><td>SUPRAX 400mg capsules</td></tr>
<tr><td>Cefixime trihydrate</td><td>Cefixime trihydrate</td></tr>
<tr><td>Colloidal silicon dioxide</td><td>Colloidal silicon dioxide</td></tr>
<tr><td></td><td>Crospovidone</td></tr>
<tr><td>Microcrystalline cellulose 102</td><td>Low Substituted Hydroxy Propyl Cellulose,</td></tr>
<tr><td>Magnesium Stearate,</td><td>Magnesium Stearate,</td></tr>
</table></td><td>• The response is submitted in subsection 3.2.P.2.1.1
• Quantity of cefixime per unit dose and per batch have been explained and justified based upon the salt factor calculation and assay results. The justification is submitted.
• Firm has used the theoretical factor for adjustment of water content while dispensing, instead of the actual results of “water content test” reported in the drug substance analysis.
• The firm submitted that we have used no overages in our formulation</td></tr>
</table>

	<table><tr><td>EHG Capsule shell '0' size</td><td>Mannitol</td></tr><tr><td></td><td></td></tr></table> • Quantity of cefixime per unit dose shall be justified with equivalency factor for cefixime trihydrate. • You have mentioned the use of overages in your formulation to compensate the potency of the product during process loss, justify?	
3.2.P.2.2.1	• Firm has performed pharmaceutical equivalence against the product Cefspan Capsule 400mg by M/s Barrett Hodgson (Pvt) Ltd. Justification is required as comparator product fails the dissolution test, then how product is pharmaceutical equivalent. ***(Limit NLT 80%, test result 69.82%.)*** • Time point for CDP conducted is 30, 45, 60min. 15 min time point is not considered being necessary as per WHO guidelines.	• Firm has again submitted pharmaceutical equivalence of applied product against the product Cefspan Capsule 400mg by M/s Barrett Hodgson (Pvt) Ltd and the results of tests are within range. • ***No reply submitted***
3.2.P.2.1.1	Compatibility studies of the Drug Substance(s) with excipients shall be provided as the qualitative composition of the formulation is not similar to innovator / reference product.	The firm have submitted that applied formulation contains colloidal silicon dioxide, magnesium stearate and microcrystalline cellulose as per reference formulation. The stability studies of the product show that all the test, physical appearance dissolution and assay are within limits and there are no changes developed during stability.
3.2.P.5.2	• Provide signed copy of analytical methods used for applied product • Justification for proposed analytical procedure is required as the official monograph is available in JP • The firm have proposed UV spectrophotometric method for assay of drug product while the JP monograph recommends HPLC for assay analysis	• The firm submitted that product complies JP specifications and analytical method and JP monograph is submitted. ***However, JP monograph for applied product was not submitted and analytical was submitted only for assay test and dissolution test.*** • The firm submitted that there was a typographical mistake we have use the submitted method and HPLC chromatograms are attached. ***However, no chromatograms were submitted***
3.2.P.5.4	• In finished product specifications under section 3.2.P.5.1 you have applied in house specifications while in Batch Analyses you confirmed that product complies with USP specifications, clarify?	The firm submitted that product complies JP specifications and stated that JP monograph is attached. ***However, no JP monograph was submitted***
3.2.P.6	• The working standard used during analysis states that it should be used before July 2020 while 3rd month stability study performed in august 2020 and 6th month stability study performed at November 2020 using the same working standard	• The firm have submitted valid COA of working standard. • The firm have submitted COA of primary reference standard and standardization of working standard has been performed against the same primary reference standard.

	• The firm have provided COA of primary reference standard for drug substance analysis and COA of working standard. However, the standardization of working standard is performed with other Reference Standards, the COA of which is not provided	
3.2.P.8	• Submit Raw data sheets, COA & analytical record for both assay & dissolution test containing detail of sample preparation, standard preparation for various performance parameters. • The date of initiation mentioned in stability study is 13.05.2020 while the date of manufacturing mentioned in BMR is 18.05.2021. Clarify how stability study started before the manufacturing of batch.	• Firm have submitted Raw data sheets, including actual details of sample solution preparation & standard preparation, weight of standard & calculation formula applied for assay test only. ***Raw data sheets and COA for dissolution test containing detail of sample preparation, standard preparation for various performance parameters is not submitted.*** • The firm submitted that there was a typographic mistake. The initiation date is 18-05-2021 as mentioned in BMR

Previous Decision (321-DRB): Deferred for following:

- Submission of analytical procedures & analytical record for testing of the Drug substance by Drug Product manufacturer as per USP monograph.
- Submission of Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) for drug substance performed by the Drug Product manufacturer
- Justification how same batch of drug substance (Batch No. 00243/078/2020) is used both as compacted and micronized.
- Submission of CDP as per WHO guidelines against innovator product
- Revision of specification as approved by Registration Board in its 313th meeting and notified vide letter No. F.14-I/2022-PEC dated 14th March 2022.
- Performance of batch analysis as per the monograph approved by Registration Board in its 313th meeting and notified vide letter No. F.14-I/2022-PEC dated 14th March 2022.

Evaluation by PEC:

- Firm has submitted analytical procedures and COA of Drug substance for testing of the Drug substance by Drug Product manufacturer as per USP monograph
- Firm has submitted Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) for drug substance performed by the Drug Product manufacturer
- The firm submitted that batch Number of Drug substance used is 00244/078/2020 of cefixime compacted. Firm has submitted COA of Drug substance manufacturer and drug product manufacturer
- Firm has submitted dissolution instead of CDP
- Firm has not submitted revised specification as approved by Registration Board in its 313th meeting and notified vide letter No. F.14-I/2022-PEC dated 14th March 2022.
- Firm has not submitted performance of batch analysis as per the monograph approved by Registration Board in its 313th meeting and notified vide letter No. F.14-I/2022-PEC dated 14th March 2022.

Decision: Approved with manufacturer specifications as approved by Registration Board in its 313th meeting and notified vide letter No. F.14-I/2022-PEC dated 14th March 2022.

Registration Board further decided that registration letter will be issued upon submission of following:

- **Performance of analysis as per the monograph approved by Registration Board in its 313th meeting and notified vide letter No. F.14-I/2022-PEC dated 14th March 2022 before issuance of registration letter.**
- **CDP studies with sampling time points as recommended by relevant guidelines.**

- **Fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

Case No. 06: Routine application of Human Drugs on Form 5

85.	Name and address of manufacture / Applicant	M/s Iqra Pharmaceuticals., Plot No. 02, Street No. S-9, Natic Industrial Zone, Rawat, Islamabad, Pakistan
	Brand Name + Dosage Form and Strength	Pilzide 600mg Tablet
	Composition	Each Film Coated Tablet Contains: Linezolid……..…600mg
	Dairy No. date of R &I fee	Form-5 Dy.No 15573 dated 07-03-2019 Rs.20,000/- Dated 07 03-2019
	Pharmacological Group	Oxazolidinone Antibiotic
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	12's; As per SRO
	Approval status of product in Reference Regulatory Authorities	ZYVOX 600mg film coated Tablets USFDA Approved.
	Me-too-status	Nezocin Tablets 600mg by M/s Brookes Pharmaceuticals (Reg No.55005)
	GMP Status	New License (inspection dated 19-02-2019 the panel unanimou recommends the grant of DML)
	Remark of the Evaluator [XI]	• The firm submitted revised master formulation and removed addition of overage along with undertaking at the end of for signed by the technical persons
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500/- correction/pre-approval change/ in product specifications, as per notification No.F.7-11/20 B&A/DRAP dated 13-07-2021.	
86.	Name and address of manufacture / Applicant	M/s Iqra Pharmaceuticals., Plot No. 02, Street No. S-9, Natic Industrial Zone, Rawat, Islamabad, Pakistan
	Brand Name + Dosage Form and Strength	Biopride 50mg Tablets
	Composition	Each Film Coated Tablet Contains: Itopride HCl…….50mg
	Dairy No. date of R &I fee	Form-5 Dy.No 15568 dated 07-03-2019 Rs.20,000/- Dated 07 03-2019
	Pharmacological Group	Propulsives
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Ganaton 50mg film coated tablet (PMDA) Japan Approved
	Me-too-status	Xepride tablet 50mg of M/s Usawa Pharmaceuticals (Reg. # 076818)
	GMP Status	New License (inspection dated 19-02-2019 the panel unanimou recommends the grant of DML)
	Remark of the Evaluator [XI]	•
	Decision: Approved with innovator's specifications. Firm shall submit the fee of Rs. 7,500/- correction/pre-approval change/ in product specifications, as per notification No.F.7-11/20 B&A/DRAP dated 13-07-2021.	

87	Name and address of manufacture / Applicant	M/s Iqra Pharmaceuticals., Plot No. 02, Street No. S-9, Natio Industrial Zone, Rawat, Islamabad, Pakistan
	Brand Name + Dosage Form and Strength	Mcam 7.5mg Tablets
	Composition	Each Tablet Contains: Meloxicam…….7.5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 15514 dated 07-03-2019 Rs.20,000/- Dated 07 03-2019
	Pharmacological Group	Non-steroidal anti-inflammatory drugs (NSAIDs)
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's, 2x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	MOBIC (7.5mg, 15mg) uncoated Tablets USFDA Approved
	Me-too-status	Melflam 7.5mg Tablets by M/s Aries Pharmaceuticals (Reg#84265)
	GMP Status	New License (inspection dated 19-02-2019 the panel unanimou recommends the grant of DML)
	Remark of the Evaluator [XI]	
	Decision: Approved.	
88	Name and address of manufacture / Applicant	M/s Iqra Pharmaceuticals., Plot No. 02, Street No. S-9, Natio Industrial Zone, Rawat, Islamabad, Pakistan
	Brand Name + Dosage Form and Strength	Airmax 5mg Tablet
	Composition	Each Film Coated Tablet Contains: Montelukast Sodium Eq. to Montelukast…….5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 15616 dated 07-03-2019 Rs.20,000/- Dated 07 03-2019
	Pharmacological Group	Leukotriene receptor antagonists
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x14's, 3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Singulair (4mg, 5 mg) Chewable Tablet USFDA Approved
	Me-too-status	Nohist Chewable Tablet 5mg by M/s Bio-Mark Pharmaceutica (Reg.# 85712)
	GMP Status	New License (inspection dated 19-02-2019 the panel unanimou recommends the grant of DML)
	Remark of the Evaluator [XI]	• The firm revised the formulation from film coated tablets chewable tablets without submission of applicable fee. The f submitted revised form 5 and master formulation. The revi label claim is as under: Each chewable Tablet Contains: Montelukast Sodium Eq. to Montelukast…….5mg
	Decision: Approved with following label claim: **Each chewable Tablet Contains:** **Montelukast Sodium Eq. to Montelukast…….5mg** **Firm shall submit the fee of Rs. 30,000/- for correction/pre-approval change in composit (correction/change of formulation from from film coated to chewable tablets), as per notificat No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
89	Name and address of manufacture / Applicant	M/s Iqra Pharmaceuticals., Plot No. 02, Street No. S-9, Natio Industrial Zone, Rawat, Islamabad, Pakistan

	Brand Name + Dosage Form and Strength	Q-Flam 50mg Tablet
	Composition	Each Film Coated Tablet Contains: Diclofenac potassium…….50mg
	Dairy No. date of R &I fee	Form-5 Dy.No 15517 dated 07-03-2019 Rs.20,000/- Dated 07 03-2019
	Pharmacological Group	NSAID
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	2x10's, 3x10's;As per SRO
	Approval status of product in Reference Regulatory Authorities	Diclofenac potassium 50mg Film Coated Tablets MHRA Approved.
	Me-too-status	Kalfen 50mg tablets by M/s Candid Pharmaceuticals (Reg#100912)
	GMP Status	New License (inspection dated 19-02-2019 the panel unanimou recommends the grant of DML)
	Remark of the Evaluator [XI]	•
	Decision: Approved with change of brand name.	

Deferred cases of Human Drugs on Form 5

90.	Name and address of manufacture / Applicant	M/s Efroze Chemical Industries Pvt Ltd. 146/23, Korangi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Dufanor 10mg Tablet
	Composition	Each Film Coated Tablet Contains: Dydrogesterone……..…10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11400 dated 05-03-2019 Rs.20,000/- 05-03-2019
	Pharmacological Group	Progestogens
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	20's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Duphaston 10mg film-coated tablets by M/s Mylan IRE Healthcare Limited (Ireland Approved)
	Me-too-status	Dydrstone 10mg Tablet by M/s Pharmasol (Pvt) Ltd (Reg#096477)
	GMP Status	GMP certificate issued to Efroze Chemical Industries (Pvt.) Ltd on dated 03-05-2020 based on inspection conducted on 17-03-2021
	Previous Remark of Evaluator [XI]	• Dydrogesterone is available as Cis and Trans isomer. The firm did not clarify about the type of isomer that will be used in formulation. (Trans Isomeric Form active) • The firm did not provide evidence of required manufacturing facility / section approval letter for the applied formulation
	Previous Decision (307-DRB)	Deferred for following: • Clarification about the type of isomer of Dydrogesterone that will be used in formulation • Evidence of required manufacturing facility / section from Licensing Division
	Evaluation by PEC	• The firm submitted that they will be using Trans-Isomer of dydrogesterone in their formulation and provided COA of API and GMP certificate of supplier M/s Yangzhou Aurisco Pharmaceutical Co., Ltd China.

		• The firm submitted letter No. F. 2-11/2000-Lic (Vol-V) dated 22nd November 2021 issued by Secretary Central Licensing Board showing the presence of Tablet section (Hormone)
	Previous Decision (316-DRB)	• Deferred for review of submitted COA of Dydrogesterone for compliance against the Pharmacopoeial monograph
	Evaluation by PEC	• The firm submitted that they will be using Trans-Isomer of dydrogesterone in their formulation and provided COA of API from supplier M/s Yangzhou Aurisco Pharmaceutical Co., Ltd China. • The submitted COA states that the API Dydrogesterone conforms to EP10.0 standard. The limits and number of tests are as per European Pharmacopeia monograph
	Decision: Deferred for confirmation of already registered products in section of "Tablet (Hormone) section.)	

91.	Name and address of manufacturer / Applicant	M/s Helix Pharma Pvt Ltd. Hakimsons House, A/56, S.I.T.E Manghopir Road, Karachi, Pakistan By M/s Mediate Pharmaceutical Pvt Ltd. Plot No. 150-151, Sector 24, Korangi Industrial Area, Karchi, Pakistan
	Brand Name +Dosage Form + Strength	Nurosa Injection 10mg/ml
	Composition	Each Vial Contains: Lacosamide…10mg
	Diary No. Date of R& I & fee	Dy. No. 13056 dated 06.03.2019 Rs. 50,000/- dated 05.03.2019
	Pharmacological Group	Other antiepileptics
	Type of Form	Form 5
	Finished Product Specification	The firm has claimed in-house specs.
	Pack size & Demanded Price	1's (20ml); As per SRO
	Approval status of product in Reference Regulatory Authorities.	Vimpat 10 mg/ml solution for infusion (20ml). Approved in MHRA.
	Me-too status	Vimpat 10 mg/ml solution for infusion (20ml). Approved in MHRA.
	GMP status	Inspected on 16.06.2020 with the following conclusion: Keeping in view above mentioned rectification status in Liquid Sterile Ampoule/Infusion/Opthalmic/Otic Section of the firm and positive intention towards improvement, panel unanimously "Recommends the Resumption of production in Liquid Sterile Ampoule/Infusion/Opthalmic/Otic Section".
	Previous Remark of Evaluator (Evaluator PEC-IX)	• The drug product specifications have not been evaluated. • The address in the application is Helix Pharma Pvt Ltd. Hakimsons House, A/56, S.I.T.E Manghopir Road, Karachi, Pakistan, while it is Helix Pharma Pvt Ltd., A/56, S.I.T.E Karachi in the DML. • Stamped signatures of qualified persons are placed in the application.
		• The firm added vial washing, vial sterilization and vial sealing, and packing to the manufacturing outlines along with submission of Rs. 25,000/- fee (challan- 314211675442)
	Previous Decision (317-DRB)	Deferred for:

		• Revision of "Each Vial Contains: Lacosamide…10mg" to "Each ml contains: Lacosamide…10mg". • Submission of differential fee of Rs. 50,000. • Valid contract manufacturing agreement between the contract giver and contract acceptor.
	Evaluation by PEC	• The firm has revised the label claim as: Each ml contains: Lacosamide……10mg • The firm has submitted differential fee Rs. 50000/- on deposit slip No#3596152433. • The firm has submitted copy of contract manufacturing agreement between the contract giver and contract acceptor made on 3rd December 2019 valid for a period of three years from date of agreement.
	Decision: Approved with nnovator's specifications and following label claim: **Each ml contains:** **Lacosamide……10mg**	

Deferred cases of Veterinary Drugs on Form 5

92.	Name and address of manufacture / Applicant	M/s Star Laboratories Pvt Ltd. 23-km, Multan Road, Lahore
	Brand Name+Dosage Form+Strength	Tylexin M powder
	Composition	Each 1000gm powder contains: Doxycycline HCl……200gm Tylosin Tartrate……100gm Bromhexine ……..5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 8164 dated 25-02-2019 Rs.20,000/- 20-02-2019
	Pharmacological Group	Antibiotic & Mucolytic
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	100gm, 500gm, 1000gm; As per SRO
	Me-too-status	T D Shell Water Soluble Powder by M/s. Inshal Pharmaceutical Industries, (Reg#093236)
	GMP Status	Decision of the 270th Meeting of CLB: After thorough discussion/deliberations and recommendation of the panel of experts in its report dated 14-05-2019, the Central Licensing Board decided to: I- Resume production activities in Human Liquid Injection Section (Genera-Ampoule) Only. II- However production will remain suspended in Human Injectable Section (Psychotropic), till the improvements made by the firm, verification by the panel of experts.
	Previous Remark of Evaluator XI	• Letter of deficiencies sent on 29-07-2020 and reminder on 27-01-2021 but no reply received yet • Master formulation is missing, submit accordingly • Manufacturing outline is missing, submit accordingly • You have applied incorrect label claim. The me-too product contains Each 1000gm powder contains: Doxycycline HCl……200gm Tylosin Tartrate……100gm

		Bromhexine HCl…5gm while you have applied for Each ml contains: Doxycycline HCl……200gm Tylosin Tartrate……100gm Bromhexine ……..5mg. Revise the label claim as per available me-too product along with submission of applicable fee.
	Previous Decision (308-DRB)	Deferred for following: • Submission of master formulation of applied product • Submission of manufacturing outline of applied product • Revision of the label claim as per available me-too product along with submission of applicable fee.
	Evaluation by PEC	• The firm has revised label claim as per available me-too along with submission of Rs. 30000/- on deposit slip # 9944140616. The revised label claim is as under: Each 1000gm powder contains: Doxycycline HCl……200gm Tylosin Tartrate……100gm Bromhexine HCl…5gm • The firm has submitted master formulation and manufacturing outline for the applied product. • The firm has submitted cGMP certificate issued on 20-07-2020 base on inspection conducted on 24-01-2020
	Decision: Approved with nnovator's specifications and following label claim: **Each 1000gm powder contains:** **Doxycycline HCl……200gm** **Tylosin Tartrate……100gm** **Bromhexine HCl…5gm**	
93.	Name and address of manufacture / Applicant	M/s Star Laboratories Pvt Ltd.23-km, Multan Road, Lahore
	Brand Name+Dosage Form+Strength	Tylexin powder
	Composition	Each kg contains: Doxycycline HCl……..…200gm Tylosin Tartrate…….100gm Bromhexine ……..20gm
	Dairy No. date of R &I fee	Form-5 Dy.No 8163 dated 25-02-2019 Rs.20,000/- 20-02-2019
	Pharmacological Group	Antibiotic & Mucolytic
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	100gm, 500gm, 1000gm; As per SRO
	Me-too-status	T-DOX Water Soluble Powder by M/s Elegance Pharmaceuticals, (Reg#078285)
	GMP Status	Decision of the 270th Meeting of CLB: After thorough discussion/deliberations and recommendation of the panel of experts in its report dated 14-05-2019, the Central Licensing Board decided to: I- Resume production activities in Human Liquid Injection Section (Genera-Ampoule) Only.

		II- However production will remain suspended in Human Injectable Section (Psychotropic), till the improvements made by the firm, verification by the panel of experts.
	Previous Remark of Evaluator XI	• Letter of deficiencies sent on 29-07-2020 and reminder on 27-01-2021 but no reply received yet • You have applied incorrect label claim. Me-too of applied product shows the hydrochloride salt of Bromhexine while the applied formulation contains the base form of Bromhexine. Clarify or revise the salt form of Bromhexine in the label claim as per available me-too product along with submission of applicable fee. • In label claim you have applied with Doxycycline HCl while in master formulation you have mentioned Doxycycline Hyclate, clarify? Furthermore, in master formulation you have considered the salt factor in case of doxycycline and tylosin which is not as per label claim, clarify?
	Previous Decision (308-DRB)	Deferred for following: • Revision of the label claim as per available me-too product along with submission of applicable fee. • Clarification since firm have mentioned Doxycycline HCl in label claim while Doxycycline Hyclate in master formulation and considered the salt factor in master formulation in case of doxycycline and tylosin which is not as per label claim,
	Evaluation by PEC	• The firm has revised label claim as per available me-too along with submission of Rs. 30000/- on deposit slip # 9144522360. The revised label claim is as under: Each kg contains: Doxycycline HCl……..…200gm Tylosin Tartrate…….100gm Bromhexine HCl……..20gm. • The firm has submitted revised master formulation and mentioned correct salt form of doxycycline and revised the salt factor as per label claim. • The firm has submitted cGMP certificate issued on 20-07-2020 base on inspection conducted on 24-01-2020
	Decision: Approved with nnovator's specifications and following label claim: **Each kg contains:** **Doxycycline HCl……..…200gm** **Tylosin Tartrate…….100gm** **Bromhexine HCl……..20gm.**	
94.	Name and address of manufacture / Applicant	M/s Star Laboratories Pvt Ltd. 23-km, Multan Road, Lahore
	Brand Name+Dosage Form+Strength	Colidox T Powder
	Composition	Each 100g Contains: Doxycycline Hyclate……40gm Tylosin Tartrate……20gm Colistin sulphate……..10gm Bromhexine……..2gm
	Dairy No. date of R &I fee	Form-5 Dy.No 7400 dated 20-02-2019 Rs.20,000/- 20-02-2019
	Pharmacological Group	Antibiotic & Mucolytic
	Type of form	Form 5

	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	100gm, 500gm, 1000gm; As per SRO
	Me-too-status	Brocotyd Powder by M/s Univet Pharmaceutical (Reg#058962)
	GMP Status	Decision of the 270th Meeting of CLB: After thorough discussion/deliberations and recommendation of the panel of experts in its report dated 14-05-2019, the Central Licensing Board decided to: I- Resume production activities in Human Liquid Injection Section (Genera-Ampoule) Only. II- However production will remain suspended in Human Injectable Section (Psychotropic), till the improvements made by the firm, verification by the panel of experts.
	Previous Remark of Evaluator XI	• Letter of deficiencies sent on 29-07-2020 and reminder on 27-01-2021 but no reply received yet • 1st page of form 5 is missing • You have applied incorrect label claim. Me-Too of applied product shows the hydrochloride salt of Bromhexine while the applied formulation contains the base form of Bromhexine. Clarify or revise the salt form of Bromhexine in the label claim and master formulation as per available me-too product along with submission of applicable fee. • Master formulation is missing, submit accordingly • Manufacturing outline is missing, submit accordingly
	Previous Decision (308-DRB)	Deferred for following: • Submission of master formulation of applied product • Submission of manufacturing outline of applied product • Revision of label claim as per available me-too product along with submission of applicable fee.
	Evaluation by PEC	• The firm has revised label claim as per available me-too along with submission of Rs. 30000/- on deposit slip # 5518579780. The revised label claim is as under: Each 100g Contains: Doxycycline Hyclate……40gm Tylosin Tartrate……20gm Colistin sulphate……..10gm Bromhexine HCl……..2gm • The firm has submitted master formulation and manufacturing outline for the applied product. • The firm has submitted cGMP certificate issued on 20-07-2020 base on inspection conducted on 24-01-2020
	Decision: Approved with innovator's specifications and following label claim: **Each 100g Contains:** **Doxycycline Hyclate……40gm** **Tylosin Tartrate……20gm** **Colistin sulphate……..10gm** **Bromhexine HCl……..2gm**	

Case No. 07; Registration application of human drugs on Form 5 whose Replies are not received

95.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Beclonate 200mcg Rotacaps

	Composition	Each rotacap contains: Beclomethasone dipropionate……..…200mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11814 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Other Drugs for Obstructive Airway Diseases, Inhalants (Glucocorticoids)
	Type of form	Form-5
	Finished product specifications	BP
	Pack size and Demand Price	30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Pulvinal Beclometasone Dipropionate 200 micrograms/metered dose inhalation powder (MHRA Approved) ……..as provided by the firm but could not be verified
	Me-too-status	Betatec 200 Rotacaps by M/s Highnoon Laboratories (Reg#43459)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery

		system under defined test conditions (i.e., flow rate, duration). • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink. • Undertaking at the end of form 5 is missing. • The applicant have claimed manufacturer's specifications but the official monograph is available in BP.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
96.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Beclotide 100mcg Rotacaps
	Composition	Each rotacap Contains: Beclomethasone dipropionate…….100mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11813 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Other Drugs for Obstructive Airway Diseases, Inhalants (Glucocorticoids)
	Type of form	Form-5
	Finished product specifications	BP
	Pack size and Demand Price	30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Pulvinal Beclometasone Dipropionate 100 micrograms/metered dose inhalation powder (MHRA Approved) ……..as provided by the firm but could not be verified
	Me-too-status	Betatec 100 Rotacaps by M/s Highnoon Laboratories (Reg#43458)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for

		manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink. • Undertaking at the end of form 5 is missing. • The applicant have claimed manufacturer's specifications but the official monograph is available in BP.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
97.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Beclonate 400mcg Rotacaps
	Composition	Each rotacap contains: Beclomethasone dipropionate……400mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11815 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Other Drugs for Obstructive Airway Diseases, Inhalants (Glucocorticoids)
	Type of form	Form-5
	Finished product specifications	BP
	Pack size and Demand Price	30'S; As per SRO
	Approval status of product in Reference Regulatory Authorities	Pulvinal Beclometasone Dipropionate 400 micrograms/metered dose inhalation powder (MHRA Approved)……..as provided by the firm but could not be verified

	Me-too-status	Betatec 400 Rotacaps by M/s Highnoon Laboratories (Reg#44703)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • Undertaking at the end of form 5 is missing. • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink. • The applicant have claimed manufacturer's specifications but the official monograph is available in BP.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	

98.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Bisonid 400 mcg Rotacaps
	Composition	Each rotacap contains: Budesonide……400mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11810 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Other Drugs for Obstructive Airway Diseases, Inhalants (Glucocorticoids)
	Type of form	Form-5
	Finished product specifications	BP
	Pack size and Demand Price	30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Budesonide 400 Micrograms Dry Powder Inhaler (MHRA Approved) ……..as provided by the firm but could not be verified
	Me-too-status	Budevair 400 Rotacaps by M/s Highnoon Laboratories (Reg#54318)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery

		system under defined test conditions (i.e., flow rate, duration). • Undertaking at the end of form 5 is missing. • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
99.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Bisonid 100 mcg Rota Caps
	Composition	Each rotacap contains: Budesonide……..…100mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11808 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Other Drugs for Obstructive Airway Diseases, Inhalants (Glucocorticoids)
	Type of form	Form-5
	Finished product specifications	BP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Budesonide 100 Micrograms Dry Powder Inhaler (MHRA Approved) ……..as provided by the firm but could not be verified
	Me-too-status	Budevair 100 Rotacaps by M/s Highnoon Laboratories (Reg#54313)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and

		"Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • Undertaking at the end of form 5 is missing. • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
100.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Bisonid 200 mcg Rotacaps
	Composition	Each rotacap contains: Budesonide……..…200mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11809 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Other Drugs for Obstructive Airway Diseases, Inhalants (Glucocorticoids)
	Type of form	Form-5
	Finished product specifications	BP
	Pack size and Demand Price	30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Budesonide 200 Micrograms Dry Powder Inhaler (MHRA Approved) ……..as provided by the firm but could not be verified
	Me-too-status	Budevair 200 Rotacaps by M/s Highnoon Laboratories (Reg#54312)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.

	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • Undertaking at the end of form 5 is missing. • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
101.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Bisonid-F 100mcg/6mcg Rotacaps
	Composition	Each rotacap contains: Budesonide……..100mcg Formoterol fumarate…..…6mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11811 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Adrenergics, Inhalants (Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics)
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Symbicort 100mcg/6mcg Turbohaler, Inhalation Powder (MHRA Approved)

	Me-too-status	Combivair 100 Rotacaps by M/s Highnoon Laboratories (Reg#054311)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • The reference formulation have mentioned the hydrated form (dihydrate) of Formoterol fumarate in the label claim while you have not mentioned the hydrated form. Revise the label claim as per reference formulation mentioning the hydrated form along with submission of applicable fee.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
102.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Bisonid-F 200mcg/6mcg Rotacaps

	Composition	Each rotacap contains: Budesonide…….200mcg Formoterol fumarate……..…6mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11812 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Adrenergics, Inhalants (Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics)
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Symbicort 200mcg/6mcg Turbohaler, Inhalation Powder (MHRA Approved)
	Me-too-status	Combivair 200 Rotacaps by M/s Highnoon Laboratories Ltd (Reg#054316)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration).

		• Form 5 is missing. • The reference formulation have mentioned the hydrated form (dihydrate) of Formoterol fumarate in the label claim while you have not mentioned the hydrated form. Revise the label claim as per reference formulation mentioning the hydrated form along with submission of applicable fee.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
103.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Stardi Tablets 0.035mg/2mg Tablet
	Composition	Each film coated tablet contains: Cyproterone Acetate……..2mg Ethinylestradiol……..0.035mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11806 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Estrogen / Anti-androgen
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	5x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Co-Cyprindiol 2000/35 film coated Tablets (MHRA approved)
	Me-too-status	Fam-21 Tablet by M/s Pharma Health (Reg.#77106)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	• Undertaking at the end of form 5 is missing. • Evidence of manufacturing facility/section approval for the applied formulation i.e. Steroidal Tablet section
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
104.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Meste 25mg Tablet
	Composition	Each film coated tablet contains: Exemestane…….25mg

	Dairy No. date of R &I fee	Form-5 Dy.No 11803 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Aromatase Inhibitor
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	3x5's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Exemestane 25mg Film-coated Tablets (MHRA Approved)
	Me-too-status	PH&T Exemestane 25mg coated tablets of M/s Mehran International (Reg. # 078122) (does not depict film coating)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	• Evidence of manufacturing facility/section approval for the applied formulation i.e. Steroidal Tablet section.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
105.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Finsat 1mg Tablet
	Composition	Each film coated tablet contains: Finasteride ……1mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11804 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Drugs Used In Benign Prostatic Hypertrophy G04CB01 Testosterone-5-alpha reductase inhibitors
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Finasteride 1mg Film-coated Tablets (MHRA Approved)
	Me-too-status	Prosin Tablet by M/s Himont Pharmaceutical (Reg#83852)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production,

		quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	• Evidence of manufacturing facility/section approval for the applied formulation i.e. Steroidal Tablet section. • Master formulation and manufacturing outline not submitted
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
106.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Salzone 50mcg/25mcg Rotacap
	Composition	Each rotacap contains: Fluticasone Propionate……50mcg Salmeterol (as Xinafoate)……..25mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11816 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Adrenergics in combination with corticosteroids or other drugs, excluding Anticholinergics.
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	30'S; As per SRO
	Approval status of product in Reference Regulatory Authorities	Seretide Evohaler 25 microgram/50 microgram per metered dose pressurised **inhalation, suspension** (MHRA Approved)
	Me-too-status	Wiltide Plus 25/50Mcg Automized Capsules by M/s Wilson's Pharmaceuticals (Reg. #38486)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board:

		• Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • Undertaking at the end of form 5 is missing. • The firm has claimed manufacturer's specifications and the product is available in USP.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
107.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Salzone 250mcg/25mcg Rotacap
	Composition	Each rotacap contains: Fluticasone Propionate……..250mcg Salmeterol (as Xinafoate)……25mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11817 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Adrenergics in combination with corticosteroids or other drugs, excluding Anticholinergics.
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Seretide Evohaler 25 microgram/250 microgram per metered dose pressurised **inhalation, suspension** (MHRA Approved)
	Me-too-status	Wiltide Plus 25/250Mcg Automized Powder capsules by M/s Wilson's Pharmaceuticals (Reg#38470)

	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • Undertaking at the end of form 5 is missing. • The firm has claimed manufacturer's specifications and the product is available in USP.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
108.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Gestyl Plus Tablet 0.075mg/0.02mg
	Composition	Each film coated tablet contains: Gestodene…….0.075mg Ethinylestradiol……...0.02mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11805 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019

	Pharmacological Group	Hormonal contraceptives for systemic use, (progestogens and estrogens, fixed combinations)
	Type of form	Form-5
	Finished product specifications	Manufacturing specifications
	Pack size and Demand Price	21's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Aidulan 20/75 microgram film-coated tablets (MHRA Approved)
	Me-too-status	Meliane Tablets by M/s Medipharm (Pvt) Ltd (Reg#024076) (doesnot depict coating)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	• Evidence of manufacturing facility/section approval for the applied formulation i.e. Steroidal Tablet section. • Undertaking at the end of form 5 is missing.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
109.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Saydocit Sachet
	Composition	Each sachet contains: Sodium bicarbonate…….0.428g/g Citric Acid……...0.176g/g Sodium citrate……0.153g/g Tartaric Acid……..0.215g/g
	Dairy No. date of R &I fee	Form-5 Dy.No 11818 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Antacids & Antiflatulents
	Type of form	Form-5
	Finished product specifications	Manufacturer's Specifications
	Pack size and Demand Price	20's, 100's; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Citro-soda of Abbott laboratories (as provided by the Firm but strength of ingredients is different)

	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	• Undertaking at the end of form 5 is missing. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting along with weblink • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm as the provided me too contains ingredients in different strengths.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
110.	Name and address of manufacture / Applicant	M/s Neutro Pharma (Pvt) Ltd., Sheikhupura Road, Lahore
	Brand Name + Dosage Form and Strength	Tromo Rota Capsule 0.18mcg
	Composition	Each rotacap contains: Tiotropium bromide monohydrate…0.18mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 11807 dated 06-03-2019 Rs.20,000/- Dated 05-03-2019
	Pharmacological Group	Anticholinergic
	Type of form	Form-5
	Finished product specifications	Manufacturer specification
	Pack size and Demand Price	10's, 15's, 20's: As per SRO
	Approval status of product in Reference Regulatory Authorities	SPIRIVA tiotropium 18 microgram powder for inhalation (in capsule) (TGA Australia Approved)
	Me-too-status	Tiovair Rotacaps by M/s Highnoon Laboratories (Reg#54315)
	GMP Status	The firm was inspected on 21,23-08-2017 by a panel of inspectors and conclusion of inspections was: Panel inspected the unit and evaluated documentation regarding production, quality control and quality assurance. Panel discussed various technical

		aspects with the technical staff at length. Panel decided to recommend the renewal of DML of M/s Neutro Pharma for the approved sections by the Central Licensing Board.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • You have applied for label claim Tiotropium bromide monohydrate…0.18mcg while reference formulation contain Tiotropium bromide monohydrate equivalent to Tiotropium …18mcg. Revise the label claim as per reference formulation along with submission of applicable fee. Furthermore revise the master formulation adjusting the weight of API considering the hydrated form. • Undertaking at the end of form 5 is missing.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
111.	Name and address of manufacture / Applicant	M/s Wimits Pharmaceuticals (Pvt.) Ltd., Plot No. 129, Sundar Industrial Estate, Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Provinate Ointment
	Composition	Each gram contains: Gentamicin (as sulphate) …….. 1mg (0.1% w/w)

		Betamethasone (as valerate)…….. 1mg (0.1% w/w)
	Dairy No. date of R &I fee	Form-5 Dy.No 12117 dated 06-03-2019 Rs.20,000 Dated 06-03-2019
	Pharmacological Group	Antibiotic+Corticosteroid
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	15g, 30g; As per SRO
	Approval status of product in Reference Regulatory Authorities	Valisone-G Ointment Health Canada Approved
	Me-too-status	Genticyn B Ointment by M/s Reckitt & Colman (Reg#010185)
	GMP Status	cGMP certificate issued to firm on the basis of evaluation conducted on 08-09-2021
	Remark of the Evaluator [XI]	• Firm has Cream/Ointment/Lotion/Gel (General) section as per Sceretary CLB Letter No. F. 1-10/2012-Lic dated 07th june 2022. • Revise the weight of API in master formulation considering the salt factor. In label claim you have applied Gentamicin (as sulphate) …1mg (0.1% w/w). However in master formulation gentamicin mentioned as gentamicin sulphate 0.5%, clarify?
	Decision: Approved. • **Firm shall submit revised master formulation mentioning correct strength of gentamycin sulphate as per submitted label claim before issuance of registration letter.** • **Firm shall submit fee of Rs.30,000/- for correction/pre-approval change in the master formulation, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
112.	Name and address of manufacture / Applicant	M/s Wimits Pharmaceuticals (Pvt.) Ltd., Plot No. 129, Sundar Industrial Estate, Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Difluzim-D cream
	Composition	Each gram contains: Diflucortolone valerate ……..… 1mg Isoconazole Nitrate ……. 10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 12125 dated 06-03-2019 Rs.20,000 Dated 06-03-2019
	Pharmacological Group	Corticosteroid, Antifungal
	Type of form	Form-5
	Finished product specifications	Manufacturer's Specification
	Pack size and Demand Price	10g, 15g, 30g, 45g; As per SRO
	Approval status of product in Reference Regulatory Authorities	Travocort 0.1 + 1% w/w Cream (AIFA Italy Approved)
	Me-too-status	Difzole Cream by M/s Vega Pharmaceuticals (Reg#69084)

	GMP Status	cGMP certificate issued to firm on the basis of evaluation conducted on 08-09-2021
	Remark of the Evaluator [XI]	• Firm has Cream/Ointment/Lotion/Gel (General) section as per Sceretary CLB Letter No. F. 1-10/2012-Lic dated 07th june 2022.In master formulation mometasone furoate is mentioned as the active ingredients, clarify?
	Decision: Approved with innovator's specifications. • **Firm shall submit revised master formulation mentioning correct API before issuance of registration letter.** • **Firm shall submit fee of Rs.30,000/- for correction/pre-approval change in the master formulation and product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
113.	Name and address of manufacture / Applicant	M/s Wimits Pharmaceuticals (Pvt.) Ltd., Plot No. 129, Sundar Industrial Estate, Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Eflowim 13.9% w/w cream Eflomit 13.9% w/w cream
	Composition	Each g contains: Eflornithine Hydrochloride ……..… 139mg (13.9% w/w)
	Dairy No. date of R &I fee	Form-5 Dy.No 12116 dated 06-03-2019 Rs.20,000 Dated 06-03-2019
	Pharmacological Group	Anti-Hirsutism Agent
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10g, 15g, 30g,45g; As per SRO
	Approval status of product in Reference Regulatory Authorities	VANIQA (13.9%) Cream, USFDA Approved
	Me-too-status	Hairid Cream by M/s Saffron Pharma, (Reg#85721)
	GMP Status	cGMP certificate issued to firm on the basis of evaluation conducted on 08-09-2021
	Remark of the Evaluator [XI]	• Firm has Cream/Ointment/Lotion/Gel (General) section as per Sceretary CLB Letter No. F. 1-10/2012-Lic dated 07th june 2022. • You have applied incorrect label claim. The reference formulation contain 13.9% (139 mg/g) of anhydrous eflornithine hydrochloride as eflornithine hydrochloride monohydrate (150 mg/g) while you have applied eflornithine hydrochloride only and not considering the hydrochloride and monohydrate form. Revise the

		label claim as per reference formulation along with submission of applicable fee. • In master formulation hydroquinine is mentioned as the active ingredients, clarify?
	Decision: Approved with innovator's specifications and following label claim: **Each g contains:** **Eflornithine Hydrochloride as monohydrate……..… 139mg (13.9% w/w)** • **Submission of revised master formulation as per applied product before issuance of registration letter** • **Firm shall submit the fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of hydrated form of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
114.	Name and address of manufacture / Applicant	M/s Wimits Pharmaceuticals (Pvt.) Ltd., Plot No. 129, Sundar Industrial Estate, Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Fuvate 0.1% w/w cream Fuvim 0.1% w/w cream
	Composition	Each gm contains: Mometasone Furoate……..1 mg (0.1%)
	Dairy No. date of R &I fee	Form-5 Dy.No 12129 dated 06-03-2019 Rs.20,000 Dated 06-03-2019
	Pharmacological Group	Corticosteroids
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	15g, 30g, 45g; As per SRO
	Approval status of product in Reference Regulatory Authorities	ELOCON 0.1% w/w Cream for topical use USFDA Approved
	Me-too-status	Edme Cream by Amarant Pharmaceuticals (Reg #67020)
	GMP Status	cGMP certificate issued to firm on the basis of evaluation conducted on 08-09-2021
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format. • • Firm has Cream/Ointment/Lotion/Gel (General) section as per Sceretary CLB Letter No. F. 1-10/2012-Lic dated 07th june 2022.
	Decision: Approved. Firm shall submit 1st page of form 5 as per prescribed format before issuance of registration letter along with applicable fee for revision of Form 5, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
115.	Name and address of manufacture / Applicant	M/s Wimits Pharmaceuticals (Pvt.) Ltd., Plot No. 129, Sundar Industrial Estate, Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Polywim Ointment Polymit Ointment
	Composition	Each gram contains: Polymyxin B Sulphate

		……..10000IU Bacitracin Zinc …… 500IU
	Dairy No. date of R &I fee	Form-5 Dy.No 12127 dated 06-03-2019 Rs.20,000 Dated 06-03-2019
	Pharmacological Group	Antibacterials
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	20g, 30g, 45g; As per SRO
	Approval status of product in Reference Regulatory Authorities	Polyfax Ointment MHRA Approved
	Me-too-status	Multifax Ointment by Xenon Pharmaceuticals (Reg#32328)
	GMP Status	cGMP certificate issued to firm on the basis of evaluation conducted on 08-09-2021.
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format. • Firm has Cream/Ointment/ Lotion/Gel (General) section as per Sceretary CLB Letter No. F. 1-10/2012-Lic dated 07th june 2022.
	Decision: Approved. Firm shall submit 1st page of form 5 as per prescribed format before issuance of registration letter along with applicable fee for revision of Form 5, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
116.	Name and address of manufacture / Applicant	M/s Wimits Pharmaceuticals (Pvt.) Ltd., Plot No. 129, Sundar Industrial Estate, Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Quaz 1% w/w cream Quazim 1% w/w Cream
	Composition	Each gram contains: Silver Sulphadiazine …….10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 12123 dated 06-03-2019 Rs.20,000 Dated 06-03-2019
	Pharmacological Group	Antibiotics And Chemotherapeutics For Dermatological Use
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	15g, 30g, 45g; As per SRO
	Approval status of product in Reference Regulatory Authorities	Flamazine Cream 1%w/w MHRA Approved
	Me-too-status	Derma 1% w/w Cream by M/s Mafins Pharma (Reg#81178)
	GMP Status	cGMP certificate issued to firm on the basis of evaluation conducted on 08-09-2021
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format. • • Firm has Cream/Ointment/Lotion/Gel (General) section as per Sceretary

		CLB Letter No. F. 1-10/2012-Lic dated 07th june 2022.
	Decision: Approved. Firm shall submit 1st page of form 5 as per prescribed format before issuance of registration letter along with applicable fee for revision of Form 5, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
117.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Azabex 200mg Tablet
	Composition	Each film coated Tablet Contains: Carbamazepine……200mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16324 da ted 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antiepileptics
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10's, 50's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Carbagen 200mg tablets MHRA Approved
	Me-too-status	Carbawel 200 mg Tablets by M/s Welmark Pharmaceuticals (Reg#77462)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• The firm has applied for manufacturer's specifications but the official monograph is available in USP. • You have applied for film coated tablet but the reference formulation is uncoated. Revise the label claim and master formulation along with submission of applicable fee.
	Decision: Approved with USP specifications and following label claim: **Each Tablet Contains:** **Carbamazepine……200mg** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications and correction/pre-approval change in composition (correction/change of formulation from film coated tablet to un-coated tablet) as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	

	• **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
118.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Rotavin 40mg/2ml Injection
	Composition	Each 2ml contains: Drotaverine HCl…..…40mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16363 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Drugs for functional gastrointestinal disorders
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10x4ml, 25x2ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Hi-Spa 40mg/2ml injection of M/s Helix Karachi (Reg.#073604)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied for two different volume i.e. 2ml and 4ml in same application, mention only a single volume. • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink. • Submit complete manufacturing outline • Mention type of primary packaging material of applied formulation whether it is type I, II or III glass container
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	

119.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Diflozin 25mg Tablet
	Composition	Each tablet contains: Empagliflozin ……..…25mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16346 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Blood Glucose Lowering Drugs, Excl. Insulins
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	14's; As per SRO
	Approval status of product in Reference Regulatory Authorities	JARDIANCE (10mg, 25mg) film-coated tablets USFDA Approved
	Me-too-status	Empoli 25mg Tablet by M/s Sami Pharmaceuticals (Reg#098701)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied incorrect label claim. The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee. • You have not mentioned coating, blistering and packing in manufacturing outline. Submit complete manufacturing outline. • Submission of stability studies data of three batches as per Requirements of Registration Board decision of 293rd meeting.
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of DRB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
120.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Lamot 50mg Tablet

	Composition	Each tablet contains: Lamotrigine…….50mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16338 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Other antiepileptics
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	LAMICTAL 50mg Tablets (USFDA approved) **Discontinued** **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**
	Me-too-status	Epictal 50mg Tablet of M/s Pakistan Pharmaceuticals (Reg#089242)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• The firm have applied for manufacturer's specifications but the official monograph for the applied product is available in USP.
	Decision: Approved with USP specifications. • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
121.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Lemox 20mg Tablet
	Composition	Each tablet contains: Olmesartan Medoxomil……20mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16332 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Angiotensin II receptor blockers (ARBs)
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10's; As per SRO

	Approval status of product in Reference Regulatory Authorities	BENICAR tablets USFDA Approved
	Me-too-status	Olmisan 20mg tablets by Highnoon Laboratories (Reg. 092273)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• The firm have applied for manufacturer's specifications but the official monograph for the applied product is available in USP. • You have applied incorrect label claim. The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee.
	Decision: Approved with USP specifications and following label claim: **Each film coated tablet contains:** **Olmesartan Medoxomil……20mg** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications and correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to film coated tablet) as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
122.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Cetarac 800mg Tablet
	Composition	Each tablet contains: Piracetam……..…800mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16341 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Other psychostimulants and nootropics
	Type of form	Form-5
	Finished product specifications	Manufacturer's specification
	Pack size and Demand Price	3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Nootropil 800 mg film-coated Tablets (MHRA Approved)

	Me-too-status	Nootropil Tablet 800mg by M/s GSK (Reg# 82277)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied incorrect label claim. The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee. • You have not mentioned coating, blistering and packing in manufacturing outline. Submit complete manufacturing outline.
	Decision: Approved with following label claim: **Each film coated tablet contains:** **Piracetam……..…800mg** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to film coated tablet) as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit complete manufacturing outline before issuance of registration letter** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
123.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Perbex 20mg Tablet
	Composition	Each tablet contains: Rabeprazole Sodium……..20mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16330 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Proton pump inhibitors
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10's, 14's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Rabeprazole 20mg Gastro-resistant Tablets MHRA approved
	Me-too-status	Rabro 20mg Tablet by M/s Genix Pharma (Reg#83775)

	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied incorrect label claim. The reference formulation is enteric coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee. • You have not mentioned coating, blistering and packing in manufacturing outline. Submit complete manufacturing outline.
	Decision: Approved with innovator's specifications and following label claim: **Each enteric coated tablet contains:** **Rabeprazole Sodium……..20mg** • **Firm shall submit the fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to enteric coated tablet), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit complete manufacturing outline before issuance of registration letter** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
124.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Rivox 200mg Tablet
	Composition	Each Tablet Contains: Rifaximin……..…200mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16328 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antibiotics
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	XIFAXAN (200mg, 550mg) film-coated tablets, **USFDA** approved
	Me-too-status	Nimixa 200mg film-coated tablet by M/s Getz Pharma (Reg# 70734)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was:

		Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied incorrect label claim. The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee. • You have not mentioned coating, blistering and packing in manufacturing outline. Submit complete manufacturing outline.
	Decision: Approved with innovator's specifications and following label claim: **Each film coated tablet contains:** **Rifaximin……..…200mg** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications and correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to film coated tablet) as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit complete manufacturing outline before issuance of registration letter** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
125.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Faxet 10mg Tablet
	Composition	Each tablet contains: Rivaroxaban……10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16340 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antithrombotic Agents
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	5's, 10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Xarelto film-coated tablets (2.5mg, 10mg, 15mg, 20mg) by USFDA Approved.
	Me-too-status	Roxaban 10mg Tablet by M/s Genetics Pharmaceuticals (Reg# 85163)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was:

		Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied incorrect label claim. The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee. • You have not mentioned coating, blistering and packing in manufacturing outline. Submit complete manufacturing outline.
	Decision: Approved with innovator's specifications and following label claim: **Each film coated tablet contains:** **Rivaroxaban……10mg** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications and correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to film coated tablet) as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit complete manufacturing outline before issuance of registration letter** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
126.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Rovastin 10mg Tablet
	Composition	Each tablet contains: Rosuvastatin Calcium……..…10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16359 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	HMG CoA reductase inhibitors
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	CRESTOR (5, 10, 20, or 40 mg) film coated tablets USFDA Approved
	Me-too-status	R-Vastin-10 Tablet by M/s Rasco Pharma, (Reg#80208)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was: Based on the areas inspected, the people met and the documents

		reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied for label claim Each tablet contains: Rosuvastatin Calcium……10mg while the reference formulation contain Each film coated tablet contains: Rosuvastatin as Calcium……10mg. Revise the label claim as per reference formulation along with submission of applicable fee. • You have not mentioned coating, blistering and packing in manufacturing outline. Submit complete manufacturing outline.
	Decision: Approved with innovator's specifications and following label claim: **Each film coated tablet contains:** **Rosuvastatin as Calcium……..…10mg** • **Firm shall submit the differential fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of salt factor of the drug substance) and change of formulation from un-coated tablet to film coated tablet, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit complete manufacturing outline before issuance of registration letter** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
127.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Rovastin 5mg Tablet
	Composition	Each tablet contains: Rosuvastatin Calcium……5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16335 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	HMG CoA reductase inhibitors
	Type of form	Form-5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	1x10's, 2x10's, 3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	CRESTOR (5, 10, 20, or 40 mg) film coated tablets USFDA Approved
	Me-too-status	R-Vastin-5 Tablet by M/s Rasco Pharma, (Reg#80210)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was:

		Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied for label claim Each tablet contains: Rosuvastatin Calcium…….5mg while the reference formulation contain Each film coated tablet contains: Rosuvastatin as Calcium…….5mg. Revise the label claim as per reference formulation along with submission of applicable fee. • You have not mentioned coating, blistering and packing in manufacturing outline. Submit complete manufacturing outline.
	Decision: Approved with innovator's specifications and following label claim: **Each film coated tablet contains:** **Rosuvastatin as Calcium……..…5mg** • **Firm shall submit the differential fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of salt factor of the drug substance) and change of formulation from un-coated tablet to film coated tablet, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit complete manufacturing outline before issuance of registration letter** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
128.	Name and address of manufacture / Applicant	M/s Trigon Pharmaceuticals Pvt Limited., 8 km, Thoker Raiwind Road, Lahore
	Brand Name + Dosage Form and Strength	Primot 25mg Tablet
	Composition	Each Tablet Contains: Topiramate……25mg
	Dairy No. date of R &I fee	Form-5 Dy.No 16327 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antiepileptics
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	30's, 60's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Topiramate Cadila 25mg film-coated tablets MHRA Approved
	Me-too-status	Neutop 25mg tablets by M/s Nabiqasim Industries (Reg#076387)
	GMP Status	The firm was inspected on 25-03-2019 and Conclusion of inspection was:

		Based on the areas inspected, the people met and the documents reviewed, and considering the findings of inspection M/s Trigon Pharmaceuticals Pvt Ltd Lahore was considered to be operating at a satisfactory level of GMP compliance with refrence to GMP guidelines as per Dugs Act, 1976 and rules framed there under.
	Remark of the Evaluator [XI]	• You have applied incorrect label claim. The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim as per reference formulation along with submission of applicable fee. • You have not mentioned coating, blistering and packing in manufacturing outline. Submit complete manufacturing outline.
	Decision: Approved with following label claim: **Each film coated tablet contains:** **Topiramate……25mg** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to film coated tablet) as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit complete manufacturing outline before issuance of registration letter** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
129.	Name and address of manufacture / Applicant	M/s Medimarker's Laboratories Pvt Ltd., A-104, S.I.T.E Area, Hyderabad
	Brand Name + Dosage Form and Strength	Markxim Dry Powder 500mg Injection IV
	Composition	Each Vial Contains: Cefotaxime Sodium……...500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 8445 dated 26-02-2019 Rs.20,000/- Dated 21-02-2019
	Pharmacological Group	Cephalosporine
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Cefotaxime 500mg powder for solution for injection/infusion MHRA Approved
	Me-too-status	Efatax 500mg Injection by M/s Cure Laboratories (Reg# 098017)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format

		• Firm has Injectable section (Cephalosporine) as per Sceretary CLB Letter No. F. 2-4/2003-Lic (Vol-I) dated 03rd December 2018. • You have applied incorrect label claim. Revise the label claim after considering the salt factor as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Approved with following label claim: **Each Vial Contains:** **Cefotaxime as Sodium……...500mg** • **Firm shall submit 1st page of form 5 as per prescribed format alonwith GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit the fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of salt factor of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
130.	Name and address of manufacture / Applicant	M/s Medimarker's Laboratories Pvt Ltd., A-104, S.I.T.E Area, Hyderabad
	Brand Name + Dosage Form and Strength	Rifodime Dry Powder Injection 500mg
	Composition	Each Vial Contains: Ceftazidime Pentahydrate……500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 8456 dated 26-02-2019 Rs.20,000/- Dated 21-02-2019
	Pharmacological Group	Cephalosporine
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Ceftazidime 500mg Powder for Solution for Injection MHRA Approved
	Me-too-status	Kefamin Injection 500mg IM/IV by M/s Maxitech Pharma (Reg# 097038)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • Firm has Injectable section (Cephalosporine) as per Sceretary CLB Letter No. F. 2-4/2003-Lic (Vol-I) dated 03rd December 2018. • You have applied incorrect label claim. Revise the label claim after considering the hydrated form as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years

	Decision: Approved with following label claim: **Each Vial Contains:** **Ceftazidime as Pentahydrate……500mg** • **Firm shall submit 1st page of form 5 as per prescribed format alonwith GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit the fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of hydrated factor of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
131.	Name and address of manufacture / Applicant	M/s Medimarker's Laboratories Pvt Ltd., A-104, S.I.T.E Area, Hyderabad
	Brand Name + Dosage Form and Strength	Cefmark Dry Powder Injection 500mg IV
	Composition	Each Vial Contains: Ceftriaxone Sodium……500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 8450 dated 26-02-2019 Rs.20,000/- Dated 21-02-2019
	Pharmacological Group	Cephalosporin
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Ceftriaxone 500mg powder for solution for injection MHRA Approved
	Me-too-status	Ceftro Injection 500mg IV by Curexa Health, (Reg#82738)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • Firm has Injectable section (Cephalosporine) as per Sceretary CLB Letter No. F. 2-4/2003-Lic (Vol-I) dated 03rd December 2018. • You have applied incorrect label claim. Revise the label claim after considering the salt factor as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Approved with following label claim: **Each Vial Contains:** **Ceftriaxone as Sodium……500mg** • **Firm shall submit 1st page of form 5 as per prescribed format alongwith GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit the fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of salt factor of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
132.	Name and address of manufacture / Applicant	M/s Medimarker's Laboratories Pvt Ltd., A-104, S.I.T.E Area, Hyderabad
	Brand Name + Dosage Form and Strength	Halexin Dry Powder Suspension 125mg/5ml

	Composition	Each 5ml contains: Cephalexin Monohydrate……..125mg
	Dairy No. date of R &I fee	Form-5 Dy.No 8471 dated 26-02-2019 Rs.20,000/- Dated 21-02-2019
	Pharmacological Group	Cephalosporine
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Cefalexin 125mg/5ml Powder for Oral Suspension MHRA Approved
	Me-too-status	Imlax 125mg Dry Powder Suspension by M/s Daneen Pharma (Reg#101555)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • Firm has Dry syrup section (Cephalosporine) as per Sceretary CLB Letter No. F. 2-4/2003-Lic (Vol-I) dated 03rd December 2018. • You have applied incorrect label claim. Revise the label claim after considering the hydrated form as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Approved with following label claim: **Each 5ml contains:** **Cephalexin as Monohydrate……..125mg** • **Firm shall submit 1st page of form 5 as per prescribed format alongwith GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit the fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of hydrated factor of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
133.	Name and address of manufacture / Applicant	M/s Medimarker's Laboratories Pvt Ltd., A-104, S.I.T.E Area, Hyderabad
	Brand Name + Dosage Form and Strength	Halexin Dry Powder Suspension 250mg/5ml
	Composition	Each 5ml contains: Cephalexin Monohydrate…….250mg
	Dairy No. date of R &I fee	Form-5 Dy.No 8472 dated 26-02-2019 Rs.20,000/- Dated 21-02-2019
	Pharmacological Group	Cephalosporine
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Cefalexin 250mg/5ml Powder for Oral Suspension MHRA Approved

	Me-too-status	Imlax 250mg Dry Powder Suspension by M/s Daneen Pharma (Reg# 101556)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • Firm has Dry syrup section (Cephalosporine) as per Sceretary CLB Letter No. F. 2-4/2003-Lic (Vol-I) dated 03rd December 2018. • You have applied incorrect label claim. Revise the label claim after considering the hydrated form as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Approved with following label claim: **Each 5ml contains:** **Cephalexin as Monohydrate……..250mg** • **Firm shall submit 1st page of form 5 as per prescribed format alongwith GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit the differential fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of hydrated factor of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
134.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Fexodine 120mg Tablet
	Composition	Each Tablet Contains: Fexofenadine as HCl……..…120mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7286 dated 19-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	Antihistamines
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Telfast 120mg film-coated tablets, MHRA Approved.
	Me-too-status	Axofed 120mg Tablet by M/s Akson Pharmaceuticals, (Reg# 101789)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee.

		Furthermore, you have applied the label claim considering the salt factor. Revise the label claim without considering the salt factor along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
135.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Fexodine 60mg Tablet
	Composition	Each Tablet Contains: Fexofenadine as HCl……60mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7288 dated 19-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	Antihistamines
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	FEXOTABS 60mg film coated tablet, TGA Approved.
	Me-too-status	Axofed 60mg Tablet by M/s Akson Pharmaceuticals, (Reg# 101788)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. Furthermore, you have applied the label claim considering the salt factor. Revise the label claim without considering the salt factor along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
136.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi

	Brand Name + Dosage Form and Strength	Fexodine 180mg Tablet
	Composition	Each Tablet Contains: Fexofenadine as HCl……180mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7287 dated 19-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	Antihistamines
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	FEXOTABS 180mg film coated tablet, TGA Approved.
	Me-too-status	Axofed 180mg Tablet by M/s Akson Pharmaceuticals, (Reg# 101790)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. Furthermore, you have applied the label claim considering the salt factor. Revise the label claim without considering the salt factor along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
137.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Nacdium Gel 2gm
	Composition	Each 100gm Contains: Diclofenac diethylamine ammonium salt as Diclofenac Sodium…….2gm (2%w/w)
	Dairy No. date of R &I fee	Form-5 Dy.No 30939 dated 13-09-2018 Rs.20,000/- Dated 13-09-2018
	Pharmacological Group	NSAIDS
	Type of form	Form 5
	Finished product specifications	BP
	Pack size and Demand Price	20gm, 100gm; As per SRO
	Approval status of product in Reference Regulatory Authorities	Voltarol 12 Hour Emulgel 2.32% Gel MHRA Approved
	Me-too-status	Diclofil Gel by M/s Murfy Pharmaceuticals (Reg# 049917)

	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format duly signed by the signatory • Submit manufacturing procedure for the applied product • Provide evidence of required manufacturing facility/section approval letter • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
138.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	RapidCam 8mg Tablet
	Composition	Each Tablet Contains: Lornoxicam……..8mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7294 dated 19-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	NSAID
	Type of form	Form 5
	Finished product specifications	Innovator's specifications
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Xefo 8mg film-coated tablet (EMA approved)
	Me-too-status	Lufam 8mg Tablet by M/s Martin Dow Ltd (Reg# 083309)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • You have applied for uncoated tablets while the reference formulation is film coated. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.Verification of validity status of DML from Licensing Divison.**	
139.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Atrolip 10mg Tablet

	Composition	Each Tablet Contains: Atorvastatin……..10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7289 dated 19-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	HMG CoA reductase inhibitors
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Lipitor 10mg film-coated tablets MHRA Approved
	Me-too-status	Atorviz 10mg tablets by Tabros Pharma (Reg#098542)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. Furthermore, mention the salt and hydrated form of atorvastatin in the label claim along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
140.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Atrolip 20mg Tablet
	Composition	Each Tablet Contains: Atorvastatin……..20mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7307 dated 20-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	HMG CoA reductase inhibitors
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Lipitor 20mg film-coated tablets MHRA Approved
	Me-too-status	Atorviz 20mg tablets by Tabros Pharma (Reg#098541)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The reference formulation is film coated while you have applied for

		uncoated tablets. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. Furthermore, mention the salt and hydrated form of atorvastatin in the label claim along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
141.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Atrolip 40mg Tablet
	Composition	Each Tablet Contains: Atorvastatin……..…40mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7308 dated 20-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	HMG CoA reductase inhibitors
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Lipitor 40mg film-coated tablets MHRA Approved
	Me-too-status	Atorviz 40mg tablets by Tabros Pharma (Reg#098540)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. Furthermore, mention the salt and hydrated form of atorvastatin in the label claim along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	

142.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Erythrobax 500mg Tablet
	Composition	Each 5ml Contains: Erythromycin Stearate……500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7285 dated 19-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	Macrolides
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Erythrocin 500 film coated tablets MHRA Approved
	Me-too-status	Wotez 500mg Tablet by M/s Martin Dow Marker Ltd (Reg#090772)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The cover letter, fee challan and 1st page of form 5 shows that you have applied for tablet while the label claim shows that you have applied for suspension/solution, clarify and Revise the label claim as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
143.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Erythrobax 250mg Tablet
	Composition	Each 5ml Contains: Erythromycin (Stearate)…250mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7284 dated 19-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	Macrolides
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Erythrocin 250 film coated tablets MHRA Approved
	Me-too-status	Wotez 250mg Tablet by M/s Martin Dow Marker Ltd (Reg#090773)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format

		• The cover letter, fee challan and 1st page of form 5 shows that you have applied for tablet while the label claim shows that you have applied for suspension/solution, clarify and Revise the label claim as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
144.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Zoline 400mg Tablet
	Composition	Each Tablet Contains: Linezolid……400mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7293 dated 19-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	Oxazolidinone Antibacterial
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	ZYVOX 400mg film-coated tablets Tablet USFDA Approved. **Discontinued** **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons* (as per USFDA website)
	Me-too-status	Zvox 400mg Tablet by M/s Arreta Pharmaceuticals (Reg# 084279)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	

145.	Name and address of manufacture / Applicant	M/s Baxter Pharmaceuticals., A-1/A, Scheem No.33,Phase-1,S.I.T.E,Super Highway, Karachi
	Brand Name + Dosage Form and Strength	Lowstat 20mg Tablet
	Composition	Each Tablet Contains: Simvastatin……..…20mg
	Dairy No. date of R &I fee	Form-5 Dy.No 7305 dated 20-02-2019 Rs.20,000/- Dated 19-02-2019
	Pharmacological Group	HMG CoA reductase inhibitors
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Simvastatin 20mg film coated Tablets MHRA Approved
	Me-too-status	Simvital 20mg Tablet by M/s Lisko Pakistan (Reg# 092908)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise the 1st page of form 5 as per prescribed format • The reference formulation is film coated while you have applied for uncoated tablets. Revise the label claim, master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. • Submit latest GMP Inspection report conducted within last three years
	Decision: Registration Board deferred the case for following: • **Submission of reply to the above cited shortcomings within six months.** • **Verification of validity status of DML from Licensing Divison.**	
146.	Name and address of manufacture / Applicant	M/s Faas Pharmaceuticals (Pvt.) Ltd., F-748/L, S.I.T.E Karachi, Pakistan ***Contract Manufactured by:*** M/s Pharmevo Private Limited. Plot # A-29, North Western Industrial Zone, Port Qasim, Karachi
	Brand Name + Dosage Form and Strength	Fasxime 100mg/5ml Powder for Suspension
	Composition	Each reconstituted 5ml Contains: Cefixime as Trihydrate…….100mg
	Dairy No. date of R &I fee	Form-5 Dy.No 30876 dated 13-09-2018 Rs.50,000/- Dated 13-09-2018
	Pharmacological Group	Cephalosporin
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	30ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	Cefixime 100mg/5ml Powder for Oral Suspension MHRA Approved

	Me-too-status	Mixo Dry Powder Suspension 100mg/5ml by M/s Maxitech Pharma (Reg# 096373)
	GMP Status	"GMP certificate issued to M/s Faas Pharmaceuticals (Pvt.) Ltd on 08-05-2018". M/s Pharm Evo was visited by the above panel on 7th Feb,2019. Detailed report has been prepared on prescribed format and is being attached. Keeping in view the people met, documents observed and observations made during the inspection, the panel is of the view TO issue GMP certificate to the Firm.
	Remark of the Evaluator [XI]	• Mention the correct weight of API in master formulation considering the hydrated form • Submit contract manufacturing agreement between M/s Faas Pharmaceuticals and M/s PharmEvo Pvt Ltd
	Decision: Approved. Registration Board further decied that registration letter will be issue dupon submission of following: • **Revised master formulation mentioning the correct weight of API considering the hydrated form** • **Contract manufacturing agreement between M/s Faas Pharmaceuticals and M/s PharmEvo Pvt Ltd.** • **Ffee of Rs. 75,000/- for correction/pre-approval change in master formulation (correction/change of weight of API considering the hydrated form), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Latest GMP inspection report for both M/s Faas Pharmaceuticals (Pvt.) Ltd and M/s Pharmevo Private Limited from QA&LT Division, conducted within last three years**	
147.	Name and address of manufacture / Applicant	M/s Faas Pharmaceuticals (Pvt.) Ltd., F-748/L, S.I.T.E Karachi, Pakistan ***Contract Manufactured by:*** M/s Pharmevo Private Limited. Plot # A-29, North Western Industrial Zone, Port Qasim, Karachi
	Brand Name + Dosage Form and Strength	Feltrix 1g IV Dry Powder for Injection
	Composition	Each Vial Contains: Ceftriaxone Sodium eq. to Ceftriaxone……1000mg
	Dairy No. date of R &I fee	Form-5 Dy.No 30883 dated 13-09-2018 Rs.50,000/- Dated 13-09-2018
	Pharmacological Group	Cephalosporin
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO

	Approval status of product in Reference Regulatory Authorities	Rocephin 1g Powder for solution for injection or infusion MHRA Approved
	Me-too-status	Ceftro Injection 1gm IV by Curexa Health, (Reg#82740)
	GMP Status	"GMP certificate issued to M/s Faas Pharmaceuticals (Pvt.) Ltd on 08-05-2018". M/s Pharm Evo was visited by the above panel on 7th Feb,2019. Detailed report has been prepared on prescribed format and is being attached. Keeping in view the people met, documents observed and observations made during the inspection, the panel is of the view TO issue GMP certificate to the Firm.
	Remark of the Evaluator [XI]	• Submit contract manufacturing agreement between M/s Faas Pharmaceuticals and M/s PharmEvo Pvt Ltd • Provide evidence of required manufacturing facility/section approval letter. • Firm has Sterile Dry Powder Injectable (Cephalosporine) section as per Secretary CLB letter No. F. 2-1/98-Lic (Vol-III) dated 10th November 2022.
	Decision: Approved. Registration Board further decied that registration letter will be issue dupon submission of following: • **Contract manufacturing agreement between M/s Faas Pharmaceuticals and M/s PharmEvo Pvt Ltd** • **Latest GMP inspection report for both M/s Faas Pharmaceuticals (Pvt.) Ltd and M/s Pharmevo Private Limited from QA&LT Division, conducted within last three years**	
148.	Name and address of manufacture / Applicant	M/s Linta Pharmaceuticals Pvt Ltd., Plot No. 03, Street No S-5, National Industrial Zone, Rawat, Islamabad
	Brand Name + Dosage Form and Strength	Dom-C 15mg/20mg Tablets
	Composition	Each Film Coated Tablet Contains: Domperidone Maleate eq. to Domperidone……15mg Cinnarizine…….20mg
	Dairy No. date of R &I fee	Form-5 Dy.No 31550 dated 18-09-2018 Rs.20,000/- Dated 18-09-2018
	Pharmacological Group	Antiemetic & Antihistamine
	Type of form	Form 5
	Finished product specifications	Manufacturer specification
	Pack size and Demand Price	1x10's, 2x10's, 5x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	

	GMP Status	The firm was inspected on 10-07-2019 and conclusion of inspection was: Keeping in view the above it may be concluded that M/s Linta Pharmaceuticals is operating at acceptable level of GMP standard.
	Remark of the Evaluator [XI]	• Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink • Provide evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
149.	Name and address of manufacture / Applicant	M/s Farm Aid Group., Plot # 3/2, Phase I & II, Hattar Industrial Estate, Haripur
	Brand Name + Dosage Form and Strength	Panto-Aid 40mg Capsule
	Composition	Each hard gelatin capsule contains: Pantoprazole Sodium EC pellets 22.5% w/w eq to Pantoprazole……40mg Source of pellets: Vision Pharmaceuticals
	Dairy No. date of R &I fee	Form-5 Dy.No 21658 dated 20-06-2018 Rs.20,000/- Dated 13-06-2018
	Pharmacological Group	Proton pump inhibitors
	Type of form	Form 5
	Finished product specifications	Innovator's specifications
	Pack size and Demand Price	14's; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Aprant 40mg Capsule by M/s Adamjee Pharmaceuticals (Reg#076139)
	GMP Status	
	Remark of the Evaluator [XI]	• Provide evidence of required manufacturing facility/section approval letter • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink • Valid GMP certificate of supplier of pellets

	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
150.	Name and address of manufacture / Applicant	M/s Gillman Pharmaceuticals., 41/2-A, Phase I & II, Industrial Estate, Hattar, Pakistan ***Contract Manufactured by:*** M/s Aulton Pharmaceuticals. Plot No. 84/1, Block A, Phase V, Industrial Estate, Hattar, K.P.K
	Brand Name + Dosage Form and Strength	Feromax 100mg/5ml Injection
	Composition	Each 5ml Amber Glass Ampoule Contains: Iron Sucrose eq. to Elemental Iron……..100mg
	Dairy No. date of R &I fee	Form-5 Dy.No 41702 dated 07-12-2018 Rs.50,000/- Dated 07-12-2018
	Pharmacological Group	Anti-anaemic
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	5ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	Venofer (50mg/2.5mL, 100mg/5mL, 200mg/10mL) (20mg/mL) in single-dose vials. Injection USFDA Approved
	Me-too-status	Irofit Injection 100mg/5ml by M/s Zafa Pharma (Reg#82291)
	GMP Status	The firm M/s Aulton Pharmaceuticals was inspected on 27-06-2019 and conclusion of inspection was: As per observations made during inspection, the manufacturing, quality control and environmental facilities, provided the qualified staff employed, the documentation maintained, implementation of the SOP's the GMP compliance status of the firm M/s Aulton Pharma is found to be satisfactory
	Remark of the Evaluator [XI]	• You have applied on form 5D while mee too of the product is available. Apply on prescribed form 5 for the applied product • Application must be submitted by the applicant i.e. M/s Gillman Pharmaceuticals. • Undertaking at the end of form 5 is missing • You have not performed terminal sterilization, justify • Submit latest GMP Inspection report of M/s Gillman Pharmaceuticals conducted within last three years

		• Submit contract manufacturing agreement between M/s M/s Gillman Pharmaceuticals and M/s M/s Aulton Pharmaceuticals
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
151.	Name and address of manufacture / Applicant	M/s Ferroza International Pharmaceuticals Pvt. Ltd., 33 Km, Ferozepur Road, Lahore
	Brand Name + Dosage Form and Strength	Fer-Antinal 5mg Tablet
	Composition	Each Tablet Contains: Desloratadine……5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11236 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Antihistamine
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Clarinex 5mg film coated tablet USFDA Approved.
	Me-too-status	Desatil Tablets 5mg by Aries Pharmaceuticals (Reg#84270)
	GMP Status	
	Remark of the Evaluator [XI]	• Form 5 submitted without signature by the applicant • Undertaking at the end of form 5 is missing • You have applied for uncoated tablets while the reference formulation is film coated. Revise the label claim as per reference formulation along with submission of applicable fee. • Submit latest GMP inspection report conducted within last three years
	Decision: Approved with following label claim: **Each film coated tablet contains:** **Desloratadine……5mg** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to film coated tablet) as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit duly signed Form 5 submitted undertaking at the end of form 5** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
152.	Name and address of manufacture / Applicant	M/s Ferroza International Pharmaceuticals Pvt. Ltd., 33 Km, Ferozepur Road, Lahore
	Brand Name + Dosage Form and Strength	Gemi-Fer 320mg Tablet
	Composition	Each Tablet Contains: Gemifloxacin……320mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11239 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Fluoroquinolones

	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Disconitnued
	Me-too-status	Gemibid 320mg Tablet by M/s Evolution Pharmaceuticals (Reg#095377)
	GMP Status	
	Remark of the Evaluator [XI]	• Form 5 submitted without signature by the applicant • Undertaking at the end of form 5 is missing • You have applied for uncoated tablets while the reference formulation is film coated. Revise the label claim as per reference formulation along with submission of applicable fee. Furthermore, you have not mentioned the salt of gemifloxacin in the label claim. Mention the salt form of gemifloxacin in label claim and adjust its weight in master formulation considering the salt factor along with submission of applicable fee. • Submit latest GMP inspection report conducted within last three years
	Decision: Deferred for confirmation of regulatory status in reference regulatoty authorities as the product is withdrawn from market in EMA	
153.	Name and address of manufacture / Applicant	M/s Ferroza International Pharmaceuticals Pvt. Ltd., 33 Km, Ferozepur Road, Lahore
	Brand Name + Dosage Form and Strength	Lornofer 8mg Tablet
	Composition	Each Tablet Contains: Lornoxicam……8mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11235 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	NSAID
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	2x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Xefo 8mg film-coated tablet (EMA approved)
	Me-too-status	Xonica 8mg Tablet by M/s Zephyr Pharmatec (Reg#086983)
	GMP Status	
	Remark of the Evaluator [XI]	• Form 5 submitted without signature by the applicant • Undertaking at the end of form 5 is missing

		• You have applied for uncoated tablets while the reference formulation is film coated. Revise the label claim as per reference formulation along with submission of applicable fee. • You have mentioned the addition of 5% overage in master formulation. Provide scientific justification for addition overage • Submit latest GMP inspection report conducted within last three years
	Decision: Approved with innovator's specifications and following label claim: **Each film coated tablet contains:** **Lornoxicam……8mg** • **Firm shall submit the fee of Rs. 30000/- for correction/pre-approval change in composition (correction/change of formulation from un-coated tablet to film coated tablet) and revision of master formulation without overages as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit duly signed Form 5 submitted undertaking at the end of form 5** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
154.	Name and address of manufacture / Applicant	M/s Ferroza International Pharmaceuticals Pvt. Ltd., 33 Km, Ferozepur Road, Lahore
	Brand Name + Dosage Form and Strength	Sitafer-Met 50/1000 mg Tablet
	Composition	Each Tablet Contains: Sitagliptin Phosphate……50mg Metformin HCl…….1000mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11240 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Antidiabetic
	Type of form	Form 5
	Finished product specifications	Innovator's specifications
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Janumet film coated tablet (50mg/500mg, 50mg/1000mg) USFDA Approved.
	Me-too-status	Sildomet M 50/1000mg Tablet by M/s High-Q Pharmaceuticals (Reg#76400)
	GMP Status	
	Remark of the Evaluator [XI]	• You have mentioned the label claim without considering the salt factor in case of sitagliptin. Revise the label claim considering the salt factor along with submission of applicable fee. Furthermore, mention the hydrated form of sitagliptin in label claim and adjust its weight in master

		formulation considering the hydrated form • Mention the salt and hydrated form of sitagliptin in master formulation • You have applied for uncoated tablets while the reference formulation is film coated. Revise the label claim as per reference formulation along with submission of applicable fee. • Form 5 submitted without signature by the applicant • Undertaking at the end of form 5 is missing • Submit latest GMP inspection report conducted within last three years
	Decision: Approved with following label claim: **Each film coated tablet contains:** **Sitagliptin as Phosphate monohydrate……50mg** **Metformin HCl…….1000mg** • **Firm shall submit the differential fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of salt factor and hydrated form of the drug substance) and revision of master formulation mentioning the salt and hydrated form of sitagliptin, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm shall submit duly signed Form 5 submitted undertaking at the end of form 5** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
155.	Name and address of manufacture / Applicant	M/s Ferroza International Pharmaceuticals Pvt. Ltd., 33 Km, Ferozepur Road, Lahore
	Brand Name + Dosage Form and Strength	Sitafer-Met 50/500 mg Tablet
	Composition	Each Tablet Contains: Sitagliptin Phosphate……..…50mg Metformin HCl…….500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11234 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Antidiabetic
	Type of form	Form 5
	Finished product specifications	Innovator's specifications
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Janumet film coated tablet (50mg/500mg, 50mg/1000mg) USFDA Approved.
	Me-too-status	Silomet M 50/500mg Tablet by M/s High-Q Pharmaceuticals (Reg#76399)
	GMP Status	
	Remark of the Evaluator [XI]	• You have mentioned the label claim without considering the salt factor in case of sitagliptin. Revise the label claim considering the salt factor along with submission of applicable

		fee. Furthermore, mention the hydrated form of sitagliptin in label claim and adjust its weight in master formulation considering the hydrated form • Mention the salt and hydrated form of sitagliptin in master formulation • You have applied for uncoated tablets while the reference formulation is film coated. Revise the label claim as per reference formulation along with submission of applicable fee. • Form 5 submitted without signature by the applicant • Undertaking at the end of form 5 is missing • Submit latest GMP inspection report conducted within last three years
	Decision: Approved with following label claim: **Each film coated tablet contains:** **Sitagliptin as Phosphate monohydrate……50mg** **Metformin HCl…….500mg** • **Firm shall submit the differential fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of salt factor and hydrated form of the drug substance) and revision of master formulation mentioning the salt and hydrated form of sitagliptin, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021** • **Firm shall submit duly signed Form 5 submitted undertaking at the end of form 5** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years**	
156.	Name and address of manufacture / Applicant	M/s Ferroza International Pharmaceuticals Pvt. Ltd., 33 Km, Ferozepur Road, Lahore
	Brand Name + Dosage Form and Strength	Muscofer 4mg Capsule
	Composition	Each Capsule Contains: Thiocolchicoside……4mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11238 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Muscle Relaxants, Centrally Acting Agents
	Type of form	Form 5
	Finished product specifications	BP
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	MIOREL 4mg hard capsule, ANSM France approved
	Me-too-status	Musrid 4mg Capsule by M/s Genix Pharma (Reg#094856)
	GMP Status	
	Remark of the Evaluator [XI]	• Form 5 submitted without signature by the applicant • Undertaking at the end of form 5 is missing

		• Submit latest GMP inspection report conducted within last three years • The firm have claimed for BP specifications and the official monograph is not available in any pharmacopeia
	Decision: Approved with innovator's specifications. • **Firm shall submit duly signed Form 5 submitted undertaking at the end of form 5** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change/ in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
157.	Name and address of manufacture / Applicant	M/s Ferroza International Pharmaceuticals Pvt. Ltd., 33 Km, Ferozepur Road, Lahore
	Brand Name + Dosage Form and Strength	Feroflex-P 37.5/325 mg Tablet
	Composition	Each Tablet Contains: Tramadol……37.5mg Paracetamol……325mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11237 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Opioids in combination with non-opioid analgesics
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Tramadol hydrochloride/Paracetamol 37.5mg/325mg Film-coated Tablets MHRA Approved
	Me-too-status	Distalgesic Tablets by M/s Atco Lab (Reg#73865)
	GMP Status	
	Remark of the Evaluator [XI]	• You have not mentioned the salt form of tramadol in label claim. Revise the label claim mentioning the salt form of tramadol along with submission of applicable fee. • You have applied for uncoated tablets while the reference formulation is film coated. Revise the label claim as per reference formulation along with submission of applicable fee. • Form 5 submitted without signature by the applicant • Undertaking at the end of form 5 is missing • Submit latest GMP inspection report conducted within last three years
	Decision: Approved with following label claim: **Each film coated tablet contains:** **Tramadol HCl……37.5mg** **Paracetamol……325mg**	

	• **Firm shall submit duly signed Form 5 submitted undertaking at the end of form 5** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit the differential fee of Rs. 30,000/- for correction/pre-approval change in composition (correction/change of salt form of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
158.	Name and address of manufacture / Applicant	M/s Goodman Laboratories., No.5, Street No. S-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name + Dosage Form and Strength	Pine 100mg Tablet
	Composition	Each Film Coated Tablet Contains: Quetiapine as Fumarate…….100mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10293 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Antipsychotics
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	10's, 14's, 20's, 30's, 50's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Quetiapine 100mg film coated tablet MHRA Approved.
	Me-too-status	Q-Med 100mg Tablets by M/s Medera Pharmaceuticals, (Reg#092163)
	GMP Status	GMP certificate issued to Goodman Laboratories based on inspection conducted on 08.08.2018
	Remark of the Evaluator [XI]	• Submit undertaking at the end of form 5 duly signed by the technical persons
	Decision: Deferred for following: • **Verification of validity status of DML from Licensing Divison.** • **Submission of undertaking at the end of form 5 duly signed by the technical persons**	
159.	Name and address of manufacture / Applicant	M/s Goodman Laboratories., No.5, Street No. S-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name + Dosage Form and Strength	Pine 25mg Tablet
	Composition	Each Film Coated Tablet Contains: Quetiapine as Fumarate……..…25mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10292 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Antipsychotics
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	10's, 14's, 20's, 30's, 50's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Quetiapine 25mg film coated tablet MHRA Approved.
	Me-too-status	Q-Med 25mg Tablets by M/s Medera Pharmaceuticals, (Reg#075431)

	GMP Status	GMP certificate issued to Goodman Laboratories based on inspection conducted on 08.08.2018
	Remark of the Evaluator [XI]	• Submit undertaking at the end of form 5 duly signed by the technical persons
	Decision: Deferred for following: • **Verification of validity status of DML from Licensing Divison.** • **Submission of undertaking at the end of form 5 duly signed by the technical persons**	
160.	Name and address of manufacture / Applicant	M/s Goodman Laboratories., No.5, Street No. S-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name + Dosage Form and Strength	Losap Plus Tablet 50/12.5mg
	Composition	Each Film Coated Tablet Contains: Losartan Potassium……50mg Hydrochlorothiazide……..12.5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10291 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Angiotensin II receptor blockers (ARBs) and diuretics
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	10's, 14's, 20's, 30's, 50's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Cozaar Comp 50mg/12.5mg film-coated tablets MHRA approved
	Me-too-status	Losmart-H Tablet 50mg/ 12.5 mg by M/s Scilife Pharma (Reg#100197)
	GMP Status	GMP certificate issued to Goodman Laboratories based on inspection conducted on 08.08.2018
	Remark of the Evaluator [XI]	• Submit undertaking at the end of form 5 duly signed by the technical persons • You have mentioned the quantity of losartan potassium in master formulation (54.24mg/tab) more than the label claim, clarify
	Decision: Deferred for following: • **Verification of validity status of DML from Licensing Divison.** • **Submission of undertaking at the end of form 5 duly signed by the technical persons** • **Submission of revised master formulation mentioning the quantity of API as per label claim**	
161.	Name and address of manufacture / Applicant	M/s Goodman Laboratories., No.5, Street No. S-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name + Dosage Form and Strength	Pride 200mg Tablet
	Composition	Each Tablet Contains: Amisulpride……..200mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10283 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Antipsychotics (Benzamides)
	Type of form	Form 5

	Finished product specifications	BP
	Pack size and Demand Price	10's, 20's, 30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Amisulpride 200mg Tablets MHRA Approved
	Me-too-status	Aurlex Tablets 200mg by M/s Bio-mark Pharmaceuticals (Reg#093592)
	GMP Status	GMP certificate issued to Goodman Laboratories based on inspection conducted on 08.08.2018
	Remark of the Evaluator [XI]	• Submit undertaking at the end of form 5 duly signed by the technical persons • You have not submitted manufacturing outline for the applied product. Submit complete manufacturing outline for the applied product
	Decision: Deferred for following: • **Verification of validity status of DML from Licensing Divison.** • **Submission of undertaking at the end of form 5 duly signed by the technical persons** • **Submission of complete manufacturing outline for the applied product**	
162.	Name and address of manufacture / Applicant	M/s Goodman Laboratories., No.5, Street No. S-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name + Dosage Form and Strength	Pride 50mg Tablet
	Composition	Each Tablet Contains: Amisulpride…….50mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10300 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Antipsychotics (Benzamides)
	Type of form	Form 5
	Finished product specifications	BP
	Pack size and Demand Price	10's, 20's, 30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Amisulpride 50mg Tablets MHRA Approved
	Me-too-status	Aurlex Tablets 50mg by M/s Bio-mark Pharmaceuticals (Reg#093591)
	GMP Status	GMP certificate issued to Goodman Laboratories based on inspection conducted on 08.08.2018
	Remark of the Evaluator [XI]	• Submit undertaking at the end of form 5 duly signed by the technical persons • You have not submitted manufacturing outline for the applied product. Submit complete manufacturing outline for the applied product
	Decision: Deferred for following: • **Verification of validity status of DML from Licensing Divison.** • **Submission of undertaking at the end of form 5 duly signed by the technical persons** • **Submission of complete manufacturing outline for the applied product**	

163.	Name and address of manufacture / Applicant	M/s Goodman Laboratories., No.5, Street No. S-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name + Dosage Form and Strength	E-Cit Tablet 5mg
	Composition	Each Film Coated Tablet Contains: Escitalopram as Oxalate……..5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10287 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Selective serotonin reuptake inhibitors
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	10's, 14's, 20's, 28's, 30's, 60's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Lexapro (5mg, 10mg, 20mg) film-coated tablets USFDA Approved
	Me-too-status	Avulus 5mg Tablet by M/s Seatle (Pvt) Ltd (Reg#098266)
	GMP Status	GMP certificate issued to Goodman Laboratories based on inspection conducted on 08.08.2018
	Remark of the Evaluator [XI]	• Submit undertaking at the end of form 5 duly signed by the technical persons • You have not submitted manufacturing outline for the applied product. Submit complete manufacturing outline for the applied product
	Decision: Deferred for following: • **Verification of validity status of DML from Licensing Divison.** • **Submission of undertaking at the end of form 5 duly signed by the technical persons** • **Submission of complete manufacturing outline for the applied product**	
164.	Name and address of manufacture / Applicant	M/s Goodman Laboratories., No.5, Street No. S-5, National Industrial Zone, Rawat, Rawalpindi
	Brand Name + Dosage Form and Strength	Dil Tablet 25mg
	Composition	Each Film Coated Tablet Contains: Carvedilol……25mg
	Dairy No. date of R &I fee	Form-5 Dy.No 10286 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Alpha and beta blocking agents
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	10's, 20's, 30's, 50's:As per SRO
	Approval status of product in Reference Regulatory Authorities	COREG (3.125mg, 6.25mg, 12.5mg, 25mg) film-coated tablet USFDA Approved
	Me-too-status	Vidocar 25mg Tablet by M/s Horizon Healthcare (Reg#099537)
	GMP Status	GMP certificate issued to Goodman Laboratories based on inspection conducted on 08.08.2018

	Remark of the Evaluator [XI]	• Submit undertaking at the end of form 5 duly signed by the technical persons • You have not submitted manufacturing outline for the applied product. Submit complete manufacturing outline for the applied product
	Decision: Deferred for following: • **Verification of validity status of DML from Licensing Divison.** • **Submission of undertaking at the end of form 5 duly signed by the technical persons** • **Submission of complete manufacturing outline for the applied product**	
165.	Name and address of manufacture / Applicant	M/s Hamaz Pharmaceuticals (Pvt.) Ltd. 13-km, Bosan Road, Lutfabad, Multan
	Brand Name + Dosage Form and Strength	Cpine Injection 250mg
	Composition	Each Vial Contains Cefepime as HCl with L Arginine eq. to Cefepime.…250mg
	Dairy No. date of R &I fee	Form-5 Dy.No 13035 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Fourth-generation cephalosporins
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Cefstar Injection IV/IM 250mg by M/s Barrett Hodgson Pakistan (Reg#076005)
	GMP Status	The firm was inspected on 17-01-2018 and recommendations of inspection were: In view of all the above it is observed that the management has addressed most of the short comings, which were pointed out during the last inspection which leads the panel of inspectors to the conclusions that the firm is presently operating at satisfactory level of GMP compliance of M/s Hamaz Pharmaceuticals is situated at Multan hence it is advised to the management to continue their efforts to further upgrade their systems.
	Remark of the Evaluator [XI]	• The firm have mentioned different names and dosage form on cover letter, form 5 and fee challan. The name mentioned on cover letter Cefnir suspension 125mg/5ml, fee challan is Cefnir / Cefdinir125mg/5ml while name mentioned on form 5 is Cpine

		injection 250mg, clarify? You have also not mentioned the dosage form on fee challan • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink • Provide evidence of required manufacturing facility/section approval letter • Submit latest GMP inspection report conducted within last three years • You have mentioned the addition of 3% overage in master formuation, provide scientific justification for addition of overage • The firm have mentioned the use of type II glass vial as primary packaging material of the applied formulation
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
166.	Name and address of manufacture / Applicant	M/s Hamaz Pharmaceuticals (Pvt.) Ltd. 13-km, Bosan Road, Lutfabad, Multan
	Brand Name + Dosage Form and Strength	Ketorol Injection 30mg/ml
	Composition	Each ml Contains: Ketorolac Tromethamine…30mg
	Dairy No. date of R &I fee	Form-5 Dy.No 13037 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	NSAID
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1mlx5's; As per SRO
	Approval status of product in Reference Regulatory Authorities	TORADOL Injection (15mg/ml, 30mg/ml) USFDA approved. **Discontinued** **Federal Register determination that product was not discontinued or withdrawn for safety or efficacy reasons**
	Me-too-status	Xevolac 30mg/ml Injection by M/s Danas Pharmaceuticals (Reg#099867)
	GMP Status	The firm was inspected on 17-01-2018 and recommendations of inspection were: In view of all the above it is observed that the management has addressed most of the short comings, which were pointed out during the last inspection which leads the panel of inspectors to

		the conclusions that the firm is presently operating at satisfactory level of GMP compliance of M/s Hamaz Pharmaceuticals is situated at Multan hence it is advised to the management to continue their efforts to further upgrade their systems.
	Remark of the Evaluator [XI]	• The firm have mentioned different names, molecule and dosage form on cover letter, form 5 and fee challan. The name mentioned on cover letter is Fosimax suspension 250mg/5ml, fee challan is Fosimax / Fosfomycin calcium dry suspension while name mentioned on form 5 is Ketorol injection 30mg/ml (ketorolactromethamine), clarify? *Furthermore, the above mentioned product on form 5 is already applied, clarify why you applied the same product again.* • You have not mentioned terminal sterilization in manufacturing outline, justify? • Mention type of primary packaging material of applied formulation whether it is type I, II or III • Provide evidence of required manufacturing facility/section approval letter • Submit latest GMP inspection report conducted within last three years • You have mentioned the addition of 5% overage of API in master formulation, clarify? • You have mentioned Ketorolac trometamol in master formulation while Ketorolac trometamine in label calim, clarify? • Submit complete manufacturing outline of the applied product • ***Same molecule and dosage form already considered by the Registration board in 321st DRB meeting***
	Decision: Registration Board decided to reject the application as same molecule and dosage form has already been considered by the Registration board in 321st meeting	
167.	Name and address of manufacture / Applicant	M/s Hamaz Pharmaceuticals (Pvt.) Ltd. 13-km, Bosan Road, Lutfabad, Multan
	Brand Name + Dosage Form and Strength	Trama Injection 100mg/2ml
	Composition	Each 2ml Contains: Tramadol HCl……100mg

	Dairy No. date of R &I fee	Form-5 Dy.No 13036 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Opioids Analgesic
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	2mlx5's; As per SRO
	Approval status of product in Reference Regulatory Authorities	TRAMAL tramadol hydrochloride 100mg/2mL injection ampoule TGA Approved
	Me-too-status	Amadrol Injection 100mg/ 2ml by M/s Amarant Pharmacetuicals (Reg#83042)
	GMP Status	The firm was inspected on 17-01-2018 and recommendations of inspection were: In view of all the above it is observed that the management has addressed most of the short comings, which were pointed out during the last inspection which leads the panel of inspectors to the conclusions that the firm is presently operating at satisfactory level of GMP compliance of M/s Hamaz Pharmaceuticals is situated at Multan hence it is advised to the management to continue their efforts to further upgrade their systems.
	Remark of the Evaluator [XI]	• The firm have mentioned different names, molecule and dosage form on cover letter, form 5 and fee challan. The name mentioned on cover letter is Cefnir suspension 250mg/5ml, fee challan is Cefnir / cefdinir 250mg/5ml while name mentioned on form 5 is Trama injection 100mg/2ml (Tramadol Hydrochloride), clarify? *Furthermore, the above mentioned product on form 5 is already applied, clarify why you applied the same product again.* • You have mentioned the weight of Tramadol HCl 105mg/2m in master formulation instead of 100mg/2ml as per label claim, clarify? • You have not mentioned terminal sterilization in manufacturing outline, justify? • Provide evidence of required manufacturing facility/section approval letter • Submit latest GMP inspection report conducted within last three years

		• Submit complete manufacturing outline of the applied product • ***Same molecule and dosage form already approved by the Registration board in 321st DRB meeting***
	Decision: Registration Board decided to reject the application as same molecule and dosage form has already been approved by the Registration board in 321st meeting	
168.	Name and address of manufacture / Applicant	M/s Hudson Pharma Private Limited., Site-Plot No. D-93, North Western Industrial Zone, Port Qasim Authority, Pakistan
	Brand Name + Dosage Form and Strength	Vilavent 100mcg/25mcg Rotacaps
	Composition	Each Rotacaps Contains: Fluticasone furoate…….100mcg Vilanterol as Trifenatate……...25mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 10355 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	BREO ELLIPTA (100/25mcg, 200/25mcg, inhalation powder) USFDA approved
	Me-too-status	Relvar Ellipta Dry Powder Inhaler 100mcg/25mcg by M/s Glaxo Smith Kline Pakistan (Reg# 085722)
	GMP Status	The firm was inspected on 03-04-2019 and conclusion of inspection was: Overall cGMP is found at acceptable level and the management is committed for continual improvement and has assured further cGMP compliance.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia.

		• Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • Submitted undertaking at the of form 5 submitted with stamped signature • Provide evidence of required manufacturing facility/section approval letter • Submit stability studies data of three batches as per the guidelines approved in 293rd meeting of Registration Board
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
169.	Name and address of manufacture / Applicant	M/s Hudson Pharma Private Limited., Site-Plot No. D-93, North Western Industrial Zone, Port Qasim Authority, Pakistan
	Brand Name + Dosage Form and Strength	Vilavent 200mcg/25mcg Rotacaps
	Composition	Each Rotacaps Contains: Fluticasone furoate……200mcg Vilanterol as Trifenatate…….25mcg
	Dairy No. date of R &I fee	Form-5 Dy.No 10354 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	30's; As per SRO
	Approval status of product in Reference Regulatory Authorities	BREO ELLIPTA (100/25mcg, 200/25mcg, inhalation powder) USFDA approved
	Me-too-status	Relvar Ellipta Dry Powder Inhaler 200mcg/25mcg by M/s Glaxo Smith Kline Pakistan (Reg# 085723)
	GMP Status	The firm was inspected on 03-04-2019 and conclusion of inspection was: Overall cGMP is found at acceptable level and the management is committed for continual improvement

		and has assured further cGMP compliance.
	Remark of the Evaluator [XI]	As per decision of 290th meeting of Registration Board: • Provide evidence of separate manufacturing facility/section for manufacturing of Rotacaps (DPIs) including specialized mixing facility to ensure the required particle size of the formulation blend. • Provide evidence of equipments for performing the test of "Uniformity of Delivered Dose" and "Aerodynamic Particle Size Distribution" as per Pharmacopoeia. • Provide description of Drug Delivery Device, which is compatible with the intended product and will be used for delivering the required "Target Delivery Dose". • Submit the label claim for "Target Delivery Dose" based upon the studies with the intended delivery system under defined test conditions (i.e., flow rate, duration). • Submitted undertaking at the of form 5 submitted with stamped signature • Provide evidence of required manufacturing facility/section approval letter • Submit stability studies data of three batches as per the guidelines approved in 293rd meeting of Registration Board
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
170.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Istisone Cream 1% w/w
	Composition	Contains: Hydrocortisone……1% w/w
	Dairy No. date of R &I fee	Form-5 Dy.No 11267 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Corticosteroids
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	10gm; As per SRO
	Approval status of product in Reference Regulatory Authorities	Hydrocortisone Cream BP 1.0% MHRA approved

	Me-too-status	Corteroid Cream by M/s FYNK Pharmaceuticals (Reg#081261)
	GMP Status	
	Remark of the Evaluator XI	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant • Submit latest GMP inspection report conducted within last three years • The applied label claim is not as per reference product. Revise the label claim as per reference product along with submission of applicable fee.
	Decision: Approved with following label claim: **Each gram Contains:** **Hydrocortisone……1% w/w** • **Firm shall submit the fee of Rs. 7,500/- for correction/pre-approval change in label claim in form 5 as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit 1st page of form 5 as per prescribed format duly signed by the applicant**	
171.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Isfyl Cough Syrup 45mg/8mg
	Composition	Each 5ml Contains: Acefylline Piperazine……45mg Diphenhydramine HCl……..8mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11276 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Xanthine/ Anti-histamine
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	60ml, 120ml, 450ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Acelyf Syrup by M/s Hicon Pharmaceuticals (Reg#077431)
	GMP Status	
	Remark of the Evaluator XI	• Revise 1st page of form 5 as per rescribed format duly signed by the applicant • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink • Submit latest GMP inspection report conducted within last three years

	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
172.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Iszyl Tablet 300mg
	Composition	Each Tablet Contains: Allopurinol……300mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11273 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Antigout Preparations
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	3x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	ZYLOPRIM (100mg, 300mg) tablets USFDA approved
	Me-too-status	Parinol 300mg Tablet by M/s Pulse Pharmaceuticals (Reg#102404)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant • Submit latest GMP inspection report conducted within last three years
	Decision: Approved. • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit 1st page of form 5 as per prescribed format before issuance of registration letter along with applicable fee for revision of Form 5, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
173.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Isget Tablet 10mg
	Composition	Each Film Coated Tablet Contains: Atorvastatin as Atorvastatin Calcium trihydrate…..…10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11275 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	HMG CoA reductase inhibitors
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Lipitor 10mg film-coated tablets MHRA Approved
	Me-too-status	Atorviz 10mg tablets by Tabros Pharma (Reg#098542)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant

		• Renewal of DML granted on 15-06-2021
	Decision: Approved. Firm shall submit 1st page of form 5 as per prescribed format before issuance of registration letter along with applicable fee for revision of Form 5, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
174.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Issacic Tablet 500mg
	Composition	Each Tablet Contains: Basic Aluminium Sucrose Sulfate (Sucralfate)……500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11272 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Other drugs for peptic ulcer and gastro-oesophageal reflux disease (GORD)
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	10x10's, 1x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Acenil Tablet 500mg by M/s Medisave Pharmaceuticals (Reg#068189)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink • Renewal of DML granted on 15-06-2021
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
175.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Is-Ferate Syrup
	Composition	Each 5ml Contains: Ferrous sulphate……200mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11268 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Iron bivalent, oral preparations
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	120ml; As per SRO

	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Ferrous Sulphate Syp by M/s Hameedsons F Abad (Reg#004676)…strength per ml could not be verified
	GMP Status	
	Remark of the Evaluator [XI]	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink • Renewal of DML granted on 15-06-2021
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
176.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Isphage Tablet 500mg
	Composition	Each Film Coated Tablet Contains: Metformin HCl……500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11271 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Biguanide (Antidiabetic)
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	10x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Metformin Hydrochloride 500mg film coated Tablets MHRA Approved
	Me-too-status	Glucomin 500mg Tablet by M/s Lisko Pakistan (Reg#082146)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant • Renewal of DML granted on 15-06-2021
	Decision: Approved. Firm shall submit 1st page of form 5 as per prescribed format before issuance of registration letter along with applicable fee for revision of Form 5, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
177.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Istamazole Tablet 400/500mg

	Composition	Each Tablet Contains: Metronidazole……400mg Diloxanide Furoate…….500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11274 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Nitroimidazole derivatives
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10x10's; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Disenite Tablets by M/s Hizat Pharmaceutical Industry (Reg#078409)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant • Provide evidence of approval of applied formulation in reference regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink • Renewal of DML granted on 15-06-2021
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
178.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Iszinc Oral Suspension 20mg/5ml
	Composition	Each 5ml Contains: Zinc Sulphate Monohydrate eq. to elemental zinc ……20mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11266 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Other Mineral Supplements
	Type of form	Form 5
	Finished product specifications	Manufacturer's specifictations
	Pack size and Demand Price	30ml, 60ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	
	Me-too-status	Zincor 200mg Dry Susp by M/s Genome Pharmaceuticals (Reg#075533)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant • Provide evidence of approval of applied formulation in reference

		regulatory authorities / agencies which were adopted by the Registration Board in its 275th meeting along with weblink • Renewal of DML granted on 15-06-2021. • Applied formulation is dry powder suspension
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
179.	Name and address of manufacture / Applicant	M/s ISIS Pharmaceuticals & Chemical Works., 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi
	Brand Name + Dosage Form and Strength	Iszinc Syrup 20mg/5ml
	Composition	Each 5ml Contains: Zinc Sulphate Monohydrate eq. to elemental zinc..…20mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11265 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Other Mineral Supplements
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	60ml, 120ml, 450ml; As per SRO
	Approval status of product in Reference Regulatory Authorities	Available in IP of WHO as solution (Available strengths: 10mg & 20mg of zinc per 5 mL)
	Me-too-status	ZNC 20mg/5ml Syrup by M/s Rotex Pharma (Reg#099950)
	GMP Status	
	Remark of the Evaluator [XI]	• Revise 1st page of form 5 as per prescribed format duly signed by the applicant • Renewal of DML granted on 15-06-2021
	Decision: Approved. Firm shall submit 1st page of form 5 as per prescribed format before issuance of registration letter along with applicable fee for revision of Form 5, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
180.	Name and address of manufacture / Applicant	M/s Nabiqasim Industries Pvt Ltd. 17/24, Korangi Industrial Area, Karachi, Pakistan
	Brand Name + Dosage Form and Strength	Glitab Tablet 5mg/500mg
	Composition	Each Film Coated Tablet Contains: Dapagliflozin Popanediol Monohydrate eq to Dapagliflozins……..5mg Metformin HCl…….500mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11407 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Combinations of oral blood glucose lowering drugs
	Type of form	Form 5
	Finished product specifications	Innovator's specifications

	Pack size and Demand Price	10's, 14's, 28's; As per SRO
	Approval status of product in Reference Regulatory Authorities	XIGDUO XR (2.5mg/1000mg, 5mg/500mg, 5mg/1000mg, 10mg/500mg, 10mg/1000mg) USFDA Approved
	Me-too-status	
	GMP Status	The firm was inspected on 05-08-2019 and conclusion of inspection was: Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection M/s Nabi Qasim Karachi is considered to be operating at an acceptable level of compliance of GMP requirements.
	Remark of the Evaluator [XI]	• Provide evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm OR submit application on requisite form 5D, stability studies data of three batches as per the guidelines approved in 293rd meeting of Registration Board, along with submission of differential fee. • The reference formulation is film coated extended release tablets and contain immediate release dapagliflozine and extended release metformin hydrochloride drug substance. Revise your formulation and manufacturing outline as per reference formulation along with submission of applicable fee.
	Decision: Deferred for evaluation of stability study data on its turn	
181.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Empozin 25mg Tablet
	Composition	Each Film Coated Tablet Contains: Empagliflozin……25mg
	Dairy No. date of R &I fee	Form-5D Dy.No 11222 dated 05-03-2019 Rs.50,000/- dated 05-03-2019
	Pharmacological Group	Blood Glucose Lowering Drugs, Excl. Insulins
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	7x1's, 10x1's, 14x1's, 28x1's, 30x1's, 60x1's, 70x1's, 90x1's, 100x1's; As per SRO

	Approval status of product in Reference Regulatory Authorities	JARDIANCE (10mg, 25mg) film-coated tablets USFDA Approved
	Me-too-status	Empoli 25mg Tablet by M/s Sami Pharmaceuticals (Reg#098701)
	GMP Status	
	Remark of the Evaluator [XI]	• You have applied on form 5D. Apply on prescribed form 5 for the applied product • Submit stability study data of three batches as per the guidelines approved in 293rd meeting of Registration Board. • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of DRB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
182.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Empozin 10mg Tablet
	Composition	Each Film Coated Tablet Contains: Empagliflozin……10mg
	Dairy No. date of R &I fee	Form-5D Dy.No 11221 dated 05-03-2019 Rs.50,000/- dated 05-03-2019
	Pharmacological Group	Blood Glucose Lowering Drugs, Excl. Insulins
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	7x1's, 10x1's, 14x1's, 28x1's, 30x1's, 60x1's, 70x1's, 90x1's, 100x1's; As per SRO
	Approval status of product in Reference Regulatory Authorities	JARDIANCE (10mg, 25mg) film-coated tablets USFDA Approved
	Me-too-status	Empoli 10mg Tablet by M/s Sami Pharmaceuticals (Reg#098702)
	GMP Status	
	Remark of the Evaluator [XI]	• You have applied on form 5D. Apply on prescribed form 5 for the applied product • Submit stability study data of three batches as per the guidelines approved in 293rd meeting of Registration Board. • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of DRB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
183.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Recoxia 90mg Tablet
	Composition	Each Film Coated Tablet Contains: Etoricoxib……90mg

	Dairy No. date of R &I fee	Form-5D Dy.No 11219 dated 05-03-2019 Rs.50,000/- dated 05-03-2019
	Pharmacological Group	NSAID
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	2's, 5's, 7's, 10's, 14's, 20's, 28's, 30's, 50's, 84's, 100's; As per SRO
	Approval status of product in Reference Regulatory Authorities	ARCOXIA 90mg film coated tablet MHRA Approved.
	Me-too-status	
	GMP Status	
	Remark of the Evaluator [XI]	• Submit stability study data of three batches as per the guidelines approved in 293rd meeting of Registration Board. • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of DRB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
184.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Recoxia 120mg Tablet
	Composition	Each Film Coated Tablet Contains: Etoricoxib…….120mg
	Dairy No. date of R &I fee	Form-5D Dy.No 11218 dated 05-03-2019 Rs.50,000/- dated 05-03-2019
	Pharmacological Group	NSAID
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	2's, 5's, 7's, 10's, 14's, 20's, 28's, 30's, 50's, 84's, 100's; As per SRO
	Approval status of product in Reference Regulatory Authorities	ARCOXIA 120mg film coated tablet MHRA Approved.
	Me-too-status	
	GMP Status	
	Remark of the Evaluator [XI]	• Submit stability study data of three batches as per the guidelines approved in 293rd meeting of Registration Board. • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of DRB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
185.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Zolaxen Tablets
	Composition	Each Tablet Contains: 375mg enteric coated Naproxen 20mg immediate release Esomeprazole magnesium

	Dairy No. date of R &I fee	Form-5D Dy.No 11223 dated 05-03-2019 Rs.50,000/- dated 05-03-2019
	Pharmacological Group	NSAID and PPI combination
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10's, 20's, 30's, 60's, 100's; As per SRO
	Approval status of product in Reference Regulatory Authorities	VIMOVO (naproxen and esomeprazole magnesium trihydrate) delayed-release tablets, for oral use (375 mg enteric-coated naproxen /20 mg immediate-release esomeprazole film-coated or 500 mg enteric-coated naproxen /20 mg immediate-release esomeprazole film-coated). US-FDA approved
	Me-too-status	
	GMP Status	
	Remark of the Evaluator [XI]	• Mention hydrated form of esomeprazole in label claim. Revise label claim considering the salt factor along with submission of applicable fee, and adjust the weight of API in Master formula considering the salt and hydrated form. • The reference formulation is delayed release tablet while you have applied otherwise. Revise label as per reference formulation along with submission of applicable fee • The submitted manufacturing outline is not as per reference product. Submit manufacturing outline as per reference product accordingly • Submit stability study data of three batches as per the guidelines approved in 293rd meeting of Registration Board. • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of DRB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
186.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Zolaxen plus Tablets
	Composition	Each Tablet Contains: 500mg enteric coated Naproxen 20mg immediate release Esomeprazole magnesium

	Dairy No. date of R &I fee	Form-5D Dy.No 11224 dated 05-03-2019 Rs.50,000/- dated 05-03-2019
	Pharmacological Group	NSAID and PPI combination
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10's, 20's, 30's, 60's, 100's; As per SRO
	Approval status of product in Reference Regulatory Authorities	VIMOVO (naproxen and esomeprazole magnesium trihydrate) delayed-release tablets, for oral use (375 mg enteric-coated naproxen /20 mg immediate-release esomeprazole film-coated or 500 mg enteric-coated naproxen /20 mg immediate-release esomeprazole film-coated). US-FDA approved
	Me-too-status	
	GMP Status	
	Remark of the Evaluator [XI]	• Mention hydrated form of esomeprazole in label claim. Revise label claim considering the salt factor along with submission of applicable fee, and adjust the weight of API in Master formula considering the salt and hydrated form. • The reference formulation is delayed release tablet while you have applied otherwise. Revise label as per reference formulation along with submission of applicable fee • The submitted manufacturing outline is not as per reference product. Submit manufacturing outline as per reference product accordingly • Submit stability study data of three batches as per the guidelines approved in 293rd meeting of Registration Board. • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of DRB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
187.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Lesart 10/40mg Tablet
	Composition	Each Film Coated Tablet Contains: Telmisartan……40mg Amlodipine as Besylate……10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11213 dated 05-03-2019 Rs.20,000/- dated 05-03-2019

	Pharmacological Group	Calcium channel blockers and Angiotensin II receptor blockers (ARBs)
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	TWYNSTA (40/5mg, 40/10mg, 80/5mg, 80/10mg) Tablets USFDA Approved
	Me-too-status	Cresar AM Tablet 10mg/40mg by M/s Tabros Pharma (Reg#094851)
	GMP Status	
	Remark of the Evaluator [XI]	• You have applied for film coated tablets while the reference formulation is bilayered tablets. Revise your label claim, formulation and manufacturing outline as per reference formulation along with submission of applicable fee. • Provide evidence of availability of bilayered compression tablet facility • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months of issuance of minutes of 322nd meeting. In case Pharmaceutical Evaluation Cell does not receive any response from firm within the given time, the case will be placed before Registration Board for decision.	
188.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Lesart 10/80mg Tablet
	Composition	Each Film Coated Tablet Contains: Telmisartan……..80mg Amlodipine as Besylate……..10mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11215 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Calcium channel blockers and Angiotensin II receptor blockers (ARBs)
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	TWYNSTA (40/5mg, 40/10mg, 80/5mg, 80/10mg) Tablets USFDA Approved
	Me-too-status	Cresar AM Tablet 10mg/80mg by M/s Tabros Pharma (Reg#094853)
	GMP Status	
	Remark of the Evaluator [XI]	• You have applied for film coated tablets while the reference formulation is bilayered tablets. Revise your label claim, formulation and manufacturing outline as per

		reference formulation along with submission of applicable fee. • Provide evidence of availability of bilayered compression tablet facility • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
189.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Lesart 5/40mg Tablet
	Composition	Each Film Coated Tablet Contains: Telmisartan……40mg Amlodipine as Besylate…….5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11212 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Calcium channel blockers and Angiotensin II receptor blockers (ARBs)
	Type of form	Form 5
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	TWYNSTA (40/5mg, 40/10mg, 80/5mg, 80/10mg) Tablets USFDA Approved
	Me-too-status	Cresar AM Tablet 5mg/40mg by M/s Tabros Pharma (Reg#094850)
	GMP Status	
	Remark of the Evaluator [XI]	• You have applied for film coated tablets while the reference formulation is bilayered tablets. Revise your label claim, formulation and manufacturing outline as per reference formulation along with submission of applicable fee. • Provide evidence of availability of bilayered compression tablet facility • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
190.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Lesart 5/80mg Tablet
	Composition	Each Film Coated Tablet Contains: Telmisartan……...80mg Amlodipine as Besylate……..5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11214 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Calcium channel blockers and Angiotensin II receptor blockers (ARBs)
	Type of form	Form 5

	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	TWYNSTA (40/5mg, 40/10mg, 80/5mg, 80/10mg) Tablets USFDA Approved
	Me-too-status	Cresar AM Tablet 5mg/80mg by M/s Tabros Pharma (Reg#094852)
	GMP Status	
	Remark of the Evaluator [XI]	• You have applied for film coated tablets while the reference formulation is bilayered tablets. Revise your label claim, formulation and manufacturing outline as per reference formulation along with submission of applicable fee. • Provide evidence of availability of bilayered compression tablet facility • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
191.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Rovan Tablet 15mg
	Composition	Each Tablet Contains: Tolvaptan……..15mg
	Dairy No. date of R &I fee	Form-5D Dy.No 11220 dated 05-03-2019 Rs.50,000/- dated 05-03-2019
	Pharmacological Group	Vasopressin antagonists
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10, 30, 90, blister, or 500 count bottle; As per SRO
	Approval status of product in Reference Regulatory Authorities	JYNARQUE (15mg, 30mg, 45mg, 60mg, 90mg) tablets USFDA approved
	Me-too-status	
	GMP Status	
	Remark of the Evaluator [XI]	• Submit stability study data of three batches as per the guidelines approved in 293rd meeting of Registration Board. • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of RB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
192.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Rovan Tablet 30mg
	Composition	Each Tablet Contains: Tolvaptan……...30mg

	Dairy No. date of R &I fee	Form-5D Dy.No 11217 dated 05-03-2019 Rs.50,000/- dated 05-03-2019
	Pharmacological Group	Vasopressin antagonists
	Type of form	Form 5D
	Finished product specifications	Manufacturer's specifications
	Pack size and Demand Price	10, 30, 90, blister, or 500 count bottle; As per SRO
	Approval status of product in Reference Regulatory Authorities	JYNARQUE (15mg, 30mg, 45mg, 60mg, 90mg) tablets USFDA approved
	Me-too-status	
	GMP Status	
	Remark of the Evaluator [XI]	• Submit stability study data of three batches as per the guidelines approved in 293rd meeting of Registration Board. • Submit latest GMP inspection report conducted within last three years
	Decision: Registration Board deferred the case for submission of reply to above cited shortcomings along with stability studies data as per checklist of 293rd meeting of RB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
193.	Name and address of manufacturer / Applicant	M/s Radiant Pharma Pvt Ltd., 43-E, Sundar Industrial Estate, Lahore
	Brand Name + Dosage Form and Strength	Belock Tablet 80mg/5mg
	Composition	Each Film Coated Tablet Contains: Valsartan……80mg Amlodipine as Besylate…….5mg
	Dairy No. date of R &I fee	Form-5 Dy.No 11216 dated 05-03-2019 Rs.20,000/- dated 05-03-2019
	Pharmacological Group	Calcium channel blockers and Angiotensin II receptor blockers (ARBs)
	Type of form	Form-5
	Finished product specifications	USP
	Pack size and Demand Price	; As per SRO
	Approval status of product in Reference Regulatory Authorities	Amlodipine/Valsartan 5mg/80mg film-coated tablets MHRA Approved
	Me-too-status	Amlodine Tablet 5/80 by M/s Jupiter Pharma (Reg#081931)
	GMP Status	
	Remark of the Evaluator [XI]	• You have applied for film coated tablets but the master formulation does not show coating composition and manufacturing outline does not show coating procedure, clarify and revise your master formulation and manufacturing outline as per reference formulation along with submission of applicable fee. • Submit latest GMP inspection report conducted within last three years
	Decision: Approved.	

	• **Firm shall submit revised master formulation and manufacturing outline mentioning coating composition and coating procedure respectively.** • **Submission of GMP audit report of the firm from QA&LT Division, valid within last three years** • **Firm shall submit fee of Rs.7,500/- for correction/pre-approval change in the amster formulation and method of manufacture, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

Case No. 08: Registration applications of Human Drugs on Form 5F (Local) whose reply is not received

194.	Name, address of Applicant / Marketing Authorization Holder	Kaizen Pharmaceuticals (Pvt.) Ltd., E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.
	Name, address of Manufacturing site.	Kaizen Pharmaceuticals (Pvt.) Ltd., E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25693 dated 15/09/2021
	Details of fee submitted	PKR 75,000/-: dated 02/07/2021
	The proposed proprietary name / brand name	Ilazo 10mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains Vilazodone HCl……...10mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	***Angiotensin II receptor blocker***
	Reference to Finished product specifications	Manufacturer's specification
	Proposed Pack size	10's, 20's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	VIIBRYD (10mg, 20mg, 40mg) film-coated tablets USFDA Approved
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	The firm was inspected on 11-08-2020 and conclusion of inspection was:

		The overall cGMP compliance of the firm with respect to building, facilities and procedures demonstrated was satisfactory at the time of inspection.
	Name and address of API manufacturer.	***Section 1.6.5:*** M/s Symed Labs Limited Sy.No.744, 745, ***750, 751, 752*** & 751. Mandollagudem Village, Choutuppal Mandal, Yadadri District, Telangana India***. (expired 24-04-2018)*** ***3.2.S.2:*** Symed Labs Limited (Unit-I) Survey No.353, Domadugu (Village), Jinnaram (Mandal), Medak (Dist) – 502 313. Telangana, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(VLH Ex No: 001, VLH Ex No: 002, VLH Ex No: 003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Viibryd 10mg tablet performing quality tests (Identification, Assay, Dissolution).

		CDP has been performed against the same brand that is Viibryd 10mg Tablet in Acid media (pH 0.1N HCl), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, accuracy, precision, specificity, LOD, LOQ)

STABILITY STUDY DATA			
Manufacturer of API	Symed Labs Limited (Unit I), Survey No.353, Domadugu (Village), Jinnaram (Mandal), Medak (Dist.) - 502 313. Telangana, India ***(Applied)***		
API Lot No.	VLH0060616		
Description of Pack (Container closure system)	PVC/ aluminum blister pack		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24(Months)		
Batch No.	TF-01	TF-02	TF-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	13-09-2017	19-12-2017	19-12-2017
Date of Initiation	28-09-2017	18-01-2018	18-01-2018
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted reference of previous inspection report of Rofair 500 mcg Tablet which is conducted on 25-06-2019 and considered in 290th meeting of Registration Board. The report confirms that: • HPLC system is 21 CFR part II compliant and Audit trail reports were available • Firm has adequate monitoring and controls for stability chambers. Chambers are controlled and monitored through software having alarm system for alerts as well
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm submitted certificate No. L.Dis.No.6592/A3/2017 of M/s Symed Labs Limited Sy.No.744, 745 & 751. Mandollagudem Village, Choutuppal Mandal, Yadadri District, Telangana India issued by Drugs Control Administration Govt. of Telangana. ***(valid upto 24-04-2018)***
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted FedEx receipt dated 28-March-2017. However, the contents of receipt are not readable

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with attested respective documents like chromatograms, Raw data sheets, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator [XI]:

Section	Observations	Response
1.5.5.	• Mention correct Pharmacological class of the API (drug substance) along with WHO ATC code for each distinct therapeutic indication.	
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer issued by relevant regulatory authority of country of origin is required • Clarification shall be submitted since the submitted GMP, COA, stability summary sheet of drug substance and section 3.2.S.2.1 of form 5F reflects different manufacturing site	
3.2.S.4	• Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	
3.2.S.6	• Description of the container closure system(s) for the shipment and storage of the API including materials of construction of each primary packaging component.	
3.2.P.2.2.1	• A brief description of formulation development shall be given.	
3.2.P.5.1.	• Justify the acceptance criteria of dissolution test NLT Q in 45min in product specifications since FDA review documents specifies that dissolution criteria shall be NLT Q in 30 min for the applied product	
3.2.P.5.3	• No chromatographic conditions are mentioned in analytical method validation	
3.2.P.5.4	• Identification test as mentioned in specification is by HPLC while in Batch analysis performed by IR, clarify?	
3.2.P.6	• COA of Reference Standards or Materials is not submitted, instead COA of Drug substance is submitted. COA of primary / secondary reference standard including source and lot number shall be provided.	

3.2.P.8	• The quantity of imported drug substance as per submitted COA is 40gm (DS COA) / 0.039KG (Drug product COA) and three batches of 10mg & 20mg Ilazo tablets each of 1500 tablets were manufactured from it. Justification is required as how the imported drug substance was sufficient enough to manufacture three batches of each strength. *(drug substance required for three batches of 10mg tab 45.33 gm and 20mg tab is 90.54gm)* • COAs of performed stability study are not submitted • Compliance Record of HPLC software 21CFR & audit trail reports on product testing is not submitted • Submit readable copy of documents for the procurement of API with approval from DRAP. • Sampling and testing date of API by drug product manufacturer is 13-11-2017 while manufacturing date of the drug product batch No. TF-01 is 13-09-2017 which is prior to sampling and testing date of API, clarify?	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

195.	Name, address of Applicant / Marketing Authorization Holder	Kaizen Pharmaceuticals (Pvt.) Ltd., E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.
	Name, address of Manufacturing site.	Kaizen Pharmaceuticals (Pvt.) Ltd., E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25694 dated 15/09/2021
	Details of fee submitted	PKR 75,000/-: dated 02/07/2021
	The proposed proprietary name / brand name	Ilazo 20mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains Vilazodone HCl……...20mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Antidepressant Agent

	Reference to Finished product specifications	Manufacturer's specification
	Proposed Pack size	10's, 20's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	VIIBRYD (10mg, 20mg, 40mg) film-coated tablets USFDA Approved
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	The firm was inspected on 11-08-2020 and conclusion of inspection was: The overall cGMP compliance of the firm with respect to building, facilities and procedures demonstrated was satisfactory at the time of inspection.
	Name and address of API manufacturer.	***Section 1.6.5:*** M/s Symed Labs Limited Sy.No.744, 745, ***750, 751, 752*** & 751. Mandollagudem Village, Choutuppal Mandal, Yadadri District, Telangana India***. (expired 24-04-2018)*** ***3.2.S.2:*** Symed Labs Limited (Unit-I) Survey No.353, Domadugu (Village), Jinnaram (Mandal), Medak (Dist) – 502 313. Telangana, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(VLH Ex No: 001, VLH Ex No: 002, VLH Ex No: 003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and

		controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Viibryd 20mg tablet performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is Viibryd 20mg Tablet in Acid media (pH 0.1N HCl), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, accuracy, precision, specificity, LOD, LOQ)

STABILITY STUDY DATA			
Manufacturer of API	Symed Labs Limited (Unit I), Survey No.353, Domadugu (Village), Jinnaram (Mandal), Medak (Dist.) - 502 313. Telangana, India ***(Applied)***		
API Lot No.	VLH0060616		
Description of Pack (Container closure system)	PVC/ aluminum blister pack		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24(Months)		
Batch No.	TF-01	TF-02	TF-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	13-09-2017	19-12-2017	19-12-2017
Date of Initiation	28-09-2017	04-01-2018	04-01-2018
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted reference of previous inspection report of Rofair 500 mcg Tablet which is conducted on 25-06-2019 and considered in 290th meeting of Registration Board. The report confirms that: • HPLC system is 21 CFR part II compliant and Audit trail reports were available • Firm has adequate monitoring and controls for stability chambers. Chambers are controlled and monitored through software having alarm system for alerts as well

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm submitted certificate No. L.Dis.No.6592/A3/2017 of M/s Symed Labs Limited Sy.No.744, 745 & 751. Mandollagudem Village, Choutuppal Mandal, Yadadri District, Telangana India issued by Drugs Control Administration Govt. of Telangana. ***(valid upto 24-04-2018)***
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted FedEx receipt dated 28-March-2017. However, the contents of receipt are not readable
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches along with attested respective documents like chromatograms, Raw data sheets, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator [XI]:

Section	Observations	Response
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer issued by relevant regulatory authority of country of origin is required • Clarification shall be submitted since the submitted GMP, COA, stability summary sheet of drug substance and section 1.6.5 and section 3.2.S.2.1 of form 5F reflects different manufacturing site	
3.2.S.4	• Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	
3.2.S.6	• Description of the container closure system(s) for the shipment and storage of the API including materials of construction of each primary packaging component.	
3.2.P.2.2.1	• A brief description of formulation development shall be given.	
3.2.P.5.1.	• Justify the acceptance criteria of dissolution test NLT Q in 45min in product specifications since FDA review documents specifies that dissolution criteria shall be NLT Q in 30 min for the applied product	
3.2.P.5.3	• No chromatographic conditions are mentioned in analytical method validation	
3.2.P.6	• COA of primary / secondary reference standard including source and lot number shall be provided.	

3.2.P.8	• The quantity of imported drug substance as per submitted COA is 40gm (DS COA) / 0.039KG (Drug product COA) and three batches of 10mg & 20mg Ilazo tablets each of 1500 tablets were manufactured from it. Justification is required as how the imported drug substance was sufficient enough to manufacture three batches of each strength. *(drug substance required for three batches of 10mg tab 45.33 gm and 20mg tab is 90.54gm)* • COAs of performed stability study are not submitted • Compliance Record of HPLC software 21CFR & audit trail reports on product testing is not submitted • Submit readable copy of documents for the procurement of API with approval from DRAP. • Sampling and testing date of API by drug product manufacturer is 13-11-2017 while manufacturing date of the drug product batch No. TF-01 is 13-09-2017 which is prior to sampling and testing date of API, clarify?	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

196.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad, Pakistan
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22581 dated 17/08/2021
	Details of fee submitted	PKR 30,000/-: dated 16/07/2021
	The proposed proprietary name / brand name	Deglu-Met 5mg/850mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Dapagliflozin…….5mg Metformin HCL….850mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	sodium-glucose co-transporter 2 (SGLT2) inhibitors. biguanide class of antidiabetics

	Reference to Finished product specifications	Innovator specs
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	XIGDUO 5mg/850mg Tablet. (Health Canada approved)
	For generic drugs (me-too status)	Dapa-Met 5mg/850mg Tablet by M/s Hilton Pharma (Reg# 093071)
	GMP status of the Finished product manufacturer	GMP certificate issued on 24-12-2018 based on inspection conducted on 24-10-2018.
	Name and address of API manufacturer.	**Dapagliflozin:** Fuxin Long Rui Pharmaceutical Co. Ltd., Fluoride Industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCL:** Aarti Drugs Limited., Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Dapagliflozin:** Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (160108, 160124, 160220)
		Metformin HCL: Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 48 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (MEF/1410027, MEF/1410028, MEF/1410029)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers,

		description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence and comparative dissolution profile of their developed formulation Deglu-Met 5mg/850mg Tablet (B # ST21A033) with comparator product Dapa-Met 5mg/850mg Tablet (B #136549) of M/s Hilton Pharma. Pvt. Ltd. in pH 1.2, acetate buffer pH 4.5 and phosphate buffer pH 6.8. The results of CDP showed that release profile of both test and comparator products were comparable. Calculation of f2 factor is not required as both metformin and dapagliflozin releases from test and comparator product more than 85 % in 15 minutes in all three-pH medium
	Analytical method validation/verification of product	Firm have submitted method validation studies including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**<u>Dapagliflozin:</u>** Fuxin Long Rui Pharmaceutical Co. Ltd., Fluoride Industrial park, Fuxin city, Liaoning province, 123000, China. **<u>Metformin HCL</u>:** Aarti Drugs Limited., Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155		
API Lot No.	Dapagliflozin: DG-20190327-D01-DG06-05 Metformin HCL: MEF/10030953		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3,6, 9, 12, 18, 24 (Months)		
Batch No.	ST21B033	ST21B034	ST21B035
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	04-03-2021	04-03-2021	04-03-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided

		to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. **Inspection date:** 14th March, 2019 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Dapagliflozin:** The firm has submitted GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co., Ltd, China issued by Liaoning Fuxin Management Committee for Fluoride Industrial Development Zone. The certificate is valid till 23-08-2023 Firm has submitted copy of Drug Manufacturing License (DML # Liao20150233) of Fuxin Long Rui Pharmaceutical Co. Ltd., China issued by Food & Drug Administration, Liaoning Province China. The certificate is valid till 20-12-2022. Metformin HCL: The firm has submitted GMP certificate for Aarti Drugs Limited India issued by Food & Drug Control Administration Gandhinagar India. The certificate is valid till 19-03-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Dapagliflozin: The firm has submitted attested copy of invoice for the import of dapagliflozin (1.5 Kg, Invoice # HN19120501-H) dated 05-12-2019 and attested copy of AD (I&E) DRAP, Islamabad clearance certificate dated 10-01-2020. Metformin HCL: The firm has submitted attested copy of invoice for the import of Metformin HCl (1000 Kg, Invoice # EXP/302/20-21) dated 15-5-2020, and attested AD (I&E) DRAP, Islamabad clearance certificate dated 05-08-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & Audit trail on testing reports of product submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.4	• Submit latest GMP inspection report conducted with in last three years	
1.5.2	• Mention the salt and hydrated form of dapagliflozin in label claim and adjust its weight in batch formula considering the salt and hydrated form • Submit the fee of Rs. 30,000 for correction/pre-approval change in composition (correction / change	

<table>
<tr><td></td><td>of salt and hydrated form of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.</td><td></td></tr>
<tr><td>2.3.R.1.1</td><td>• You have not mentioned the salt and hydrated form of dapagliflozin BMR. Moreover, salt factor and hydrated form was not considered while dispensing the API dapagliflozin, clarify?</td><td></td></tr>
<tr><td>3.2.S.4</td><td>• Assay test for drug substance Metformin is performed by titration by both drug substance manufacturer & drug product manufacturer instead by HPLC as per USP 44
• Verification study for metformin performed as per titration method instead by HPLC as per USP 44</td><td></td></tr>
<tr><td>3.2.P.1</td><td>• You have not mentioned the salt and hydrated form of dapagliflozin in composition as well as in batch formula section 3.2.P.3.2 as per reference product. Mention the salt and hydrated form of dapagliflozin in label claim and adjust its weight in batch formula considering the salt and hydrated form</td><td></td></tr>
<tr><td>3.2.P.2</td><td>• You have not performed CDP and pharmaceutical equivalence against the innovator brand justify?</td><td></td></tr>
<tr><td>3.2.P.2.1.1</td><td>• Compatibility studies of the Drug Substance(s) with excipients shall be provided as the qualitative composition of the formulation is not similar to innovator / reference product.
<table>
<tr><th>Applied product</th><th>XIGDUO tablet</th></tr>
<tr><td>Dapagliflozin
Metformin HCl</td><td>Dapagliflozin as dapagliflozin propanediol monohydrate
Metformin HCl</td></tr>
<tr><td>Maize Starch</td><td></td></tr>
<tr><td>Sodium starch glycolate type A</td><td>sodium starch glycolate</td></tr>
<tr><td>Magnesium Stearate</td><td>Magnesium Stearate</td></tr>
<tr><td>Microcrystalline cellulose</td><td>Microcrystalline cellulose</td></tr>
<tr><td>•</td><td>Hydroxypropyl cellulose</td></tr>
</table></td><td></td></tr>
<tr><td>3.2.P.8</td><td>• Submit 6th month stability study data at both real time and accelerated conditions
• Value for label claim mentioned in calculation formula for determining the assay of metformin at 3rd month time point of accelerated and real stability study data of Batch # ST21B033, Batch # ST21B034 and Batch # ST21B035 is not according to the applied formulation, clarify?
• Different volume of dissolution media, label claim and dilution mentioned in calculation formula for determining the dissolution of metformin at 3rd</td><td></td></tr>
</table>

	month time point of accelerated and real time stability study of Batch # ST21B033, Batch # ST21B034 and Batch # ST21B035 than that mentioned in analytical procedure, clarify? • Different volume of dissolution media mentioned in calculation formula for determining the dissolution of dapagliflozin at 3rd month time point of accelerated and real time stability study of Batch # ST21B033, Batch # ST21B034 and Batch # ST21B035 than that mentioned in analytical procedure, clarify?	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

197.	Name, address of Applicant / Marketing Authorization Holder	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad, Pakistan
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals (Pvt.) Ltd. Plot # 204-205 Industrial Triangle, kahuta Road, Islamabad, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22582 dated 17/08/2021
	Details of fee submitted	PKR 30,000/-: dated 16/07/2021
	The proposed proprietary name / brand name	Deglu-Met 5mg/1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Dapagliflozin…….5mg Metformin HCL….1000mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	sodium-glucose co-transporter 2 (SGLT2) inhibitors. biguanide class of antidiabetics
	Reference to Finished product specifications	Innovator specs
	Proposed Pack size	14’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	XIGDUO 5mg/1000mg Tablet. (Health Canada approved)
	For generic drugs (me-too status)	Dapa-Met 5mg/1000mg Tablet by M/s Hilton Pharma (Reg# 093072)

	GMP status of the Finished product manufacturer	GMP certificate issued on 24-12-2018 based on inspection conducted on 24-10-2018.
	Name and address of API manufacturer.	**Dapagliflozin:** Fuxin Long Rui Pharmaceutical Co. Ltd., Fluoride Industrial park, Fuxin city, Liaoning province, 123000, China. **Metformin HCL:** Aarti Drugs Limited., Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Dapagliflozin:** Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 24 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (160108, 160124, 160220)
		Metformin HCL: Stability study conditions: Real time: 30°C ± 2°C, RH: 65% ± 5% for 48 months Accelerated: 40°C ± 2°C, RH: 75% ± 5% for 6 months Batches: (MEF/1410027, MEF/1410028, MEF/1410029)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence and comparative dissolution profile of their developed formulation Deglu-Met 5mg/1000mg Tablet (B # ST21B030) with comparator product Dapa-Met 5mg/1000mg Tablet (B #135679) of M/s

		Hilton Pharma. Pvt. Ltd. in pH 1.2, acetate buffer pH 4.5 and phosphate buffer pH 6.8. The results of CDP showed that release profile of both test and comparator products were comparable. Calculation of f2 factor is not required as both metformin and dapagliflozin releases from test and comparator product more than 85 % in 15 minutes in all three-pH medium
	Analytical method validation/verification of product	Not submitted

STABILITY STUDY DATA

Manufacturer of API	**<u>Dapagliflozin:</u>** Fuxin Long Rui Pharmaceutical Co. Ltd., Fluoride Industrial park, Fuxin city, Liaoning province, 123000, China. **<u>Metformin HCL</u>:** Aarti Drugs Limited., Plot No. 211 - 213, Road No.2 G.I.D.C., Sarigam, Dist.: Valsad, Gujarat. INDIA.396155		
API Lot No.	Dapagliflozin: DG-20190327-D01-DG06-05 Metformin HCL: MEF/10030953		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3,6, 9, 12, 18, 24 (Months)		
Batch No.	ST21B030	ST21B031	ST21B032
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	04-03-2021	04-03-2021	04-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 289th meeting decided to approve registration of Promig Plus 500mg/20mg Tablet and Promig Plus 375mg/20mg Tablet. **Inspection date:** 14th March, 2019 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**<u>Dapagliflozin:</u>** The firm has submitted GMP certificate for M/s Fuxin Long Rui Pharmaceutical Co., Ltd, China issued by Liaoning Fuxin Management Committee for Fluoride Industrial Development Zone. The certificate is valid till 23-08-2023

		Firm has submitted copy of Drug Manufacturing License (DML # Liao20150233) of Fuxin Long Rui Pharmaceutical Co. Ltd., China issued by Food & Drug Administration, Liaoning Province China. The certificate is valid till 20-12-2022. Metformin HCL: The firm has submitted GMP certificate for Aarti Drugs Limited India issued by Food & Drug Control Administration Gandhinagar India. The certificate is valid till 19-03-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Dapagliflozin: The firm has submitted attested copy of invoice for the import of dapagliflozin (1.5 Kg, Invoice # HN19120501-H) dated 05-12-2019 and attested copy of AD (I&E) DRAP, Islamabad clearance certificate dated 10-01-2020. Metformin HCL: The firm has submitted attested copy of invoice for the import of Metformin HCl (1000 Kg, Invoice # EXP/302/20-21) dated 15-5-2020, and attested AD (I&E) DRAP, Islamabad clearance certificate dated 05-08-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & Audit trail on testing reports of product submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.4	• Submit latest GMP inspection report conducted with in last three years	
1.5.2	• Mention the salt and hydrated form of dapagliflozin in label claim and adjust its weight in batch formula considering the salt and hydrated form • Submit the fee of Rs. 30,000 for correction/pre-approval change in composition (correction / change of salt and hydrated form of the drug substance), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
2.3.R.1.1	• You have not mentioned the salt and hydrated form of dapagliflozin BMR. Moreover, salt factor and hydrated form was not considered while dispensing the API dapagliflozin, clarify?	
3.2.S.4	• Assay test for drug substance Metformin is performed by titration by both drug substance manufacturer & drug product manufacturer instead by HPLC as per USP 44 • Verification study for metformin performed as per titration method instead by HPLC as per USP 44	

<table>
<tr><td>3.2.P.1</td><td>• You have not mentioned the salt and hydrated form of dapagliflozin in composition as well as in batch formula section 3.2.P.3.2 as per reference product. Mention the salt and hydrated form of dapagliflozin in label claim and adjust its weight in batch formula considering the salt and hydrated form</td><td></td></tr>
<tr><td>3.2.P.2</td><td>• You have not performed CDP and pharmaceutical equivalence against the innovator brand justify?</td><td></td></tr>
<tr><td>3.2.P.2.1.1</td><td>• Compatibility studies of the Drug Substance(s) with excipients shall be provided as the qualitative composition of the formulation is not similar to innovator / reference product.
<table>
<tr><th>Applied product</th><th>XIGDUO tablet</th></tr>
<tr><td>Dapagliflozin Metformin HCl</td><td>Dapagliflozin as dapagliflozin propanediol monohydrate Metformin HCl</td></tr>
<tr><td>Maize Starch</td><td></td></tr>
<tr><td>Sodium starch glycolate type A</td><td>sodium starch glycolate</td></tr>
<tr><td>Magnesium Stearate</td><td>Magnesium Stearate</td></tr>
<tr><td>Microcrystalline cellulose</td><td>Microcrystalline cellulose</td></tr>
<tr><td></td><td>Hydroxypropyl cellulose</td></tr>
</table></td><td></td></tr>
<tr><td>3.2.P.5.3</td><td>• Analytical method validation report is not submitted</td><td></td></tr>
<tr><td>3.2.P.8</td><td>• Submit 6th month stability study data at both real time and accelerated conditions
• The volume of dissolution media mentioned in calculation formula for determining the dissolution of metformin at 3rd month time point of accelerated and real time stability study of Batch # ST21B030, Batch # ST21B031 and Batch # ST21B032 is different than that mentioned in analytical procedure, clarify?
• The volume of dissolution media mentioned in calculation formula for determining the dissolution of dapagliflozin at 3rd month time point of accelerated and real time stability study of Batch # ST21B030, Batch # ST21B031 and Batch # ST21B032 is different than that mentioned in analytical procedure, clarify?</td><td></td></tr>
</table>

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

198.	Name, address of Applicant / Marketing Authorization Holder	M/s Jawa Pharmaceuticals Private Limited., 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,

	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited., 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24075 dated 01-09-2021
	Details of fee submitted	PKR 30,000/-: dated 07-06-2021
	The proposed proprietary name / brand name	Cholein Tablet USP 40mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet contains: Atorvastatin (as calcium trihydrate)…… 40mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	HMG CoA reductase inhibitors
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	1 x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Atorvastatin 40 mg film coated Tablet by M/s Dexcel®-Pharma Ltd.7 Sopwith Way, Drayton Fields, Daventry, Northamptonshire, NN11 8PB, UK, MHRA Approved
	For generic drugs (me-too status)	Truva Tablet 40mg by Sami Pharmaceuticals (Reg# 100511)
	GMP status of the Finished product manufacturer	The firm have submitted cGMP certificate issued on 06-07-2020 based on inspection conducted on 04-03-2020
	Name and address of API manufacturer.	Zhejiang Haisen Pharmaceutical Co., Ltd., Xiangtan Village, Liushi Street, Dongyang City, Zhejiang Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature,

		structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (5616010201, 5616010202, 5616010203)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	CDP has been performed against the Lipitor Tablet (40mg) by Pfizer Pharma in Acid media (pH 1.2), acetate Buffer (pH 4.5) & Phosphate Buffer (pH 7). The values for f2 is in the acceptable range
	Analytical method validation/verification of product	Firm have submitted method verification studies including accuracy, precision and specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Zhejiang Haisen Pharmaceutical Co., Ltd., Xiangtan Village, Liushi Street, Dongyang City, Zhejiang Province, China		
API Lot No.	5620051201		
Description of Pack (Container closure system)	PVC/aluminum foil blister packs - then packed in the bleach board box.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	Trial 01	Trial 02	Trail 03
Batch Size	10,000 tablets	10,000 tablets	10,000 tablets
Manufacturing Date	22-07-2020	24-07-2020	27-07-2020
Date of Initiation	28-07-2020	28-07-2020	28-07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate for M/s Zhejiang Haisen Pharmaceutical Co., Ltd., Xiangtan Village, Liushi Street, Dongyang City, Zhejiang Province, China issued by China Food & Drug Administration. The certificate is valid till 21-08-201. Firm has submitted copy of Drug Manufacturing License (DML # ZHE20000394) of M/s Zhejiang Haisen Pharmaceutical Co., Ltd., China issued by State Food & Drug Administration, China. The certificate is valid till 24-09-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm have submitted Data of stability batches supported by attested respective documents like chromatograms and summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.3	In status of applicant you have mentioned "Is involved in none of the above (contract giver)", clarify?	
2.3.R.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	
3.2.S.4	• Test for enantiomeric purity is not included in specifications although given in USP monograph of drug substance, clarify? • Copies of analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug Product manufacturer is required.	
3.2.S.5	• COA of primary / secondary reference standard including source and lot number shall be provided.	
3.2.P.2.1.1	• Compatibility studies of the Drug Substance(s) with excipients shall be provided as the qualitative composition of the formulation is not similar to innovator / reference product. (**Composition of Applied Formulation**: Atorvastatin calcium, Microcrystalline cellulose (avicel 200), Magnesium stearate, Sodium starch glycolate (Primogel), silica dioxide)	

	• You have not performed Pharmaceutical equivalence of the applied drug with the innovator / reference / comparator product, justify?	
3.2.P.5	• In given specification of drug product, in identification test you have mentioned "identification for cefixime" while the applied product is atorvastatin calcium, clarify? • Test for uniformity of dosage unit (content uniformity) is not included in specifications and not performed in batch analysis although given in USP monograph of drug product, clarify?	
3.2.P.8	• Stability data reflect that dissolution test has not been performed after initial time point throughout stability studies at both accelerated and real time conditions, justify? • Submit COA, Raw data sheets & analytical record of stability studies containing calculation formula for both assay & dissolution test • Submit documents for the procurement of API with approval from DRAP.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

199.	Name, address of Applicant / Marketing Authorization Holder	ATCO Laboratories Limited., B-18, S.I.T.E., Karachi - 7500, Pakistan
	Name, address of Manufacturing site.	ATCO Laboratories Limited., B-18, S.I.T.E., Karachi - 7500, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28456 Dated 15/ 10/ 2021
	Details of fee submitted	PKR 30,000/-: Dated 04/10/2021 (Deposit Slip#489820062060)
	The proposed proprietary name / brand name	Ondansetron Tablet 4mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ondansetron……..4mg (as Ondansetron Hydrochloride Dihydrate BP)
	Pharmaceutical form of applied drug	Film coated Tablet
	Pharmacotherapeutic Group of (API)	Antiemetics and antinauseants, Serotonin (5-HT3) antagonists.
	Reference to Finished product	USP

	specifications	
	Proposed Pack size	7's, 10's, 14's, 20's, 28's, 30's.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zofran 4mg film coated tablet MHRA approved
	For generic drugs (me-too status)	Ongene 4mg Tablet by M/s High-Q Pharmaceuticals (Reg#091206)
	GMP status of the Finished product manufacturer	The firm was inspected on 22-03-2022 & 05-04-2022 by the panel for renewal of DML, regularization of section as per layout plan and additional sections and decision of panel is: Keeping in view the good facilities provided for manufacturing and quality control of pharmaceutical products registered in the name of firm being produced at the site and overall good maintenance of plan and the required documentation and SOPs, the panel recommended the grand of DML of the firm as well as regularization of sections as per layout plan and approval of additional sections
	Name and address of API manufacturer.	M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bengaluru Rural District-561203 India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Stability studies	Stability study conditions: Real time:30°C±2°C/75% ± 5%RH Accelerated:40°C±2°C/75%±5%RH Stability of all three batches at accelerated conditions (AOND-17002, AOND-17003, AOND-17004) conducted for 06 months Real time stability study of two batches AOND-17002, AOND-17003, conducted for 36 months while real time stability study of one batch AOND-17004 conducted for 24 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its

		verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Zofran 8mg Tablet by **GlaxoSmithKline Research Triangle Park, NC 27709 Marketed by: Novartis Pharmaceuticals UK Limited** performing quality tests (Identification, Assay, Dissolution, disintegration). CDP of ondansetron 8mg tablets has been performed against the zofran 8mg tablets in Acid media (pH 1.2), acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted method verification studies including range, accuracy, precision, specificity and robustness.

STABILITY STUDY DATA			
Manufacturer of API	M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bangaluru Rural District-561203 India		
API Lot No.	AOND-20013		
Description of Pack (Container closure system)	ALU-ALU Blister pack packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MA096C	MA097C	MA098C
Batch Size	4200 Tablets	4220 Tablets	4490 Tablets
Manufacturing Date	03/2021	03/2021	03/2021
Date of Initiation	25/03/2021	25/03/2021	25/03/2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection for authenticity of stability data of Rofl 500mcg tablet on the basis of which Registration Board in its 277th meeting dated 27-29 December, 2017 decided to approve registration of Rofl 500mcg tablet. Inspection date: 10-10-2017 The report shows that: The HPLC software is 21 CFR compliant. Adequate monitoring and control are available for stability chambers
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm have submitted copy of GMP certificate #DCD/SPL.CL-1/CR-1510/2020-21 dated 06-02-2021 of M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bangaluru

		Rural District-561203 India valid upto one year from the date of issue. The firm has submitted copy of DML #DCD/MFG/Applicant Id-240 dated 26/06/2020 of M/s Anugraha Chemicals, No D-47 to D-50, C-62 and C-63, KSSIDC, Industrial Estate, Doddaballapur, Bangaluru Rural District-561203 India valid upto 13/02/2025
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice # OND1200 dated 10-11-2020 for import on 300gm of Ondansetron HCl Dihydrate Batch #AOND-20014, AOND-20012 and AOND-20013 in the name of M/s Atco Laboratories Ltd Karachi form M/s Agraha Chemical India. *However, the invoice is not attested by AD (I&E) DRAP field office*
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance Record of HPLC software 21CFR & audit trail reports on product testing is submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator [XI]:

Section	Observations	Response
1.6.5	Submit valid GMP certificate of drug substance manufacturer	
3.2.S.4	• Copies of the analytical procedures used for routine testing of the Drug substance / Active Pharmaceutical ingredient by Drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	
3.2.S.5	Firm has submitted COA of primary reference standard which follows usp specifications and secondary reference standard which has followed Ph. Eu specifications while applied product follows bp specifications	
3.2.P.2	• Submit compatibility study as the qualitative composition of the applied formulation is not similar to innovator / reference product.	

Applied product	Zofran 4mg tab
Lactose anhydrous	Lactose
Sodium starch glycolate	Microcrystalline Cellulose

	<table><tr><td>Crospovidone</td><td>Pregelatinized maize starch</td></tr><tr><td>Magnesium stearate</td><td>Magnesium Stearate,</td></tr><tr><td>Opadry white</td><td>Methyl hydroxypropyl cellulose</td></tr><tr><td>Purified water</td><td>Titanium dioxide (E171)</td></tr><tr><td></td><td>Iron oxide (E172)</td></tr></table> • Justification is required as the pharmaceutical equivalence and CDP of higher strength has been submitted • Justify why the pharmaceutical equivalence study does not include complete testing of the drug product and the innovator product including the tests recommended by USP monograph (dissolution, identification, assay, uniformity of dosage unit). • Provide details of innovator product used during pharmaceutical equivalence study (batch #, mfg, exp)	
3.2.P.5.1	Justification for finished product specifications of USP is required as the drug substance has been analysed as per BP specifications by M/s Atco.	
3.2.P.6	Firm has submitted COA of secondary reference standard which has followed Ph. Eu specifications while the applied product follows USP specifications	
3.2.P.8	Submit documents for the procurement of API with approval from DRAP.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

200.	Name, address of Applicant / Marketing Authorization Holder	M/s Honig Pharmaceuticals., 14 km Adyala Road, Rawalpindi.
	Name, address of Manufacturing site.	M/s Honig Pharmaceuticals., 14 km Adyala Road, Rawalpindi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 31637 dated 17/11/2021
	Details of fee submitted	PKR 20,000/-: dated 26/02/2021
	The proposed proprietary name / brand	Valoton 40 mg tablets

	name	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated tablets contains: Valsartan…….40 mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Angiotensin II Receptor antagonist
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Diovan (40mg, 80mg, 160mg, 320mg) film coated tablets USFDA Approved
	For generic drugs (me-too status)	Valtec 40mg Tablet by M/s Tabros Pharrma (Reg#055899)
	GMP status of the Finished product manufacturer	----------
	Name and address of API manufacturer.	Zhejiang Menovo Pharmaceutical Co., Ltd., No. 8, Jing 13 Road, Hangzhou Gulf, Shangyu Economic and Technological Development Zone, 312369, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (VAL-D-4-081001, VAL-D-4-081002, VAL-D-4-081003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand Valtec 40mg tablet by M/s Tabros pharma by performing quality tests (Identification,

		Assay, Uniformity of dosage unit, dissolution). CDP has been performed against the same brand that is Valtec 40mg tablet by M/s Tabros pharma in 0.1 N HCl, 4.5 pH acetate buffer and 6.8pH phosphate buffer. The values for f2 is in the acceptable range
	Analytical method validation/verification of product	Not submitted

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Menovo Pharmaceutical Co., Ltd., No. 8, Jing 13 Road, Hangzhou Gulf, Shangyu Economic and Technological Development Zone, 312369, China		
API Lot No.	VAL-130901		
Description of Pack (Container closure system)	Alu Alu Blister Packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 and 24 (Months)		
Batch No.	T001	T002	T003
Batch Size	100000 tablets	100000 tablets	100000 tablets
Manufacturing Date	05-2019	05-2019	05-2019
Date of Initiation	05-2019	05-2019	05-2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No reference provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate #ZJ20190121 dated 28/10/2019 of M/s Zhejiang Menovo Pharmaceutical Co. Ltd., No. 8, Jing 13 Road, Hangzhou Gulf, Shangyu Economic and Technological Development Zone, 312369, China issued by China Food & Drug Administration valid upto 27/10/2024
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches supported by attested respective documents Raw data sheets, summary data sheets is submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm submitted that their HPLC system is not 21 CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of	Not submitted

	stability chambers (real time and accelerated)	

Remarks of Evaluator [XI]:

Section	Observations	Response
	• Differential fee of registration Rs. 10, 000/- shall be submitted	
1.3.5	• Latest GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	
2.3.R.1	• Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	
3.2.S.4	• Copies of the analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	
3.2.S.7	The test performed in stability study of drug substance by the drug substance manufacturer is different than that recommended by USP and submitted specifications, clarification is required **Specifications** / Accelerated conditions / Real time conditions / USP Appearance / Appearance / Appearance / Identification Identification (HPLC) / IR / IR / Residue on ignition Solubility / waters / LOD / Related substances/ impurities pH / Related substances / Impurity A, Impurity B, Impurity C, Any other Individual Impurity, Total Impurities Sulphated ash / Related substances, Single impurity, Total / Water determination Water (by K.F) / Content of Valsartan / Absorbance Heavy metals / Content of Valsartan / Assay Assay (On anhydrous basis)	
3.2.P.2	• Submit compatibility study as the qualitative composition of the applied formulation is not similar to innovator / reference product. **Applied product** / **Innovator tablet** Valsartan / Valsartan Sodium Starch Glycolate (Primojel) / colloidal silicon dioxide, and Starch(Maize) / --------- DE-Ionized Water / ----------	

	<table><tr><td>Microcrystalline Cellulose (Avicel 102)</td><td>microcrystalline cellulose,</td></tr><tr><td>Magnesium Stearate</td><td>magnesium stearate,</td></tr><tr><td>Talcum Purified</td><td>----------</td></tr><tr><td>Cross Povidone(Cross linked Carboxymethyl cellulose sodium)</td><td>crospovidone,</td></tr><tr><td>hydroxypropyl methylcellulose,</td><td>hydroxypropyl methylcellulose,</td></tr><tr><td>Titanium dioxide</td><td>Titanium dioxide.</td></tr><tr><td>Isopropyl alcohol</td><td>Iron oxides (yellow, black and/or red),</td></tr><tr><td>Off white color</td><td></td></tr><tr><td>Polyethylene glycol 6000</td><td>polyethylene glycol 8000,</td></tr></table> • Justification is required since pharmaceutical equivalence and CDP have not been conducted against the innovator product. • Provide details of reference product including batch No, mfg date and exp date • Results of CDP in pH 6.8 buffer are contradictory to the dissolution limits recommended by USP monograph.	
3.2.P.5	• The limits of average weight test given in specifications is 249mg±7.5% (subject to change with variation in potency of pellets) while applied products is tablet. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) for drug product shall be submitted.	
3.2.P.8	• Submit documents for the procurement of API with approval from DRAP (in case of import). • The API batch No# mentioned in batch analysis of drug substance is VAL-130901 while API batch No. mentioned in stability summary sheets is 40000290161. Clarification is required whether same batch number material mentioned in batch analysis is used for manufacturing of stability batches or otherwise • The stability study of all three batches at both accelerated and real time conditions at 3rd month time point is performed one month before the completion of three months and the same procedure adopted for subsequent time point respectively, clarification is required • Clarification is required since the stability study data at accelerated and real time conditions shows that Assay test has been performed on UV instead of HPLC as per USP monograph • The submitted raw data sheet at each time point doesn't specify the conditions (real time and accelerated) at which the stability study is performed, clarification is required	

	• No UV spectra provided for the performed dissolution study • Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) • COA of stability batches is not submitted.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

201.	Name, address of Applicant / Marketing Authorization Holder	M/s Honig Pharmaceuticals., 14 km Adyala Road, Rawalpindi.
	Name, address of Manufacturing site.	M/s Honig Pharmaceuticals., 14 km Adyala Road, Rawalpindi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32357 dated 26/11/2021
	Details of fee submitted	PKR 20,000/-: dated 26/02/2021
	The proposed proprietary name / brand name	Valoton 80 mg tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated tablets contains: Valsartan…….80 mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Angiotensin II Receptor antagonist
	Reference to Finished product specifications	USP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Diovan (40mg, 80mg, 160mg, 320mg) film coated tablets USFDA Approved
	For generic drugs (me-too status)	Valtec 80mg Tablet by M/s Tabros Pharrma (Reg#039772)
	GMP status of the Finished product manufacturer	----------
	Name and address of API manufacturer.	Zhejiang Menovo Pharmaceutical Co., Ltd., No. 8, Jing 13 Road, Hangzhou Gulf, Shangyu Economic and Technological Development Zone, 312369, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications,

		analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (VAL-D-4-081001, VAL-D-4-081002, VAL-D-4-081003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand Valtec 80mg tablet by M/s Tabros pharma by performing quality tests (Identification, Assay, Uniformity of dosage unit, dissolution). CDP has been performed against the same brand that is Valtec 80mg tablet by M/s Tabros pharma in 0.1 N HCl, 4.5 pH acetate buffer and 6.8pH phosphate buffer. The values for f2 is in the acceptable range
	Analytical method validation/verification of product	Not submitted

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Menovo Pharmaceutical Co., Ltd., No. 8, Jing 13 Road, Hangzhou Gulf, Shangyu Economic and Technological Development Zone, 312369, China		
API Lot No.	VAL-130901		
Description of Pack (Container closure system)	Alu Alu Blister Packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 and 24 (Months)		
Batch No.	T001	T002	T003
Batch Size	100000 tablets	100000 tablets	100000 tablets

Manufacturing Date	05-2019	05-2019	05-2019
Date of Initiation	05-2019	05-2019	05-2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	No reference provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate #ZJ20190121 dated 28/10/2019 of M/s Zhejiang Menovo Pharmaceutical Co. Ltd., No. 8, Jing 13 Road, Hangzhou Gulf, Shangyu Economic and Technological Development Zone, 312369, China issued by China Food & Drug Administration valid upto 27/10/2024
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches supported by attested respective documents Raw data sheets, summary data sheets is submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm submitted that their HPLC system is not 21 CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
	• Differential fee of registration Rs. 10, 000/- shall be submitted	
1.3.3	• Status of applicant is not specified	
1.3.5	• Latest GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	
2.3.R.1	• Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	
3.2.S.4	• Copies of the analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	
3.2.S.7	The test performed in stability study of drug substance by the drug substance manufacturer is different than that recommended by USP and submitted specifications, clarification is required	

Specifications	Accelerated conditions	Real time conditions	USP
Appearance			Identification

	Identification (HPLC) Solubility Sulphated ash Water (by K.F) Heavy metals Assay (On anhydrous basis)	Appearance IR waters pH Related substances Single impurity Total Content of Valsartan	Appearance IR LOD Related substances Impurity A Impurity B Impurity C Any other Individual Impurity Total Impurities Content of Valsartan	Residue on ignition Related substances/ impurities Water determination Absorbance Assay	

3.2.P.2

- Submit compatibility study as the qualitative composition of the applied formulation is not similar to innovator / reference product.

Applied product	**Innovator tablet**
Valsartan	Valsartan
Sodium Starch Glycolate (Primojel)	colloidal silicon dioxide, and
Starch(Maize)	---------
DE-Ionized Water	----------
Microcrystalline Cellulose (Avicel 102)	microcrystalline cellulose,
Magnesium Stearate	magnesium stearate,
Talcum Purified	----------
Cross Povidone(Cross linked Carboxymethyl cellulose sodium)	crospovidone,
hydroxypropyl methylcellulose,	hydroxypropyl methylcellulose,
Titanium dioxide	Titanium dioxide.
Isopropyl alcohol	Iron oxides (yellow, black and/or red),
Off white color	
Polyethylene glycol 6000	polyethylene glycol 8000,

-
- Justification is required since pharmaceutical equivalence and CDP have not been conducted against the innovator product.
- Provide details of reference product including batch No, mfg date and exp date

	• Justification is required since the results of weight variation test (456.2mg for valoton and 454.63 for valtec tablets) are out of specification in pharmaceutical equivalence (limits……280mg±7.5%) • Results of CDP in pH 6.8 buffer are contradictory to the dissolution limits recommended by USP monograph.	
3.2.P.5	• Specification and analytical procedure for valoton 40mg tablets is submitted instead of valoton 80mg tablets. Clarification is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) for drug product shall be submitted. • Same COA in batch analysis is submitted as that submitted in valoton 40mg tablet. Results of all test are same except average weight results	
3.2.P.8	• Submit documents for the procurement of API with approval from DRAP (in case of import). • The API batch No# mentioned in batch analysis of drug substance is VAL-130901 while API batch No. mentioned in stability summary sheets is 40000290161. Clarification is required whether same batch number material mentioned in batch analysis is used for manufacturing of stability batches or otherwise • The stability study of all three batches at both accelerated and real time conditions at 3rd month time point is performed one month before the completion of three months and the same procedure adopted for subsequent time point respectively, clarification is required • Clarification is required since the stability study data at accelerated and real time conditions shows that Assay test has been performed on UV instead of HPLC as per USP monograph • The submitted raw data sheet at each time point doesn't specify the conditions (real time and accelerated) at which the stability study is performed, clarification is required • No UV spectra provided for the performed dissolution study • Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) • COA of stability batches is not submitted. • Same stability study results have been reported as that for Valoton 40mg strength. • Same value of absorption of standard taken at all time point for assay test. Similarly, same value of absorption of standard taken at all time point for dissolution test. Clarification is required.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

202.	Name, address of Applicant / Marketing Authorization Holder	M/s Jawa Pharmaceuticals Private Limited., 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited., 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29538 dated 29-10-2021
	Details of fee submitted	PKR 30,000/-: dated 22-06-2021 (Deposit Slip#599036870370)
	The proposed proprietary name / brand name	Phencol ophthalmic solution 0.5% w/v
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Chloramphenicol BP…… 5mg
	Pharmaceutical form of applied drug	Eye Drops
	Pharmacotherapeutic Group of (API)	Ophthalmologicals-Antibiotics
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	10ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Chloramphenicol Eye Drops BP 0.5% w/v, MHRA Approved
	For generic drugs (me-too status)	Chlorin Eye drops by M/s NovaMed Pharmaceuticals (Reg#084887)
	GMP status of the Finished product manufacturer	The firm have submitted cGMP certificate issued on 06-07-2020 based on inspection conducted on 04-03-2020
	Name and address of API manufacturer.	Mehta API Pvt. Ltd., Gut No. 546, 571, 519 & 520, Village Kumbhavali, Taluka Palghar, District Palghar, 401506, Maharashtra India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and

		justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(CHL/0010108, CHL/0020108, CHL/0030108)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Not submitted
	Analytical method validation/verification of product	Firm have submitted method verification studies including accuracy, precision and specificity.

STABILITY STUDY DATA

Manufacturer of API	Mehta API Pvt. Ltd., Gut No. 546, 571, 519 & 520, Village Kumbhavali, Taluka Palghar, District Palghar, 401506, Maharashtra India.		
API Lot No.	LT-OCHL/016/20-21		
Description of Pack (Container closure system)	LDPE Plastic bottles with polypropylene nozzle and high density polyethylene (HDPE) cap. ***Pack size is 5ml in 10ml bottle***		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial-01	Trial-02	Trial-03
Batch Size	03 Litres	03 Litres	03 Litres
Manufacturing Date	30-09-2020	05-10-2020	08-10-2020
Date of Initiation			
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate of M/s Mehta API Pvt. Ltd., Gut No. 546, 571, 519 & 520, Village Kumbhavali, Taluka Palghar, District Palghar, 401506, Maharashtra India. issued by Commissioner, Food & Drugs Administration Maharashtra State India valid till 18-09-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm have submitted Data of stability batches supported by respective documents like chromatograms and summary data sheets etc.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator [XI]:

Section	Observations	Response
1.5.4	• Pack size mentioned in module 1 is 10ml while pack size mentioned in module 3 section 3.2.P.1 & 3.2.P.7 is -5ml in 10ml bottle, clarify?	
2.3.R.1	• Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	
2.3.	• Submit module II as per WHO QOS-PD template	
3.2.S.4	• Specifications and analytical procedure of drug substance by drug substance manufacturer are provided as per USP monograph while specification provided by drug product manufacturer are as per BP. Clarification is required. Furthermore, Batch analysis of drug substance by drug substance manufacturer show tests as per BP monograph • BP monograph uses HPLC method for assay test while drug product manufacturer uses uv method for assay test clarify?	
3.2.P.2	• Submit Pharmaceutical equivalence of the applied product against the innovator product • Sterilization by gama radiation in microbial attributes while by filtration in manufacturing process 3.2.P.3.3, clarify?	
3.2.P.5	• In batch analysis in assay test "assay for gentamycin is written while the applied product is chloramphenicol, clarification is required	
3.2.P.8	• In stability study protocols you have mentioned stability storage conditions as Real time: 30°C ± 2°C / 35% ± 5%RH and Accelerated: 40°C ± 2°C / 25% ± 5%RH and submit stability study at Real time: 30°C ± 2°C / 65% ± 5%RH and Accelerated: 40°C ± 2°C / 75% ± 5%RH, clarification is required • Initial page of stability summary sheet containing batch No. of FPP, API, storage conditions, date of manufacturing, date of initiation of stability study is not submitted • Clarification is required since the limits for assay test mentioned in stability summary sheet for all three	

	batches is 98-102% which is not as per pharmacopeia. • Submit documents for the procurement of API with approval from DRAP (in case of import). • Submit Compliance Record of HPLC software 21CFR & audit trail reports on product testing • COA and raw data sheets of stability batches is not submitted • The submitted chromatograms at initial time point does not contain batch no of applied product. • Submit data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

203.	Name, address of Applicant / Marketing Authorization Holder	M/s Ophth Pharma (Pvt) Ltd., Plot No. 241, Sector-24 Korangi Industrial Area, Karachi, Pakistan
	Name, address of Manufacturing site.	M/s Ophth Pharma (Pvt) Ltd., Plot No. 241, Sector-24 Korangi Industrial Area, Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 30259 dated 05-11-2021
	Details of fee submitted	Rs.20,000/- dated 26-02-2021
	The proposed proprietary name / brand name	Ophth Cyclovir Topical Cream 5%
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Gram Contains: Acyclovir BP……..…50mg/g
	Pharmaceutical form of applied drug	Topical Cream
	Pharmacotherapeutic Group of (API)	Antiviral
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	10gm tube
	Proposed unit price	Rs. 800
	The status in reference regulatory authorities	ZOVIRAX Cream 5% w/w, USFDA Approved
	For generic drugs (me-too status)	Hepex Cream 5% by M/s Evolution Pharmaceuticals (Reg# 091965)
	GMP status of the Finished product manufacturer	The firm has submitted GMP certificate issued on 02nd October 2020 based on inspection conducted on 27th September 2019

	Name and address of API manufacturer.	M/s Hubei Yitai Pharmaceutical Co. Ltd. Fengchengyuan, Suburban District of Tianmen City Hubei Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities physical form, manufacturers, description o manufacturing process and controls, specifications analytical procedures and its verification, batch analysis and justification of specification, reference standard container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature structure, general properties, solubilities, physical form manufacturers, specifications, batch analysis and stability studies of drug substance
	Stability studies	Stability study conditions: ***Real time: 30˚C ± 2˚C / 75% ± 5%RH for 12 months*** Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches:(02190501, 02190502, 02190503)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers description of manufacturing process and controls specifications, analytical procedure and its verification studies, batch analysis and justification of specification container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand that is Zovirax Topical Cream by M/s Barrett Hodgson by performing quality tests (appearance, identification, fill weight, drug release).
	Analytical method validation/verification of product	Not submitted

STABILITY STUDY DATA

Manufacturer of API	M/s Hubei Yitai Pharmaceutical Co. Ltd., Fengchengyuan, Suburban District of Tianmen City, Hubei Province, China		
API Lot No.			
Description of Pack (Container closure system)	Printed aluminum tube with nozzle and cap packed in unit carton		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 12 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)		
Batch No.	TB 101	TB 102	TB 103
Batch Size	5 Kg	5 Kg	5 Kg
Manufacturing Date	12-2019	12-2019	12-2019
Date of Initiation	9-12-2019	17-12-2019	26-12-2019

No. of Batches	03	
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	No GMP certificate submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm have submitted Data of stability batches supported by respective documents like UV spectra, raw data sheets and summary data sheets etc. ***Raw data sheets does not show the storage condition and time point at which performance is done***
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.4	• Submit valid copy of DML as the submitted DML is expired on 04-05-2021 and renewal of DML submitted on 17-05-2021	
1.3.5	• GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted	
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer issued by relevant regulatory authority of country of origin is required	
2.3.R.1	• Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	
3.2.S.4	• Copies of the analytical procedures used for routine testing of the Drug substance by Drug substance and drug Product manufacturer is required. • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	
3.2.S.4.4	• Batch analysis of drug substance by drug substance manufacturer follow USP specifications while Finished product manufacturer have tested the API as per BP monograph, clarification is required	

<table>
<tr><td></td><td>• Drug substance was tested on 18.05.2020 as per submitted COA of API by drug product manufacturer while batches were manufactured in 12-2019 before testing of API, clarify</td><td></td></tr>
<tr><td>3.2.S.5-6</td><td>• Container closure system data and reference standard details are not submitted</td><td></td></tr>
<tr><td>3.2.S.7</td><td>• Long term stability data of drug substance is submitted for 12 months only</td><td></td></tr>
<tr><td>3.2.P.1</td><td>• Justify the use of butylene paraben and methyl paraben in formulation as the innovator product does not contain these excipients.
<table>
<tr><td>Applied product</td><td>Innovator product (ZOVIRAX)</td></tr>
<tr><td>Stearic acid powder</td><td>cetostearyl alcohol,.</td></tr>
<tr><td>Ethylene glycol monostearate</td><td>mineral oil,</td></tr>
<tr><td>Isopropyl myristate</td><td>poloxamer 407,</td></tr>
<tr><td>Tween 80</td><td>propylene glycol,</td></tr>
<tr><td>Butylene paraben</td><td>sodium lauryl sulfate,</td></tr>
<tr><td>Propylene glycol</td><td>water</td></tr>
<tr><td>Methyl paraben</td><td>white petrolatum</td></tr>
<tr><td>Sorbitol solution 70%</td><td></td></tr>
<tr><td>Lavender oil</td><td></td></tr>
<tr><td>Purified water QS</td><td></td></tr>
</table>
• Pharmaceutical equivalence of applied product states that product follows the USP specification, while you have applied for BP specifications for the applied product, justification is required
• Process validation protocols for applied product shall be submitted</td><td></td></tr>
<tr><td>3.2.P.5</td><td>• The limits of assay test as per monograph of BP pharmacopeia is 95-105% while you have applied 45-55mg/g (90-110%) which is different from BP, clarification is required.
• Clarification is required since procedure of assay test given in analytical procedure is by UV while BP monograph for applied products states performance by HPLC.
• Submit Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) for drug product as per BP method.
• The copies of complete analysis of at least two batches shall be provided while you have provided batch analysis of only one batch, justify?</td><td></td></tr>
<tr><td>3.2.P.6</td><td>• No details of reference standard is submitted</td><td></td></tr>
<tr><td>3.2.P.8</td><td>• Clarification is required since assay test is performed by UV throughout stability study instead by HPLC as recommended by BP.</td><td></td></tr>
</table>

	• Submit documents for the procurement of API with approval from DRAP (in case of import). • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) • Submit data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcoming within six months.

Registration applications of New DML of human drugs on Form 5F

M/s Biogen Pharmaceuticals, 8-km Chakbeli Road Rawat Rawalpindi.

The Central Licensing Board in its 273rd meeting held on 15th January, 2020 has considered and approved the grant of Drug Manufacturing License by way of formulation with following sections of **M/s Biogen Pharmaceuticals, 8-km Chakbeli Road Rawat Rawalpindi** under Drug Manufacturing License No. 000911 by way of Formulation vide approval letter No. F. 1-2/2019-Lic dated 14th February 2020.

Ground Floor			
1	Dry Suspension (Cephalosporin) Section	2.	Capsule Section (Cephalosporin)
3	Dry Vial Section (Cephalosporin)	4.	Penem Injection Section
5	Ware House	*	**********
First Floor			
1	Tablet Section (General)	2	Capsule Section (General)
3	Sachet Section (General)	4	Cream Section (General)
5	Ointment Section (General)	6	Lotion Section (General)
7	Dry Vial Section (General)	*	**********
Second Floor			
1	Ampoule Section SVP (General)	2	Infusion Section (General)
3	Hydrocortisone Injection (Steroid)	4	Soft Gel Capsule General
5	Quality Control Lab	*	**********

Following applications have been submitted for registration by the firm.

204	Name, address of Applicant / Marketing Authorization Holder	M/s Biogen Life Sciences, 8-km Chakbeli Road Rawat Rawalpindi
	Name, address of Manufacturing site.	M/s Biogen Life Sciences, 8-km Chakbeli Road Rawat Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale

		☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 28775 dated 11-10-2022
	Details of fee submitted	Rs.30,000/- dated 14-07-2022 (Deposit Slip#01492435)
	The proposed proprietary name / brand name	OmeGen 20mg/1680mg Sachet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Sachet contains: Omeprazole……...20mg Sodium bicarbonate……1680mg
	Pharmaceutical form of applied drug	Immediate Release Powder for oral suspension
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator Specefications
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	ZEGERID (20mg/packet ; 1.68gm/packet, 40mg/packet ; 1.68gm/packet) for Oral Suspension USFDA Approved
	For generic drugs (me-too status)	Risek Insta Sachet 20mg + 1680mg by M/s Getz Pharma (Reg# 58547)
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020
	Name and address of API manufacturer.	**Omeprazole:** M/s Everest Organics limited., Aroor Village, Sadasivapet Mandal, Sangareddy Dist. Telangana India **Sodium Bicarbonate:** M/s United Chem., 18-Warlley Moor Lane Leeds West Workshire LS 12 4HX United Kingdom
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Omeprazole:**

		Firm has submitted stability study data of omeprazole. Stability study is conducted at accelerated conditions; ***25°C ± 2°C / 60% ± 5%RH for 06 months*** and at Real time conditions; ***2-8°C*** ± for 36 months Batches: OM/004/10, OM/005/10, OM/006/10)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the product that is Zegerid 20mg IR Powder for oral suspension by M/s Santarus Inc. by performing quality tests (Identification, Assay, Dissolution, content uniformity). CDP has been performed against the same brand that is Zegerid 20mg IR Powder for oral suspension by M/s Santarus Inc. in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	In method Validation studies only results for accuracy, precision is submitted.

STABILITY STUDY DATA

Manufacturer of API	**Omeprazole:** M/s Everest Organics limited., Aroor Village, Sadasivapet Mandal, Sangareddy Dist. Telangana India **Sodium Bicarbonate:** M/s United Chem., 18-Warlley Moor Lane Leeds West Workshire LS 12 4HX United Kingdom		
API Lot No.	**Omeprazole:** OME/E-143/21 **Sodium Bicarbonate:** 547908		
Description of Pack (Container closure system)	Aluminum foil Sachet packed in packing box		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3,6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	2000 Sachet	2000 Sachet	2000 Sachet
Manufacturing Date	09/2021	09/2021	09/2021
Date of Initiation	10-09-2021	10-09-2021	10-09-2021

No. of Batches		03
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Omeprazole:** Firm has submitted GMP certificate No# L.Dis.No:64180/TS/2021 dated 09/08/2021 in name of M/s Everest Organics Limited., Aroor Village, Sadasivapet Mandal, Sangareddy Dist. Telangana India valid upto 08/08/2022. **Sodium Bicarbonate:** M/s United Chem., 18-Warlley Moor Lane Leeds West Workshire LS 12 4HX United Kingdom
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not Submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.2	• The name of applicant as per form 5F is Biogen Life sciences while name mentioned on DML is Biogen Pharmaceuticals. Clarification is required	
1.5.6	• You have applied for innovator specifications while the monograph for the applied product is available in USP. Revise your specification as per USP monograph along with submission of applicable fee	
1.6.5	• Valid GMP certificate / DML of drug substance manufacturer for omeprazole and sodium bicarbonate issued by relevant regulatory authority of country of origin is required	
2.3.R.1	• Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient sodium bicarbonate by Drug substance manufacturer is required.	

	• Copies of the Drug substance analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient sodium bicarbonate by Drug product manufacturer is required. • Results of specificity test for dug substance omeprazole is not submitted • Provide evidence of Atomic Absorption Spectroscopy used for analysis of calcium, mg, copper in sodium bicarbonate as per results given in batch analysis • The limits of assay test for sodium bicarbonate in USP is 99-100.5 while drug substance manufacturer and drug product manufacture have followed 99-101 in batch analysis	
3.2.S.7	• Submit stability study data of drug substance omeprazole and sodium bicarbonate as per zone IV-A conditions	
3.2.P.5	• Test for pH is not included in specification although recommended by USP monograph • Justification is required since limits of dissolution specification of applied drug product (Q 75 in 30 min) is different than that recommended by innovator product review document (Q 75 in 15min). • Justification is required for not included the limits of sodium bicarbonate in dissolution test in submitted specifications • Submit complete analytical procedure for applied product • Submit method verification studies for applied product	
3.2.P.8	• Submit documents for the procurement of API with approval from DRAP. • Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

205.	Name, address of Applicant / Marketing Authorization Holder	M/s Biogen Life Sciences, 8-km Chakbeli Road Rawat Rawalpindi
	Name, address of Manufacturing site.	M/s Biogen Life Sciences, 8-km Chakbeli Road Rawat Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 28774 dated 11-10-2022
	Details of fee submitted	Not submitted
	The proposed proprietary name / brand name	**Fusigen-H 15gm Cream**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each gram cream contains: Fusidic Acid (BP)……..….20mg (2% w/w) Hydrocortisone Acetate……10mg (1% w/w)
	Pharmaceutical form of applied drug	White to off white color cream.
	Pharmacotherapeutic Group of (API)	Antibiotics & corticosteroid For Topical Use
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Fucidin H cream MHRA approved
	For generic drugs (me-too status)	Fusimax-H 2%+1% Cream by M/s Maxitech Pharma (Reg# 83733)
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020
	Name and address of API manufacturer.	**Fusidic Acid**: Joyang Laboratories., Haidu North Road, Sheyang Economic Development Zone, Jiangsu, China **Hydrocortisone Succinate:** Henan Lihua Pharmaceutical Co Ltd., Middle of Huanghe Street, Anyang Hi-Tech Industry Development Zone, Henan China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities impurities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance

	Stability studies	**Fusidic Acid:** Firm has submitted stability study data of fusidic acid. Stability study is conducted Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months and at Accelerated conditions 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (121002FA, 121003FA, 121004FA) Batches: (150501FB, 150502FB, 150503FB) **Hydrocortisone Acetate:** Firm has submitted stability study data of Hydrocortisone acetate. Stability study is conducted Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months and at Accelerated conditions 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (160801, 160802, 160803)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand Genidic-H Cream by performing quality tests (Identification, Assay, Uniformity of dosage, pH).
	Analytical method validation/verification of product	Method verification studies have submitted including specificity, repeatibility, recovery and accuracy.

STABILITY STUDY DATA

Manufacturer of API	**Fusidic Acid**: Joyang Laboratories., Haidu North Road, Sheyang Economic Development Zone, Jiangsu, China **Hydrocortisone Succinate:** Henan Lihua Pharmaceutical Co Ltd., Middle of Huanghe Street, Anyang Hi-Tech Industry Development Zone, Henan China		
API Lot No.	**Fusidic Acid:** 200507 FB **Hydrocortisone Acetate:** K06M20210604		
Description of Pack (Container closure system)	Cream filled in Aluminium pre-printed tube packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	500 tubes	500 tubes	500 tubes
Manufacturing Date	10-2021	10-2020	10-2021
Date of Initiation	14-10-2021	14-10-2021	14-10-2021

No. of Batches		03
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Fusidic Acid:** Firm has submitted GMP certificate No#CQ20180013 in the name of M/s Joyang Laboratories., Haidu North Road, Sheyang Economic Development Zone, Jiangsu, China issued by Chonging Food and Drug administration China valid upto 06-06-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Fusidic Acid:** Firm has submitted copy of invoice No# 00025096 dated 02-04-2020 in name of M/s Biogen Pharmaceuticals for import of 1.5kg of Fusidic Acid. ***However, the invoice is not attested by AD (I&E) DRAP Field office.***
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.1	• Fee for registration of applied product is not submitted	
1.6.5	• Details of each drug substance manufacturer should be provided in this section separately • Valid GMP certificate / DML of drug substance manufacturer for hydrocortisone acetate issued by relevant regulatory authority of country of origin is required	
1.3.2	• The name of applicant as per form 5F is Biogen Life sciences while name mentioned on DML is Biogen Pharmaceuticals. Clarification is required	
2.3.R.1	• Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	
3.2.S.4	• Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active	

	Pharmaceutical Ingredient fusidic acid by Drug product manufacturer is required. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient hydrocortisone acetate by both drug substance and Drug product manufacturer is required • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) i.e. fusidic acid and hydrocortisone acetate shall be submitted.	
3.2.P.2	• Submit details of reference / comparator product including batch numbers, manufacturing & expiry date, name of manufacturer in pharmaceutical equivalence • Justify why Pharmaceutical equivalence of the applied product has not been performed against the innovator product?	
3.2.P.3	• Description of manufacturing process does not include the step in which the hydrocortisone is added in the formulation in manufacturing process, clarification is required	
3.2.P.8	• Documents for procurement of API with approval from DRAP • Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

206.	Name, address of Applicant / Marketing Authorization Holder	M/s Biogen Life Sciences, 8-km Chakbeli Road Rawat Rawalpindi
	Name, address of Manufacturing site.	M/s Biogen Life Sciences, 8-km Chakbeli Road Rawat Rawalpindi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 27911 dated 03-10-2022

	Details of fee submitted	Rs.30,000/- dated 14-07-2022 (Deposit Slip#86318672487)
	The proposed proprietary name / brand name	**Fusigen-B Cream**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tube contains: Fusidic Acid……..….20mg Betamethasone (as valerate)……1mg
	Pharmaceutical form of applied drug	Cream.
	Pharmacotherapeutic Group of (API)	Antibiotics & corticosteroid For Topical Use
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Fusidic acid/Betamethasone 20 mg/g + 1 mg/g cream MHRA approved
	For generic drugs (me-too status)	Fudic-B Cream by M/s Shaigan Pharmaceutical (Reg# 83599)
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020
	Name and address of API manufacturer.	**Fusidic Acid**: Joyang Laboratories., Haidu North Road, Sheyang Economic Development Zone, Jiangsu, China **Betamethasone valerate:** Envee Drugs Pvt. Ltd., N. H. No. 8, Dumral-387 355, Ta. Nadiad, Dist: Kheda, Gujarat, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities impurities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Fusidic Acid:** Firm has submitted stability study data of fusidic acid. Stability study is conducted Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months and at

		Accelerated conditions 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (121002FA, 121003FA, 121004FA) Batches: (150501FB, 150502FB, 150503FB) **Betamethasone Valerate:** Firm has submitted stability study data of Betamethasone Valerate. Stability study is conducted Real time: 30°C ± 2°C / 65% ± 5%RH for 48months and at Accelerated conditions 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (EV/00808, EV/06308, EV/10507)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand Fuciden cream Cream by performing quality tests (Identification, Assay, pH, average weight).
	Analytical method validation/verification of product	Method validation studies have been submitted including accuracy, repeatability (method precision), linearity and range, specificity, system suitability.

STABILITY STUDY DATA

Manufacturer of API	**Fusidic Acid**: Joyang Laboratories., Haidu North Road, Sheyang Economic Development Zone, Jiangsu, China **Betamethasone valerate:** Envee Drugs Pvt. Ltd., N. H. No. 8, Dumral-387 355, Ta. Nadiad, Dist: Kheda, Gujarat, India		
API Lot No.	**Fusidic Acid:** 200507 FB **Betamethasone Valerate:** EV/BV-256/20		
Description of Pack (Container closure system)	Cream filled in Aluminium pre-printed tube packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**T#2004FB**	**T#2005FB**	**T#2006FB**
Batch Size	500 tubes	500 tubes	500 tubes
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	12-10-2021	12-10-2021	12-10-2021

No. of Batches		03
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Fusidic Acid:** Firm has submitted GMP certificate No#CQ20180013 in the name of M/s Joyang Laboratories., Haidu North Road, Sheyang Economic Development Zone, Jiangsu, China issued by Chonging Food and Drug administration China valid upto 06-06-2023 **Betamethasone valerate:** Firm has submitted GMP certificate No#S-GMP & GLP / 21072790 in the name of Envee Drugs Pvt. Ltd., N. H. No. 8, Dumral-387 355, Tal. Nadiad, Dist: Kheda, Gujarat, India issued by Food and Drugs control administration Gandinagar, Gujarat State India valid upto 06-07-2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Fusidic Acid:** Firm has submitted copy of invoice No# 00025096 dated 02-04-2020 in name of M/s Biogen Pharmaceuticals for import of 1.5kg of Fusidic Acid. ***However, the invoice is not attested by AD (I&E) DRAP Field office.*** **Betamethasone valerate:** Firm has submitted copy of invoice No# 93 dated 02-11-2020 in name of M/s Biogen Life sciences for import of 03kg of Betamethasone valerate. ***However, the invoice is not attested by AD (I&E) DRAP Field office.***
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

Remarks of Evaluator [XI]:

Section	Observations	Response
1.3.2	• The name of applicant as per form 5F is Biogen Life sciences while name mentioned on DML is Biogen Pharmaceuticals. Clarification is required	

1.5.2	• Revise label claim as per reference formulation along with submission of applicable fee	
2.3.R.1	• Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3>	
3.2.S.4	• Copies of the analytical procedures used for routine testing of the Drug substance fusidic acid by both drug substance manufacturer and Drug product manufacturer is required. • Copies of the Drug substance specifications of drug substance fusidic acid by Drug product manufacturer is required. • Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance Betamethasone Valerate by Drug product manufacturer is required • Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) i.e. fusidic acid and betamethasone valerate shall be submitted. • Certificate of Analysis of the same batch of fusidic acid used during product development and stability studies from Drug Substance manufacturer is required.	
3.2.P.2	• Submit details of reference / comparator product including batch numbers, manufacturing & expiry date, name of manufacturer in pharmaceutical equivalence	
3.2.P.6	• Submit readable copy of reference standard of fusidic acid and betamethasone valerate	
3.2.P.8	• Submit stability summary sheet of batch #2006FB at accelerated conditions • Documents for procurement of API with approval from DRAP • Submit Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

Item No. IV Agenda of Evaluator-IV (Mst.Farzana Raja)

Case no. 01 Registration applications for local manufacturing of (Human) drugs on form 5F

a. New cases

207	Name, address of Applicant / Marketing Authorization Holder	M/s Horizon Healthcare (Pvt.) Ltd. Plot no. 33 Sundar Industrial Estate Lahore.
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt.) Ltd. Plot no. 33 Sundar Industrial Estate Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33996 dated 29-12-2021
	Details of fee submitted	PKR 75,000/-: Deposit slip # 484307037314
	The proposed proprietary name / brand name	Tofanib XR tablet 11mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated Modified release tablet contains: Tofacitinib Citrate eq. to Tofacitinib 11mg
	Pharmaceutical form of applied drug	White to off white, oblong shape, film coated tablets
	Pharmacotherapeutic Group of (API)	Immunosuppressants
	Reference to Finished product specifications	As per innovator
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	XELJANZ XR Tablets 11mg approved by US-FDA
	For generic drugs (me-too status)	Drug is not available in Pakistan
	GMP status of the Finished product manufacturer	Last inspection report dated 18.06.2020 concluded good level of cGMP compliance.
	Name and address of API manufacturer.	M/s Kaifeng Pharmaceutical (Group) Company, Ltd. No.1 Yunan Street, Kaifeng Henan Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.

<table>
<tr><td></td><td>Module III (Drug Substance)</td><td>The firm as submitted detail of General information, General properties, Manufacturers, description of manufacturing process and process controls, Characterization, Impurities, Control of drug substance, Reference standard or materials container closure system and stability studies of drug substance.</td></tr>
<tr><td></td><td>Stability studies</td><td>Stability study conditions:
Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months
Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
<table>
<tr><th>Batch No</th><th>Accelerated</th><th>Long Term</th></tr>
<tr><td>15012401</td><td>6 Months</td><td>36 Months</td></tr>
<tr><td>15020201</td><td>6 Months</td><td>36 Months</td></tr>
<tr><td>15020301</td><td>6 Months</td><td>36 Months</td></tr>
</table></td></tr>
<tr><td></td><td>Module-III (Drug Product):</td><td>The firm has submitted detail of Drug Products including Description and composition of drug product, Pharmaceutical Development, Manufacturing process development, Microbiological attribution, Manufacturer, Master formulations, Description of Manufacturing Process and Process Controls, Control of Critical Steps and Intermediates, Process Validation and/ or Evaluation, Control of Excipients with specification and Analytical methods, Control of Drug Products including Finished product specifications and test methods, validation of Analytical methods, Batch analysis , Characterization of impurities, reference standard or impurities, Container closure and stabilities studies.</td></tr>
<tr><td></td><td>Pharmaceutical equivalence and comparative dissolution profile</td><td>Pharmaceutical Equivalence have been established against the brand leader that is Xeljanz XR 11mg Tablets approved by US-FDA by performing quality tests (Identification, Assay, and Dissolution. CDP has been performed against the same brand that is Xeljanz Tablets 11mg approved by US-FDA in Acid media (pH 1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8)</td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Method verification studies have submitted including Introduction, Verification of assay method, Specificity, Accuracy, Precision, Linearity concentration and peak range.</td></tr>
<tr><td colspan="3">STABILITY STUDY DATA</td></tr>
<tr><td colspan="2">Manufacturer of API</td><td>M/s Kaifeng Pharmaceutical (Group) Company, Ltd.
No.1 Yunan Street, Kaifeng Henan Province, China</td></tr>
<tr><td colspan="2">API Lot No.</td><td>HF210605</td></tr>
<tr><td colspan="2">Description of Pack</td><td>Alu-Alu. Blisters with aluminum foil having leaflet and packed in unit carton</td></tr>
</table>

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TC-001	TC-002	TC-003
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	17-08-2021	19-08-2021	21-08-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) and Dayzol 30mg Capsules, Dayzol 60mg Capsules (Dexlansoprazole) which was conducted on 1st June, 2021 and was presented in 307th meeting of Registration Board held on 08-10th June , 2021. . According to the report following points were confirmed. • The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. • The firm possesses stability chambers with digital data loggers
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. HA20190069 issued by NMPA valid till 28-09-2024 Copy of DML No. Yu20150031 issued by NMPA valid till 31-12-2025
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of form 3, form 7 , invoice (invoice# CIN20210701L01) dated 01-07-2021 cleared by DRAP Lahore office dated 19-07-2021 specifying import of Tofacitinib Citrate 0.25kgs (Batch# HF210605).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail reports have been submitted.

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers.

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.A.1	Evidence of manufacturing facility with laser drill	Firm submitted invoice for purchase of Laser Drilling Machine for tablet from Nimbus chemtech Invoice No# NC/029-21 Dated: 15-05-2021
2.	3.2.S.4.2	In standard preparation and Sample solution Quantity of Tofacitinib Citrate is written as proper quantity. Clarify what is proper quantity.	• The Standard analytical procedure of Tofacitinib citrate was followed by Drug substance procedure provided by the manufacturer. The proper quantity is taken: for standard and sample the final concentration is mentioned as 80 µg/mL respectively. The standard and sample quantity taken accordingly **Standard Stock Solution:** 20mg of Working Standard (Tofacitinib Citrate) into 25ml of diluent (0.8mg/mL or 800µg/mL) **Standard Solution:** 5mL from standard stock solution into 50ml diluent (0.08mg/mL or 80µg/mL) **Sample Stock Solution:** 20mg of Tofacitinib Citrate Sample into 25ml diluent (0.8mg/mL or 800µg/mL) **Sample Solution:** 5mL from sample stock solution into 50ml diluent (0.08mg/mL or 80µg/mL)
3.	3.2.S.4.3	• In standard preparation and Sample solution Quantity of Tofacitinib Citrate is written as proper quantity. Clarify what is proper quantity. • In specificity Bempedoic acid sample mentioned.	• The Standard analytical procedure of Tofacitinib citrate was followed by Drug substance procedure provided by the manufacturer. The proper quantity is taken: for standard and sample the final concentration is mentioned as 80 µg/mL respectively. The standard and sample quantity taken accordingly **Standard Stock Solution:** 20mg of Working Standard (Tofacitinib Citrate) into 25ml of diluent (0.8mg/mL or 800µg/mL) **Standard Solution:** 5mL from standard stock solution into 50ml diluent (0.08mg/mL or 80µg/mL) **Sample Stock Solution:** 20mg of Tofacitinib Citrate Sample into 25ml diluent (0.8mg/mL or 800µg/mL) **Sample Solution:**

			5mL from sample stock solution into 50ml diluent (0.08mg/mL or 80µg/mL). • In method of verification report under heading of specificity the Bempedoic acid was written it is typographical mistake.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

208	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32065 dated 23-09-2021
	Details of fee submitted	PKR 75,000/-: Deposit slip # 2358695272
	The proposed proprietary name / brand name	URSOVA Tablets 500mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Ursodeoxycholic Acid (Ursodiol) …500mg
	Pharmaceutical form of applied drug	Red colored, oblong shaped, biconvex film- coated tablet, bisect line on one side and plain on other side.
	Pharmacotherapeutic Group of (API)	Bile acids and derivatives
	Reference to Finished product specifications	USP Specs.
	Proposed Pack size	10’s
	Proposed unit price	Rs. 750/- (10’s)
	The status in reference regulatory authorities	URSO Forte Tablets 500mg by M/s Allergan USA Inc., USA. USFDA Approved.
	For generic drugs (me-too status)	Not Applicable
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of

		GMP requirements. Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Zhejiang Warrant Pharmaceutical Co., Ltd. Workshop 1 , No. 4290, Xingbin Road, Binhai Industrial Zone, Keqiao District, Shaoxing, Zhejiang, P.R. China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ursodeoxycholic Acid (Ursodiol) is present in EP pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, tests for impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 18 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (UDCA-II-20191101, UDCA-II-20191108, UDCA-II-20191202)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the comparator brand that is Ursofalk Tablet 500mg by M/s Losan Pharma GmbH, Germany by performing quality tests (Appearance, Average Weight, Assay, Dissolution). CDP has been performed against the compator brand that is Ursofalk Tablet 500mg by M/s Losan Pharma GmbH, Germany in Acidic media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The f2 values are in the acceptable range.

	Analytical method validation/verification of product	Method Verification studies have submitted including system suitability, linearity, range, accuracy, precision, specificity and stability of solution.		
STABILITY STUDY DATA				
Manufacturer of API	Zhejiang Warrant Pharmaceutical Co., Ltd. Workshop 1 No. 4290, Xingbin Road, Binhai Industrial Zone, Keqiao District, Shaoxing, Zhejiang, P.R. China.			
API Lot No.	UDCA-II-20191218 (CA20191218)			
Description of Pack (Container closure system)	Alu-PVDC blister packed in unit carton (10's)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH			
Time Period	Real time: 6 months Accelerated: 6 months			
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)			
Batch No.	539DS01	539DS02	539DS03	
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets	
Manufacturing Date	09.06.2020	29.06.2020	29.06.2020	
Date of Initiation	21.07.2020	21.07.2020	21.07.2020	
No. of Batches	03			
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product Estine (Ebastine) tablets 10mg & 20mg which was conducted on 06th May 2019 and was presented in 289th meeting of Registration Board held on 14th -16th May 2019. The case was approved and the inspection report confirms following points: • The HPLC software is 21CFR Compliant as per record available with the firm. • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. • Related manufacturing area, equipment, personnel and utilities are GMP compliant.			
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of Drug Manufacturing License no. Zhe 20070479 issued by Zhejiang Provincial Drug Administration valid till 11-05-2026.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of, invoice (invoice# 20ATGZ046) dated 02-04-2020 cleared by DRAP Karachi office dated 14-04-2020 specifying import of Ursodeoxycholic Acid 7.50Kg (Batch# CA20191218s).		

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted	Analytical Method Verification studies including specificity, linearity, repeatability and range performed by the Drug Product manufacturer are attached. Further, with reference to ICH Guidelines "VALIDATION OF ANALYTICAL PROCEDURES: TEXT AND METHODOLOGY Q2 (R1)" it is mentioned in section 4.1.1 Drug Substance "accuracy may be inferred once precision, linearity and specificity have been established". This is bring to your kind attention that since we have performed method verification studies as per ICH Q2 (R1) therefore, requirement of accuracy is not applicable. Link of ICH guideline is provided below: Q2(R1) Guideline.pdf (ich.org)
2.	3.2.P.5.2	Provide Evidence of HPLC with RI detector.	Instrument Calibration certificate as an evidence of HPLC with RI detector submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

209	Name, address of Applicant / Marketing Authorization Holder	M/S Welmark pharmaceuticals Industrial estate Hattar, Kpk Pakistan
	Name, address of Manufacturing site.	M/S Welmark pharmaceuticals Plot No 122 Block-B phase-5 Industrial estate Hattar Kpk Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 30576 dated 08-11-2021
	Details of fee submitted	PKR 20,000/-: Dated: 26-01-2021 Deposit slip # 1985094
	The proposed proprietary name / brand name	Teno 25mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tenofovir Alafenamide Fumarate eq to Tenofovir Alafenamide……25mg
	Pharmaceutical form of applied drug	Brown red color 8mm round shaped bisected one side and other plain film coated tablet.
	Pharmacotherapeutic Group of (API)	Antiviral for systemic use, nucleoside and nucleotide reverse transcriptase inhibitors.
	Reference to Finished product specifications	Manufacturer specifications
	Proposed Pack size	30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Vemlidy Tablet 25mg by Gilead Sciences Ltd. U.S.A.., USFDA Approved.
	For generic drugs (me-too status)	Tenofomide Tablet 25mg by M/s. Getz pharma ., Reg. No. 093109
	GMP status of the Finished product manufacturer	Not submitted.
	Name and address of API manufacturer.	Shandong Haiyo Freda Pharmaceutical Co Ltd Address: 666 Bianhai West Road Linshu West Industrial Zone, Shandong Province.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's,, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Monograph of Tenofovir Alafenamide Fumarate is present is as per In-house (Manufacturer's) specifications. The firm as submitted detail of nomenclature, structure, general properties, solubility's,, physical form, manufacturers,

		description of manufacturing process and controls, tests for related substances (Impurity A, PMPA, Unspecified impurity and Total impurities), specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (180702, 180713, 180725)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Tenofomide 25mg Tablets (Batch No. 004FB1, Mfg date 04-2020) by Getz Pharmaceuticals Karachi. Firm has submitted results of CDP for their product against Tenofomide 25mg Tablets (Batch No. 004FB1, Mfg date 04-2020). Firm has tested CDP in three dissolution medium ie. (0.1N Hcl pH 1.2, Acetate Buffer pH 4.5, Phosphate Buffer pH 6.8 and the results of f1, f2 factor are within the acceptable limit.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Shandong Haiyo Freda Pharmaceutical Co Ltd Address: 666 Bianhai West Road Linshu West Industrial Zone, Shandong Province.
API Lot No.	20021701
Description of Pack (Container closure system)	30's Tablets Teno 25mg Tablets will be packed in jar and Secondary Packing in Unit Carton.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	T010	T011	T012
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	09-2020	09-2020	09-2020
Date of Initiation	15-09-2020	16-09-2020	17-09-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SD20160495 issued by NMPA valid till 08-08-2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Firm has submitted copy of form 3, form 7 , invoice (invoice# JNXKYY20030302) dated 03-03-2020 specifying import of Tenofovir Alafenamide Fumarate 2 Kg (Batch# 20021701). But Not attested.**
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.1	Differential fee of Rs: 10000/-	**Fee of Rs: 10000/- Deposit slip #0874644724055 submitted.**
2.	1.3.5.	GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted.	**Not submitted.**
3.	1.6.5	• Drug substance manufacturer mentioned in this section is M/s Jinan Xinke Pharmaceuticals Sci & Tech. C0., Ltd , . While certificate of analysis an import documents are from Shandong Haiyo Freda Pharmaceutical Co Ltd	• The drug substance manufacturer is Shandong Haiyo Freda Pharmaceuticals Co Ltd. Documents submitted • Submitted GMP certificate is valid upto 08-08-2021 **(Submitted again same GMP certificate which is not valid)**

		. Clarification is required amongst them which one is drug substance manufacturer. • Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. Or Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin.	
4.	3.2.S.4.1	Copies of the Drug substance Specifications by Drug Product manufacturer is required.	Submitted
5.	3.2.S.4.2	Detailed analytical procedures used for routine testing of the Drug substance by drug product manufacturer shall be provided.	Submitted
6.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	Submitted
7.	3.2.S.5	COA of primary / secondary reference standard including source and lot number shall be provided.	Submitted
8.	3.2.P.2.3	Manufacturing process by Innovator is dry granulation while your method is Wet granulation. Clarify.	**We are following innovators manufacturing process and our method is dry granulation.**
9.	3.2.P.5.1	US FDA review document of the Innovator product, specifies the dissolution limit as "NLT Q in 15	**That was a typographic mistake, we are following innovators specification and dissolution limit is NLT Q in 15 minutes.**

		minutes" whereas submitted specifications declare the dissolution limits as "NLT 75% in 30 minutes" .	
10.	3.2.P.5.2	Submit complete analytical method for testing of drug product.	Submitted
11.		• Documents for the procurement of API with approval from DRAP. • US FDA review document of the Innovator product, specifies the dissolution limit as "NLT Q in 15 minutes" in 50mM Sodium Acetate buffer pH 4.5. whereas submitted specifications declare the dissolution limits as "NLT 75% in 30 minutes with Phosphate Buffer pH 6.8". • Compliance Record of HPLC software 21CFR & audit trail reports on product testing • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• **Not Submitted** • **We are following innovator specifications i.e. dissolution limit is NLT Q in 15 minutes in 50mM Sodium Acetate buffer pH 4.5.** • Compliance record of HPLC software 21CFR & audit trail reports on product testing submitted.

Decision: Deferred for following:

- **Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin or Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin.**
- **Documents for the procurement of API with approval from DRAP.**
- **Analytical record for the dissolution test for stability studies as per Innovator product.**

21(	Name, address of Applicant / Marketing Authorization Holder	M/s Medisure Laboratories Pakistan Private Limited at A-115, S.I.T.E., Super Highway, Karachi Pakistan
	Name, address of Manufacturing site.	M/s Medisure Laboratories Pakistan Private Limited. Plot A-115, S.I.T.E., Super Highway, Karachi

		Pakistan
	Status of the applicant	☑Manufacturer ☒ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☑ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☒ Export sale ☑Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32865 dated 13-12-2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 681236375678
	The proposed proprietary name / brand name	Tenosure 25mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tenofovir Alafenamide ----------25 mg (as Tenofovir Alafenamide Fumarate)
	Pharmaceutical form of applied drug	Light orange colored, round, biconvex, film coated tablet both sides are plain.
	Pharmacotherapeutic Group of (API)	Nucleoside analog reverse transcriptase inhibitor
	Reference to Finished product specifications	Manufacturer Specification
	Proposed Pack size	1x 30's
	Proposed unit price	As per SRO (not allotted yet)
	The status in reference regulatory authorities	Vemlidy Tablet 25mg by Gilead Sciences Ltd. U.S.A.., USFDA Approved.
	For generic drugs (me-too status)	Tefod Tablet 25mg by M/s. Sami Pharmaceuticals (Pvt.) Ltd., Reg. No. 096182
	GMP status of the Finished product manufacturer	Last inspection report on the basis of inspection conducted 07-09-2021 states that their current GMP compliance level is rated as Good.
	Name and address of API manufacturer.	Lianyungang Jari Pharmaceuticals Co. Ltd. Address: No. 18 Zhenhua Road, Lianyungang City, Jiangsu Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's,, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Tenofovir Alafenamide Fumarate is not present in any pharmacopeia. The firm as submitted detail of nomenclature, structure,

		general properties, solubility's,, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months (20171015, 20171115, 20171215)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Tenofomide Tablet 25mg by M/s. Getz pharma by performing quality tests (Identification, Disintegration, Assay, Dissolution,). CDP has been performed against the same brand that is Tenofomide Tablet 25mg by M/s. Getz pharma in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, and specificity.

STABILITY STUDY DATA

Manufacturer of API	Lianyungang Jari Pharmaceuticals Co. Ltd. Address: No. 18 Zhenhua Road, Lianyungang City, Jiangsu Province, China		
API Lot No.			
Description of Pack (Container closure system)	30 tablets are packaged in high density polyethylene (HDPE) bottles in unit carton (1×30's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9,12 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	0.73Kg	0.73Kg	0.73Kg
Manufacturing Date	09-2020	09-2020	09-2020

Date of Initiation	11-12-2020	11-12-2020	11-12-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. JS20191190 issued by National Medical products Administration valid till 29/11/2024
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice (MP-2020-AUG-003) dated 10-09-2020 cleared by DRAP Karachi office dated 28-09-2020 specifying import of Tenofovir Alafenamide Fumarate 1.5 Kg
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.3.5.	GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted.	Last inspection report on the basis of inspection conducted 07-09-2021 states that their current GMP compliance level is rated as Good.
2.	2.3.R.1.1	Justify the quantity of Tenofovir Alafenamide each tablet contains with equivalency factor of fumarate.	**Factor applied is 1.243 so the quantity each tablet contains 31mg of Tenofovir Alafenamide Fumarate** **(While actual factor is 1.122 so quantity of Each tablet contains 28 mg of Tenofovir Alafenamide Fumarate eq to 25mg of Tenofovir Alafenamide** **Molecular weight of** **Tenofovir Alafenamide Fumarate:534.50** **Tenofovir Alafenamide: 476.466)**
3.	3.2.S.4.1	Copies of the Drug substance Specifications by Drug Product manufacturer is required.	Submitted
4.	3.2.S.4.2	Detailed analytical procedures used for routine testing of the Drug	Submitted.

		substance by drug product manufacturer shall be provided.	
5.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	**Not submitted.**
6.	3.2.S.4.4	Certificate of analysis of drug substance provided by drug Product manufacture and drug substance manufacturer are of different supplier than applied in module I. Clarification is required.	**Not submitted.**
7.	3.2.S.5	COA of primary / secondary reference standard including source and lot number shall be provided.	Submitted
8.	3.2.P.1	Justify the quantity of Tenofovir Alafenamide each tablet contains with equivalency factor of fumarate.	**Not submitted**
9.	3.2.P.5.2	Justify dissolution acceptance criteria NLT 80% in 45 min with dissolution medium 0.1N hydrochloric acid pH 1.2 while dissolution specifications of innovator is NLT Q in 15 min with dissolution medium 50 mM Sodium Acetate buffer pH 4.5	**Instead of reply firm Refer to CDP.**
10.	3.2.P.8	• Documents for the procurement of API with approval from DRAP • Specify batch size in No of units/ Tablets	• Submitted. • 5214 Tablet in one batch

Decision: Deferred for following:

- **Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.**

- **Certificate of analysis of drug substance provided by drug Product manufacture and drug substance manufacturer are of different supplier than applied in module I. Clarification is required.**
- **Justify the quantity of Tenofovir Alafenamide each tablet contains with equivalency factor of fumarate.**
- **Justify dissolution acceptance criteria NLT 80% in 45 min with dissolution medium 0.1N hydrochloric acid pH 1.2 while dissolution specifications of innovator is NLT Q in 15 min with dissolution medium 50 mM Sodi**um Acetate buffer pH 4.5

b. Deferred Cases:

211.	Name, address of Applicant / Marketing Authorization Holder	M/s Citi Pharma Private Limited
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17868 dated 20-06-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 2746758563
	The proposed proprietary name / brand name	Panadol Extra Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Paracetamol……. 500mg Caffeine….. 65mg
	Pharmaceutical form of applied drug	Oral (Tablet)
	Pharmacotherapeutic Group of (API)	Analgesics and Psychoactive drug.
	Reference to Finished product specifications	USP
	Proposed Pack size	**10x10's tablets**
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Panadol Extra by GSK (GlaxosmithKline), UK Approved in UK.
	For generic drugs (me-too status)	Panadol Extra GSK (GlaxosmithKline). Pakistan
	GMP status of the Finished product manufacturer	cGMP certificate on the basis of evaluation conducted on 19-03-2019
	Name and address of API manufacturer.	**Paracetamol:** Citi Pharma Pvt Ltd 3.5-Km, Head Balloki Road, Phool Nagar Kasur-Pakistan. **Caffeine:** Aarti Industries Limited 1. Plot No D-53, phase II, M.I.D.C

		Kalyanshil RD Dombival (East) Thane 421204 Maharashtra state, India. 2. K-17/18/19, M.I.D.C, tararpur, Distict, Thane zone 4.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of **Paracetamol and** Caffeine is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Paracetamol:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (PGP14-37, PGP14-38, PGP14-39) **Caffeine:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (C-3011 C-3076, C-3115)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Panadol Extra Tablets by M/s GSK (GlaxosmithKline). Pakistan performing quality tests (Identification, Weight variation, Disintegration, Assay, Dissolution). CDP has been performed against the same brand

		that is Panadol Extra Tablets by M/s GSK (GlaxosmithKline). Pakistan in Acid media (pH-1.2),Acetate Buffer(pH-4.5) & Phosphate Buffer (pH 6.8)..		
	Analytical method validation/verification of product			
STABILITY STUDY DATA				
Manufacturer of API		Paracetamol: M/s Citi Pharma Private Limited Lahore. Caffeine: Aarti Industries Limited		
API Lot No.		**Caffeine:** **Paracetamol:** PGP21-183		
Description of Pack (Container closure system)		**10X10's Blistered in ALU-PVC packed in standard unit carton provided with leaflet inside.**		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		TRA-PE001	TRA-PE002	TRA-PE003
Batch Size		10,000 Tablets	10,000 Tablets	10,000 Tablets
Manufacturing Date		01-2022	01-2022	01-2022
Date of Initiation		01-2022	01-2022	01-2022
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)			
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Paracetamol:** Copy of cGMP certificate on the basis of evaluation conducted on 17-12-2020 and valid for 2 years **Caffeine**: Copy of GMP certificate No. 6101335 for Aarti Industries Limited (K-17/18/19, M.I.D.C, tararpur, Distict, Thane zone 4) issued by Food and Drug Administration Mahrashtra India-valid for 12-08-2022		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Paracetamol:** Purchase documents Invoice No# F20-34 Dated: 11-08-2021 of Batch No # PGP21-513. **Caffeine**: Form 6 for Caffeine submitted of dated: 15-07-21 by Lahore office		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Remarks OF Evaluator: Firm submitted NOC as follows:

M/s GlaxoSmithKline Consumer health Pakistan Limited 35-Dockyard Road, West Whraf –Karachi-Pakistan has provided no objection certificate for utilization of Panadol brand name as under :-

*"We, owners of the **"Panadol"** brand name since may decades globally and in Pakistan for last 45 years, would like to manufacture our following products at **"Citi Pharma Private Limited"** under the DRAP's Contract manufacturing policy:*

S.No.	***Brand Name***
1.	*Panadol Extra Tablets*
2.	*Panadol Migraine tablets*
3.	*Panadol Muscle Relaxant tablets*

*Further to this, Please note that we have no objection to the use of the brand Name **"Panadol"** for the aforementioned products, applied by Citi Pharma for the registration on contract manufacturing on behalf of GlaxoSmithKline consumer Healthcare Limited Pakistan."*

Remarks of Evaluator: Firm submitted NOC as follows:

M/s GlaxoSmithKline Consumer health Pakistan Limited 35-Dockyard Road, West Whraf – Karachi-Pakistan has provided no objection certificate for utilization of Panadol brand name as under :-

*"We, owners of the **"Panadol"** brand name since may decades globally and in Pakistan for last 45 years, would like to manufacture our following products at **"Citi Pharma Private Limited"** under the DRAP's Contract manufacturing policy:*

S.No.	***Brand Name***
1.	*Panadol Extra Tablets*
2.	*Panadol Migraine tablets*
3.	*Panadol Muscle Relaxant tablets*

*Further to this, Please note that we have no objection to the use of the brand Name **"Panadol"** for the aforementioned products, applied by Citi Pharma for the registration on contract manufacturing on behalf of GlaxoSmithKline consumer Healthcare Limited Pakistan."*

S.No	Section	Shortcomings Communicated
1.	1.6.5	Submitted GMP certificate of different site than documents submitted for drug substance (Caffeine)

2.	2.3.R.1.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3
3.	3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active (Caffeine)Pharmaceutical Ingredient by Drug Product manufacturer is required.
4.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) (Paracetamol and Caffeine)shall be submitted.
5.	3.2.S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / Active Pharmaceutical Ingredient (Paracetamol and Caffeine) manufacture.
6.	3.2.S.5	COA of primary / secondary reference standard including source and lot number for Caffeine shall be provided.
7.	3.2.P.2.2.1	• 6 units are used for CDP. Clarification is required in the light of FDA guidance for industry and EMA guidelines of Comparative dissolution. • F2 calculations for paracetamol and caffeine not submitted.
8.	3.2.P.3.5	Submitted Process validation protocol are general not product related. Clarification is required.
9.	3.2.P.5.1	• Specification claimed are USP while in section 1.5.6 applied as B.P. Clarification is required. • Justify your acceptance criteria for dissolution test as NLT 75% after 60 minutes of the labeled amount of paracetamol and caffeine while USP has specified as NLT 75% (Q) of the labelled amounts of acetaminophen and caffeine is dissolved.
10.	3.2.P.5.3	Analytical Method Verification studies performed by the Drug Product manufacturer for drug product shall be submitted.
11.	3.2.P.8	• Stability studies of three (03) months submitted. • Documents for the procurement of API (Caffeine) with approval from DRAP Compliance Record of HPLC software 21CFR & audit trail reports on product testing. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Previous Decision (M-321): Deferred for following:

- Submitted GMP certificate of different site than documents submitted for drug substance (Caffeine)
- Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3
- Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active (Caffeine) Pharmaceutical Ingredient by Drug Product manufacturer is required.

- Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) (Paracetamol and Caffeine) shall be submitted.
- Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / Active Pharmaceutical Ingredient (Paracetamol and Caffeine) manufacture.
- COA of primary / secondary reference standard including source and lot number for Caffeine shall be provided.
- 6 units are used for CDP. Clarification is required in the light of FDA guidance for industry and EMA guidelines of Comparative dissolution.
- F2 calculations for paracetamol and caffeine not submitted.
- Submitted Process validation protocol are general not product related. Clarification is required.
- Specification claimed are USP while in section 1.5.6 applied as B.P. Clarification is required.
- Justify your acceptance criteria for dissolution test as NLT 75% after 60 minutes of the labeled amount of paracetamol and caffeine while USP has specified as NLT 75% (Q) of the labelled amounts of acetaminophen and caffeine is dissolved.
- Analytical Method Verification studies performed by the Drug Product manufacturer for drug product shall be submitted.
- Stability studies of three (03) months submitted.
- Documents for the procurement of API (Caffeine) with approval from DRAP Compliance Record of HPLC software 21CFR & audit trail reports on product testing.
- Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Reply

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5	Submitted GMP certificate of different site than documents submitted for drug substance (Caffeine)	Firm submitted now GMP certificate # 6101335 valid upto 12-08-2022 of Aarti Industries Limited Address: K-17/18/19, M.I.D.C, tararpur, Distict, Thane zone 4.(mentioned on all documents)
2.	2.3.R.1.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3	Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3 submitted
3.	3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient (Caffeine) by Drug Product manufacturer is required.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient (Caffeine) by Drug Product manufacturer is submitted.

4.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) (Paracetamol and Caffeine)shall be submitted.	**Analytical method verification of tablet (Drug Product) submitted instead of drug substance.**
5.	3.2.S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / Active Pharmaceutical Ingredient (Paracetamol and Caffeine) manufacture.	**COA of paracetamol submitted while, COA of drug substance for Caffeine of a different Drug substance supplier (Kores India limited submitted.**
6.	3.2.S.5	COA of primary / secondary reference standard including source and lot number for Caffeine shall be provided.	Submitted.
7.	3.2.P.2.2.1	• 6 units are used for CDP. Clarification is required in the light of FDA guidance for industry and EMA guidelines of Comparative dissolution. • F2 calculations for paracetamol and caffeine not submitted.	• **No reply about 6 units used by firm** • **F2 calculations submitted but now data is different from previous submitted data.**
8.	3.2.P.3.5	Submitted Process validation protocol are general not product related. Clarification is required.	Submitted.
9.	3.2.P.5.1	• Specification claimed are USP while in section 1.5.6 applied as B.P. Clarification is required. • Justify your acceptance criteria for dissolution test as NLT 75% after 60 minutes of the labeled amount of paracetamol and caffeine while USP has specified as NLT 75% (Q) of the labelled amounts of acetaminophen and caffeine is dissolved.	• Typographical error. USP specifications are applied. Rectified and correction has been made. Revised documents submitted. • **No reply of dissolution specifications**.

10.	3.2.P.5.3	Analytical Method Verification studies performed by the Drug Product manufacturer for drug product shall be submitted.	No reply
11.	3.2.P.8	• Stability studies of three (03) months submitted. • Documents for the procurement of API (Caffeine) with approval from DRAP • Compliance Record of HPLC software 21CFR & audit trail reports on product testing. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	• **Stability studies summary sheets of 6 months submitted**. • **Import documents Not Submitted.** • Submitted • Submitted

Decision: Deferred for following:

- **Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) (Paracetamol and Caffeine) shall be submitted.**
- **Performance of CDP studies using 12 units each of sample and reference product.**
- **Justify your acceptance criteria for dissolution test as NLT 75% after 60 minutes of the labeled amount of paracetamol and caffeine while USP has specified as NLT 75% (Q) of the labelled amounts of acetaminophen and caffeine is dissolved.**
- **Analytical Method Verification studies performed by the Drug Product manufacturer for drug product shall be submitted.**
- **Documents for the procurement of API (Caffeine) with approval from DRAP.**
- **Since the submitted dossier does not reflect any details for contract manufacturing while annexed NOC from M/s GlaxoSmithKline Consumer Health declare it by way of cntract manufacturing hence firm shall submit clarity regarding the status of registration application whether it's for self-manufacturing with registration in name of M/s Citi Pharma Private Limited or for contract manufacturing with registration in name of M/s GlaxoSmithKline Consumer health Pakistan Limited. In case of contract manufacturing for M/s GlaxoSmithKline Consumer health Pakistan Limited, the application shall be re submitted as per relevant SRO of contract manufacturing policy.**
- **Clarification for using of Panadol brand name as per Rule 20A of Drugs (L,R &A) Rules, 1976.**

212.	Name, address of Applicant / Marketing Authorization Holder	M/s Citi Pharma Private Limited
	Name, address of Manufacturing site.	M/s Citi Pharma Private Limited Factory: 3 K.M, Head Balloki Road, Phool Nagar, Distt. Kasur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 17866 dated 20-06-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 66410331823
	The proposed proprietary name / brand name	Panadol Migraine Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Paracetamol……. 250mg Caffeine anhydrous….. 65mg **Aspirin…… 250mg**
	Pharmaceutical form of applied drug	Oral (Tablet)
	Pharmacotherapeutic Group of (API)	NSAID and Psychoactive drug.
	Reference to Finished product specifications	USP
	Proposed Pack size	**4 X6's**
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	EXCEDRIN (MIGRAINE) by M/s GSK (GlaxosmithKline) Consumer Health, USA, Approved in USA. (OTC product)
	For generic drugs (me-too status)	….
	GMP status of the Finished product manufacturer	cGMP certificate on the basis of evaluation conductd on 19-03-2019
	Name and address of API manufacturer.	**Paracetamol:** Citi Pharma Pvt Ltd 3.5-Km, Head Balloki Road, Phool Nagar Kasur-Pakistan. **Caffeine:** Aarti Industries Limited 1. Plot No D-53, phase II, M.I.D.C Kalyanshil RD Dombival (East) Thane 421204 Maharashtra state, India. 2. K-17/18/19, M.I.D.C, tararpur, Distict, Thane. **Aspirin:** JQC HUAYIN PHARMACEUTICAL CO., LTD. Yuqan Road,Huayian City, Shanxi Province. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of **Paracetamol and** Caffeine is present in BP and Official monograph

		of Aspirin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: **Paracetamol:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (PGP14-37, PGP14-38, PGP14-39) **Caffeine:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (C-3011 C-3076, C-3115) **Aspirin:** Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months. Batches: (A201104081, A201104082, A201104083
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Panadol Migraine Tablets by M/s GSK (GlaxosmithKline) Consumer Health, USA performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Panadol Migraine Tablets by M/s GSK (GlaxosmithKline) Consumer Health, USA in Acid media (pH-1.2),Acetate Buffer(pH-4.5) & Phosphate Buffer (pH 6.8).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	Paracetamol: M/s Citi Pharma Private Limited Lahore.	

	Caffeine: Aarti Industries Limited **Aspirin:** JQC HUAYIN PHARMACEUTICAL CO., LTD.		
API Lot No.	**Caffeine:** **Paracetamol** : PGP21-183 **Aspirin:** A201903162		
Description of Pack (Container closure system)	**Alu, PVC foil blister**		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRA-PM001	TRA-PE002	TRA-PE003
Batch Size	10,000 Tablets	10,000 Tablets	10,000 Tablets
Manufacturing Date	12-2021	12-2021	12-2021
Date of Initiation	09-2021	09-2021	09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Paracetamol:** Copy of cGMP certificate on the basis of evaluation conducted on 17-12-2020 and valid for 2 years **Caffeine**: Copy of GMP certificate No. NEW-WHO-GMP/KD/88375/2019/11/30185 issued by Food and Drug Administration Mahrashtra India-valid for 19-11-2022 **Aspirin:**
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Paracetamol:** Purchase documents Invoice No# F20-34 Dated: 11-08-2021 of Batch No # PGP21-513
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks OF Evaluator: **Firm submitted NOC as follows:**		

M/s GlaxoSmithKline Consumer health Pakistan Limited 35-Dockyard Road, West Whraf –Karachi-Pakistan has provided no objection certificate for utilization of Panadol brand name as under :-

*"We, owners of the **"Panadol"** brand name since may decades globally and in Pakistan for last 45 years, would like to manufacture our following products at **"Citi Pharma Private Limited"** under the DRAP's Contract manufacturing policy:*

S.No.	***Brand Name***
1.	*Panadol Extra Tablets*
2.	*Panadol Migraine tablets*
3.	*Panadol Muscle Relaxant tablets*

*Further to this, Please note that we have no objection to the use of the brand Name **"Panadol"** for the aforementioned products, applied by Citi Pharma for the registration on contract manufacturing on behalf of GlaxoSmithKline consumer Healthcare Limited Pakistan.*

S.No	Section	Shortcomings Communicated
1.	1.6.5	• Submitted GMP certificate of different site than documents submitted for drug substance (Caffeine). • Valid Drug Manufacturing License or Valid Good Manufacturing Practice (GMP) certificate of the Aspirin manufacturer issued by relevant regulatory authority of country of origin.
2.	2.3.R.1.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3
3.	3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active (Caffeine)Pharmaceutical Ingredient by Drug Product manufacturer is required.
4.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) (Paracetamol and Caffeine and Aspirin)shall be submitted.
5.	3.2.S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / Active Pharmaceutical Ingredient (Paracetamol and Caffeine) manufacture.
6.	3.2.S.5	COA of primary / secondary reference standard including source and lot number for Caffeine and Aspirin shall be provided.
7.	3.2.P.1	• Composition of tablet is different from reference product in terms of excipients. • Applied formulation is film coated however it is not evident from composition in section 3.2.P.1 and 3.2.P.3.2 as there are no excipients for coating.
8.	3.2.P.2.3	Manufacturing process Coating step is not included however applied product is film coated.
9.	3.2.P.2.2.1	Submitted CDP data for paracetamol and Caffeine is same as in Panadol Extra tablet. Clarification s is required.

10.	3.2.P.3.5	Submitted Process validation protocol are general not product related. Clarification is required.
11.	3.2.P.5.1	Justify your acceptance criteria for dissolution test as NLT 75% after 60 minutes of the labeled amount of paracetamol ,caffeine and Aspirin while USP has specified as NLT 75% (Q) of the labelled amounts of acetaminophen , Aspirin and caffeine is dissolved
12.	3.2.P.5.3	Analytical Method Verification studies performed by the Drug Product manufacturer for drug product shall be submitted.
13.	3.2.P.6	COA of primary / secondary reference standard including source and lot number for paracetamol, Aspirin and Caffeine shall be provided
14.	3.2.P.8	• Manufacturing of batches was done in Dec, 2021 than how stability studies started in September 2021. • Stability studies of three (03) months submitted. • Documents for the procurement of API (Caffeine and Aspirin) with approval from DRAP

Previous Decision (M-321): Deferred for following:

- Submitted GMP certificate of different site than documents submitted for drug substance (Caffeine).
- Valid Drug Manufacturing License or Valid Good Manufacturing Practice (GMP) certificate of the Aspirin manufacturer issued by relevant regulatory authority of country of origin.
- Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3
- Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active (Caffeine)Pharmaceutical Ingredient by Drug Product manufacturer is required.
- Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) (Paracetamol and Caffeine and Aspirin)shall be submitted.
- Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / Active Pharmaceutical Ingredient (Paracetamol and Caffeine) manufacture.
- COA of primary / secondary reference standard including source and lot number for Caffeine and Aspirin shall be provided.
- Composition of tablet is different from reference product in terms of excipients.
- Applied formulation is film coated however it is not evident from composition in section 3.2.P.1 and 3.2.P.3.2 as there are no excipients for coating.
- Manufacturing process Coating step is not included however applied product is film coated.
- Submitted CDP data for paracetamol and Caffeine is same as in Panadol Extra tablet. Clarification s is required.
- Submitted Process validation protocol are general not product related. Clarification is required.
- Justify your acceptance criteria for dissolution test as NLT 75% after 60 minutes of the labeled amount of paracetamol ,caffeine and Aspirin while USP has specified as

NLT 75% (Q) of the labelled amounts of acetaminophen , Aspirin and caffeine is dissolved

- Analytical Method Verification studies performed by the Drug Product manufacturer for drug product shall be submitted.
- COA of primary / secondary reference standard including source and lot number for paracetamol, Aspirin and Caffeine shall be provided
- Manufacturing of batches was done in Dec, 2021 than how stability studies started in September 2021.
- Stability studies of three (03) months submitted.
- Documents for the procurement of API (Caffeine and Aspirin) with approval from **DRAP**

Reply

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5	• Submitted GMP certificate of different site than documents submitted for drug substance (Caffeine). • Valid Drug Manufacturing License or Valid Good Manufacturing Practice (GMP) certificate of the Aspirin manufacturer issued by relevant regulatory authority of country of origin.	• Caffeine: Firm submitted now GMP certificate # 6101335 valid upto 12-08-2022 of Aarti Industries Limited Address: K-17/18/19, M.I.D.C, tararpur, District, Thane zone 4.(mentioned on all documents) • **In Chinese submitted which can not be read.**
2.	2.3.R.1.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3	Submitted.
3.	3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active (Caffeine)Pharmaceutical Ingredient by Drug Product manufacturer is required.	Copies of the Drug substance specifications (BP) and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient (Caffeine) by Drug Product manufacturer is submitted.
4.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability	**Analytical method verification of tablet (Drug Product) submitted instead of drug substance.**

		(method precision) performed by the Drug Product manufacturer for drug substance(s) (Paracetamol and Caffeine and Aspirine)shall be submitted.	
5.	3.2.S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / Active Pharmaceutical Ingredient (Paracetamol and Caffeine) manufacture.	**COA of paracetamol and Aspirin submitted while, COA of drug substance for Caffeine of a different Drug substance supplier (Kores India limited submitted.**
6.	3.2.S.5	COA of primary / secondary reference standard including source and lot number for Caffeine and Aspirin shall be provided.	Submitted.
7.	3.2.P.1	• Composition of tablet is different from reference product in terms of excipients. • Applied formulation is film coated however it is not evident from composition in section 3.2.P.1 and 3.2.P.3.2 as there are no excipients for coating.	• **Correct formulation as per reference product attached.** • **Revised section 3.2.P.1 and 3.2.P.3 are attached.**
8.	**3.2.P.2.3**	Manufacturing process Coating step is not included however applied product is film coated.	**Correct manufacturing method submitted.**
9.	3.2.P.2.2.1	Submitted CDP data for paracetamol and Caffeine is same as in Panadol Extra tablet. Clarification s is required.	**Correct CDP with F2 calculations submitted.**
10.	3.2.P.3.5	Submitted Process validation protocol are	Submitted.

		general not product related. Clarification is required.	
11.	3.2.P.5.1	• Justify your acceptance criteria for dissolution test as NLT 75% after 60 minutes of the labeled amount of paracetamol ,caffeine and Aspirin while USP has specified as NLT 75% (Q) of the labelled amounts of acetaminophen , Aspirin and caffeine is dissolved	**Correction is done and revised specifications**
12.	3.2.P.5.3	Analytical Method Verification studies performed by the Drug Product manufacturer for drug product shall be submitted.	**Not submitted.**
13.	3.2.P.6	COA of primary / secondary reference standard including source and lot number for paracetamol, Aspirin and Caffeine shall be provided	Submitted.
14.	3.2.P.8	• Manufacturing of batches was done in Dec, 2021 than how stability studies started in September 2021. • Stability studies of three (03) months submitted. • Documents for the procurement of API (Caffeine and Aspirin) with approval from DRAP	**Not submitted.**

Decision: Deferred for following:

- **Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) (Paracetamol and Caffeine and Aspirine) shall be submitted.**
- **Analytical Method Verification studies performed by the Drug Product manufacturer for drug product shall be submitted.**

- **Justification for initiating stability studies in Se [ptember 2021, whereas manufacturing of batches was done in Dec, 2021.**
- **Documents for the procurement of API (Caffeine and Aspirin) with approval from DRAP.**
- **Stability studies of three (03) months submitted.**
- **Documents for the procurement of API (Caffeine and Aspirin) with approval from DRAP**
- **Clarity regarding drug substance manufacturer since COA of drug substance for Caffeine of two different Drug substance manufacturers has been submitted.**
- **Since the submitted dossier does not reflect any details for contract manufacturing while annexed NOC from M/s GlaxoSmithKline Consumer Health declare it by way of cntract manufacturing hence firm shall submit clarity regarding the status of registration application whether it's for self-manufacturing with registration in name of M/s Citi Pharma Private Limited or for contract manufacturing with registration in name of M/s GlaxoSmithKline Consumer health Pakistan Limited. In case of contract manufacturing for M/s GlaxoSmithKline Consumer health Pakistan Limited, the application shall be re submitted as per relevant SRO of contract manufacturing policy.**
- **Clarification for using of Panadol brand name as per Rule 20A of Drugs (L,R &A) Rules, 1976.**

Case no. 02 Registration applications for local manufacturing of (Human) drugs on form 5

a. New cases

21	Name and address of manufacturer / Applicant	M/s Wnsfeild Pharmaceuticals. Plot no. 122, Phase V, Block A, Industrial Estate Hattar.
	Brand Name +Dosage Form + Strength	Betawin 16m Tablet
	)osition	Each Uncoated Tablet Contains: Betahistine Dihydrochloride …….16mg
	Diary No. Date of R& I & fee	Dy.No 39685 dated 03-12-2018 Rs.20,000/- Dated 03-12-2018
	Pharmacological Group	Anti-Vertigo
	Type of Form	Form 5
	Finished product Specifications	BP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Betahistine of MHRA Approved
	Me-too status	Betalin Tablet 16mg by Linear Pharma (081873)
	GMP status	Last GMP inspection of Wnsfeild conducted on 18-01-2018, wherein renewal of DML was recommended.
	Remarks of the Evaluator:	
	Revise your master formulation according to applied strength.	Revise master formulation according to applied strength is submitted.
	Decision: Approved. The firm shall submit full fee for correction/pre-approval change in master formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021	
21	Name and address of manufacturer / Applicant	M/s Wnsfeild Pharmaceuticals. Plot no. 122, Phase V, Block A, Industrial Estate Hattar.
	Brand Name +Dosage Form + Strength	Nazodin 100mg Tablets
	Composition	Each film coated tablet contains: Phenazopyridine Hydrochloride ……. 100mg

	Diary No. Date of R& I & fee	Dy.No 39686 dated 03-12-2018 Rs.20,000/- Dated 03-12-2018
	Pharmacological Group	Analgesic,Drugs for urological pain
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	PHENAZO of BAUSCH HEALTH, CANADA INC Health Canada approved.
	Me-too status	Uropyrine 100mg Tablet by Ontech Corporation Karachi (Reg no. 041200)
	GMP status	Last GMP inspection of Wnsfeild conducted on 18-01-2018, wherein renewal of DML was recommended.
	Remarks of the Evaluator	
	Decision: Approved.	

Case no. 03 Registration applications of newly granted DML or New section (Human)

a. New DML

M/s Fleming Pharmaceutical**. (New DML)**

CLB in its 282nd meeting held on 31st August 2021 has considered and approved the grant of Drug Manufacturing License by way of formulation with following five (05) sections to M/s M/s Fleming Pharmaceutical.

1.	Oral Dry Powder for suspension(Penicillin)
2.	Capsule (Penicillin)
3.	Tablet (Penicillin)
4.	Dry Powder Injectable (Penicillin)
5.	Dry Powder Injectable (Carbapenem)

Accordingly, firm has applied for following products for consideration by Drug Registration Board

Capsule (Penicillin)
01 Molecules/ 02 Products

21	Name, address of Applicant / Marketing Authorization Holder	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Name, address of Manufacturing site.	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale

		☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24368 dated 29-08-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 665216866218
	The proposed proprietary name / brand name	Flemox 250 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Amoxicillin …….…. 250 mg (as Amoxicillin trihydrate)
	Pharmaceutical form of applied drug	Maroon cap and yellow body Capsule shell #2 filled with white to off white powder.
	Pharmacotherapeutic Group of (API)	Penicillin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	10 x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Amoxicillin Capsules by M/s US Antibiotics, USFDA Approved.
	For generic drugs (me-too status)	Amoxil Capsules by M/s GSK, Reg. No. 000213
	GMP status of the Finished product manufacturer	New DML letter issued dated; 14-09-2021
	Name and address of API manufacturer.	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Amoxicillin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: 00013/210/2009, 00013/211/2009, 00013/212/2009)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Amoxil 250mg Capsule by GSK Pakistan Limited (Batch YJ9F) by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand by in Acid media (pH 1.2) & Acetate buffer 4.5 pH and Phosphate Buffer (pH 6.8) and water . The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.		
API Lot No.	000130/601/2021		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (10×10's)		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	12-2021	12-2021	12-2021
Date of Initiation	15-12-2021	15-12-2021	15-12-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 129/2020-DRAP (AD/1998630-530) issued by DRAP on the basis of evaluation conducted on 22-06-2022 and valid for 2 years.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	• API had been locally procured from Pharmagen Ltd.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is required.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer are attached.
2.	3.2.S.7	Justification is required for not performing the identification test, pH and determination of optical rotation during the stability study of drug substance.	Firm submitted the revised stability data in which the results of identification test, pH and determination of optical rotation test has included.
3.	3.2.P.3.5	Submitted Process validation protocol are general not product related. Clarification is required.	Revised Process validation protocol submitted.
4.	3.2.P.5.1	• Time for Q not mentioned in specifications. • USP monograph mentioned Microbial enumeration test and test for specified organism. Which is not performed. Clarification is required.	• Revised internal specifications are attached. • Firm submitted the revised specification in which microbial enumeration test and test for specified organism has included. Further, performance data of microbial enumeration test and test for specified organism on next time point has also been submitted.
5.	3.2.P.8	• Purchase documents for Amoxicillin. • Compliance Record of HPLC software 21CFR	Purchase documents of different batch no submitted. Later firm submitted the correct purchase documents of API.

		& audit trail reports on product testing • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

21(	Name, address of Applicant / Marketing Authorization Holder	M/s Fleming Pharmaceutical. 23- Km Lahore-Sheikhupura Road, Lahore.
	Name, address of Manufacturing site.	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24369 dated 29-08-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 9532870139
	The proposed proprietary name / brand name	Flemox 500 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Amoxicillin …… 500 mg (as Amoxicillin trihydrate)
	Pharmaceutical form of applied drug	Maroon cap and yellow body Capsule shell #2 filled with white to off white powder.
	Pharmacotherapeutic Group of (API)	Penicillin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	10 x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Amoxicillin Capsules by M/s US Antibiotics, USFDA Approved.
	For generic drugs (me-too status)	Amoxil Capsules by M/s GSK, Reg. No. 006669
	GMP status of the Finished product manufacturer	New DML letter issued dated; 14-09-2021

	Name and address of API manufacturer.	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Amoxicillin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: 00013/210/2009, 00013/211/2009, 00013/212/2009)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Amoxil 500mg Capsule by GSK Pakistan Limited (Batch UH2X) by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand by in Acid media (pH 1.2) & Acetate buffer 4.5 pH and Phosphate Buffer (pH 6.8) and water . The values for f1 and f2 are in the acceptable range
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.
API Lot No.	000130/601/2021

Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (10×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	24-01-2022	24-01-2022	24-01-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 129/2020-DRAP (AD/1998630-530) issued by DRAP on the basis of evaluation conducted on 22-06-2022 and valid for 2 years.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• API had been locally procured from Pharmagen Ltd.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is required.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer are attached.

2.	3.2.S.7	Justification is required for not performing the identification test, pH and determination of optical rotation during the stability study of drug substance	Firm submitted the revised stability data in which the results of identification test, pH and determination of optical rotation test has included.
3.	3.2.P.3.5	Submitted Process validation protocol are general not product related. Clarification is required.	Revised Process validation protocol submitted.
4.	3.2.P.5.1	• Time for Q not mentioned in specifications. • USP monograph mentioned Microbial enumeration test and test for specified organism. Which is not performed. Clarification is required.	• Revised internal specifications are attached. • We would like to mention that microbial enumeration test is not mentioned in specification, as it is not required to be performed on every batch. Initial testing report is attached. Firm submitted the revised specification in which microbial enumeration test and test for specified organism has included. Further, performance data of microbial enumeration test and test for specified organism on next time point has also been submitted.
5.	3.2.P.8	• Purchase documents for Amoxicillin. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Purchase documents of different batch no submitted. Later firm submitted the correct purchase documents of API.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

b. New/Additional section(s)

Deferred case

217.	Name, address of Applicant / Marketing Authorization Holder	M/s Hudson Pharma Private Limited D-93, North Western Industrial Zone, Port Qasim, Karachi, Sindh 75350,

		Pakistan.
	Name, address of Manufacturing site.	M/s Hudson Pharma Private Limited D-93, North Western Industrial Zone, Port Qasim, Karachi, Sindh 75350, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11038 dated 06/05/2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 40017019
	The proposed proprietary name / brand name	Becloson S Suspension for Nebulisation 0.8mg + 1.6mg/2ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2ml of suspension contains: Beclometasone dipropionate…….. 0.8mg Salbutamol sulphate 1.928mg equivalent to salbutamol …….1.6mg
	Pharmaceutical form of applied drug	Suspension for Nebulisation
	Pharmacotherapeutic Group of (API)	Corticosteroid and Selective beta-2-adrenoreceptor agonists
	Reference to Finished product specifications	In-house
	Proposed Pack size	2ml × 1's, 5's & 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Product is registered in Italian Medicine Agency (AIFA), with the brand name "Clenil Compositum" by Chiesi Farmaceutici, Italy.
	For generic drugs (me-too status)	Manufacturer name: Chiesi Farmaceutici, Italy. Importer: Chiesi Pharmaceutical (Pvt.) Ltd. Brand name: Clenil Compositum, Strength: 0.8mg+1.6mg/2ml, Registration number: 021199
	GMP status of the Finished product manufacturer	New section granted on 24/11/2021 Injectable Ampoule BF (steroid) - New
	Name and address of API manufacturer.	**Beclomethasone dipropionate:** FARMABIOS S.p.A.Via Pavia, 1 27027 Gropello Cairoli, (PV) Italy. **Salbutamol sulphate:** LUSOCHIMICA SpA – Via Giotto 9 – 23871 Lomagna (LC) – ITALY
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to

		nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substances. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Official monograph of Beclomethasone dipropionate is present in USP and Salbutamol sulphate is present in BP. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	**Beclomethasone dipropionate**: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Batches: (0081300, 0091300, B0111322) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (0031130, 0101515, 0111515,) **Salbutamol sulphate:** Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (SAL 104, SAL 204, SAL 304)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator product that is

		Clenil Compositum Suspension for Nebulisation 0.8mg+1.6mg/2ml Batch - 1136521 by Chiesi Farmaceutici, Italy
	Analytical method validation/verification of product	Method validation studies have submitted including specificity, linearity/range, accuracy, precision (repeatability and intermediate), Limit of Quantitation (LOQ), Limit of Detection (LOD) and robustness.

STABILITY STUDY DATA

Manufacturer of API	Beclomethasone dipropionate: M/s FARMABIOS S.p.A.Via Pavia, 1 27027 Gropello Cairoli, (PV) Italy. Salbutamol sulphate: M/s LUSOCHIMICA SpA – Via Giotto 9 – 23871 Lomagna (LC) – ITALY		
API Lot No.	Beclomethasone dipropionate: 2106DM4 Salbutamol sulphate: SALM119		
Description of Pack (Container closure system)	Two aluminium pouches present in a unit carton with leaflet. Each aluminium pouch contain 2ml x 5s product filled in plastic Ampoule (LDPE) 10 mono dose vials		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	SB-BS-NU-01	SB-BS-NU-02	SB-BS-NU-03
Batch Size	2 Liters	2 Liters	2 Liters
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	14-01-2022	14-01-2022	14-01-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Beclomethasone dipropionate: Copy of GMP certificate No.IT-API/167/H/2020 issued by Italian Medicine Agency valid till 12/06/2023. Salbutamol sulphate: Copy of GMP certificate No.IT-API/69/H/2019 issued by Italian Medicine Agency valid till 03/08/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Beclomethasone dipropionate: Firm has submitted copy of invoice (invoice# 380) Dated 19-11-2021 cleared by DRAP Karachi office dated 10-12-2021 specifying import 0.2g Beclomethasone dipropionate (Batch# 2106DM4).

		Salbutamol sulphate: Firm has submitted copy of invoice (invoice# 112) Dated 27-03-2020 cleared by DRAP Karachi office dated 23-04-2022 specifying import 5kg Salbutamol Sulphate (Batch# SALM119).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.5.2	Specify the equivalent strength of the base for Salbutamol sulfate	Each 2ml of suspension contains: Beclometasone dipropionate 0.8mg Salbutamol sulphate 1.928mg equivalent to salbutamol 1.6mg
2.	1.5.7	Aerosol for Nebulization mentioned in this section. Clarification is required about applied formulation	Our applied formulation is in suspension form which is used as nebulisation for aerosol. So, our formulation route of administration is Suspension for nebulisation for aerosol, and the same has been mentioned on the innovator (Clenil Compositum) pack.
3.	2.3.R.1.1	Source of Salbutamol Sulfate in BMR's is from Cipla. Clarification is required.	A typographical error in the BMR and we have used the salbutamol sulfate manufactured by Lusochimica and it can be verified from the CoA of FPP manufacturer for the same lot number.
4.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer of both drug substances (Beclomethasone dipropionate &Salbutamol sulphate shall be submitted..	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer of both drug substances (Beclometasone dipropionate & Salbutamol sulphate) shall be submitted.
5.	3.2.S.5	COA of primary / secondary reference standard Testosteron Propionate including source and lot number shall be provided.	With reference to this query we would like to inform you that at the time of initial testing of Beclomethasone Dipropionate, the internal standard testosterone propionate was not available to us due to

			import constraints of the USP primary reference standard. Hence, we have used the same method as per USP without internal standard and complete validation has been performed to validate our results and also compare it with manufacturer results as well. Furthermore, we have ordered for working standard of Testosterone propionate from Merck, Same will be used for the release testing in future consignment. The complete method of validation is already submitted.
6.	3.2.P.8	• Sterility testing and Uniformity of dose units not included in initial testing. • Details of Water loss test for 6 months not submitted.	• We have performed the Sterility testing and Uniformity of dose on all stability batches and the results are within range. • Details of Water loss test for 6 months submitted.

Previous Decision: Registration Board deferred the case for further deliberation regarding manufacturing requirments of products containing Steriodal and non-steriodal drug substance in one formulation.

Reply by firm: In this regard, our clear understanding is that introducing a less sensitive active into the designated steroid manufacturing area is more appropriate/safe than introducing a sensitive active into general manufacturing area, for all combination products that have both types of ingredients.

Discussion: Registraion Board deliberated the applied formulation and evoked the decision of Board regarding "Manufcaturing requirements of Dry Powder Inhaler capsules", wherein it was discussed that the drug products intended for inhlataional route of administration have local onset of action and does not go into syetmic circulation hence the same manufacturing facility/section can be used for such formulations. Moreoever relevant decision of CLB was taken in its 239th meeting and is as under:

1. Steroidal topical preparations like Eye/Ear Drops, Sterile Eye Ointment, External Preparation i.e. Cream/Ointment/Gel, Lotions, Spray/aerosols, suppositories, vaginal preparation, intra oral preparations, Nasal drops etc shall be manufactured in General facility/area subject to following conditions that the:

a. Manufacturers shall have segregated dispensing booths, cleaning validation and controls studies for processes and adequate system to minimize the potential risk of cross contamination,
b. Commercial marketing of above products shall be allowed by Registration Board after confirmation and verification of conditions as in (1.a.) above

2. Segregated manufacturing facility shall be required for the manufacturing of Steroidal Injections, Syrup and Oral Solid dosage forms (Tablet, capsules, granules etc).

In pursuance of the baove cited facts Registration Board decided to allow the manufacturing of inhalational products of a particular dosage form containing steroidal/general ingredients in the same manufacturing facility subject to the condition that manufacturers shall have segregated dispensing booths, cleaning validation and controls studies for processes and adequate system to minimize the potential risk of cross contamination.

In instant ase M/s Hudson has two approved manufacturing sections titled as "Plastic ampoule (BFS) section" and "Injectable ampoule BF (Steroid)", whereas applied formulation is of respule dosage form. Hence Board decided to ensure the distinction of the available facility of "Injectable ampoule BF (steroid)" section for the applied dosage form of "Inhalational Respules" the firm shall revise the title of the said section to avoid cross contamination of steroidal ingredients into the Injectable preparations. In case the firm intends to apply for the "Steroid injectable dosage forms", the firm shall have separatee manufacturing faciluity for it.

Decision: Registration Board approved the applied product of "Becloson S Suspension for Nebulisation 0.8mg + 1.6mg/2ml" with Innovator'specifications against the available manufacturing facility of "Injectablel ampoule BF (steroid)" section.
The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.
Registration Board further directed the firm to revise the title of the section to "Respules (Blow Fill Seal) section" from Licensing Division before issuance of registration letter.

Case no. 04 Registration applications of drugs for which stability study data is submitted

a. Exemption from onsite verification of stability data

218	Name and address of manufacturer / Applicant	M/s Sante Pvt Ltd. 245/2-Z, Block 6, PECHS, Karachi 75400"
	Brand Name +Dosage Form + Strength	Brinza Ophthalmic Suspension "Brinzolamide 1% Brimonidine Tartrate 0.2%
	Composition	Each ml contains: Brinzolamide…10mg Brimonidine Tartrate …2mg
	Diary No. Date of R& I & fee	Dy.No 22189 dated 26-06-2018 Rs.20,000/- 26-06-2018 Duplicate
	Pharmacological Group	Anti-glaucoma Preparations and Miotics
	Type of Form	Form 5
	Finished product Specifications	Manufacturer Specs
	Pack size & Demanded Price	As per PRC.
	Approval status of product in Reference Regulator Authorities	SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% USFDA Approved.
	Me-too status	
	GMP status	02-07-2019 Conclusion: Based on the current practices and keeping in view the attitude of the management towards better compliance of GMP their overall compliance level for the said dosage form is rated as Good
	Remarks of the Evaluator.	Firm has ophthalmic section. • The provided Me too could not be confirmed
	Previous Decision	Registration Board deliberated that since the referred me-too product "Simbrinza" was first approved in 268th meeting of Registration Board and Board in 240th meeting has

		already decided that stability studies data will be required for new formulation and its subsequent generic, hence Board deferred the case for submission of stability study data as per the guidelines provided in 278th meeting of Registration Board as it's a subsequent generic. (M-292)

STABILITY STUDY DATA

Drug	Brinza Ophthalmic Suspension "Brinzolamide 1% Brimonidine Tartrate 0.2%		
Name of Manufacturer	M/s Sante Pvt Ltd. 245/2-Z, Block 6, PECHS, Karachi 75400"		
Manufacturer of API	**Brinzolamide:** M/s Duke Chem S.A.U. Pol. Industrial Sante Pere Molanta Avgda. Mare de Deu de Montserrat 93-99 08799 Olerdola -Barcelona **Brimonidine Tartrate:** Farmak, a.s Na vicinci 16/3 Klasterni Hradisko, 77900 Olomouc Czech Republic		
API Lot No.	**Brinzolamide:** 332700900 **Brimonidine Tartrate:** 16021017		
Description of Pack (Container closure system)	8ml LDPE bottle		
Stability Storage Condition	Real time : 30°C ± 2° C / 35% ± 5% RH Accelerated: 40°C ± 2°C / 25% ± 5% RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated:0,3,6 (month) Real Time: 0,3,6 (month)		
Batch No.	08T	09T	10T
Batch Size	5 Liter	5 Liter	5 Liter
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	24-11-2019	24-11-2019	24-11-2019
No. of Batches	03		
Date of Submission	06-11-2020 (29596)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product "Zithrosan 1% eye drops" which was presented in 289th meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 14th March, 2019. According to inspection report, following points were confirmed. • The firm has 21CFR compliant HPLC software.

		• The firm has audit trail reports available. Adequate monitoring and control are available for stability chamber
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	**Brinzolamide:** Copy of COA of Brinzolamide (Batch# 332700900.) from M/s Duke Chem S.A.U. Pol. Industrial Sante Pere Molanta Avgda. Mare de Deu de Montserrat 93-99 08799 Olerdola -Barcelona is submitted. Copy of COA (Batch# 332700900) from M/S Sante Pvt Ltd is submitted. **Brimonidine Tartrate:** Copy of COA of Brimonidine Tartrate (Batch# 16021017.) from M/s Farmak, a.s Na vicinci 16/3 Klasterni Hradisko, 77900 Olomouc Czech Republic is submitted. Copy of COA (Batch# 16021017) from M/S Sante Pvt Ltd is submitted.
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	
4.	Stability study data of API from API manufacturer	**Brinzolamide:** The firm has submitted copy of **accelerated, 06 Months** (40°C ± 2°C & 75±5%RH) & **long term, 48 Months** (30C ± 2°C & 75±5%RH) stability study reports of 03 batches **Brimonidine Tartrate:** The firm has submitted copy of **accelerated, 06 Months** (40°C ± 2°C & 75±5%RH) & **long term, 60 Months** (30C ± 2°C & 75±5%RH) stability study reports of 03 batches and Accelerated and Real time stability study batches
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Brinzolamide:** Copy of GMP Certificate No # NFC_II/2121/001/CAT M/s Duke Chem S.A.U. Pol. Industrial Sante Pere Molanta Avgda. Mare de Deu de Montserrat 93-99 08799 Olerdola - Barcelona issued by Competent Authority of Ministry of health of Government of Catalonia-Spain, is submitted. Based on inspection conducted on 17, 19, 20 & 21 May 2021 valid for 3 years **Brimonidine Tartrate:** Copy of GMP Certificate No # sukis 1705/2019 for M/s Farmak, a.s Na vicinci 16/3 Klasterni Hradisko, 77900 Olomouc Czech Republic issued by Competent Authority of Czech Republic(SUKL), is submitted. Based on inspection conducted on 14-02-2019 valid for 3 years
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Brinzolamide:** Copy of form 3, form 7 and Commercial Invoice No: E/109709 Dated: 11-01-2018 from M/s gentec Pharmaceutical group and

<table>
<tr><td></td><td></td><td>manufacturer Not attested by AD DRAP for Brinzolamide batch No# 332700900
Brimonidine Tartrate: Copy of form 3 and Commercial Invoice No: P1800168 Dated: 04-05-2018 from M/s Farmak, a.s Na vicinci 16/3 Klasterni Hradisko, 77900 Olomouc Czech Republic Not attested by AD DRAP for Brimonidine Tartrate batch No# 16021017.
Airway bill from Farmark A.S Submitted.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Same excipients used as used by innovator.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>Brinza Ophthalmic Suspension
"Brinzolamide 1%
Brimonidine Tartrate 0.2%
<table>
<tr><th>Batch No.</th><th>Bach size</th><th>Mfg. Started</th></tr>
<tr><td>08T</td><td>5 Liter</td><td>01-10-2019</td></tr>
<tr><td>09T</td><td>5 Liter</td><td>03-10-2019</td></tr>
<tr><td>10T</td><td>5 Liter</td><td>03-10-2019</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Not applicable</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Submitted</td></tr>
<tr><td colspan="3">REMARKS OF EVALUATOR</td></tr>
<tr><td>S.No</td><td>Shortcomings communicated</td><td>Reply</td></tr>
<tr><td>1.</td><td>Documents for the procurement of API with approval from DRAP</td><td>Attested not submitted but Airway bill for Brimonidine Tartrate.</td></tr>
<tr><td>2.</td><td>Certificate of Analysis of Brinzolamide by API Manufacturer and Finished Product manufacturer of different batch No than batch No</td><td>Invoice Submitted contains 2 other batches of Brinzolamide also included but not attested</td></tr>
</table>

	mentioned on commercial invoice, form 7. Justify	
3.	Valid Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin for both API.	Brinzolamide Valid GMP certificate not submitted
4.	Stability study data of API from API manufacturer for both API's according to zone IV-A	Brimonidine Tartrate stability studies of 2 batches submitted
5.	Method used for analysis of both API from both API Manufacturer and Finished Product manufacturer.	Submitted
6.	Complete batch manufacturing record of three stability batches.	Fill volume in BMR is 08ml and in stability 05ml mentioned.
7.	Brinzolamide overage without any scientific justification.	Due to grinding process and transferring losses of API for brinzolamide suspension 5% overage was taken into account to meet the product shelf life. It would further be considered after real time stability study data till shelf life
8.	Stability initiation date not mentioned.	Initiation date submitted
9.	COA's of all time points for real time and accelerated stability studies of 3 batches of finished product.	Submitted
10.	Raw data sheets for Assay calculations of all time point of finished products	Submitted
Second letter Dated:12-10-2021		
S.No	**Shortcomings**	
1.	Documents for the procurement of API with approval from DRAP as submitted documents are not attested.	Submitted but not attested. For **Brimonidine Tartrate** Airway bill submitted.
2.	In submitted form 7 and Commercial invoice, 03 batch No of Brinzolamide mentioned while COA of only 1 batch submitted. Clarify which batch was used in manufacturing of stability batches	Stability batches 08T, 09T & 10T were manufactured using Brinzolamide batch # 332700900 having 18L0043D mentioned in Batch manufacturing record which is traceable through raw material test report. For review other two batches COA's also attached however these are not used in manufacturing of batches.
3.	Valid Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin for both API of Brinzolamide	Submitted
4.	Submit Stability study data of API from API manufacturer of 1 more	3 batches stability studies submitted according to Zone IV-B

	batch according to zone IV-A for Brimonidine Tartrate as stability studies of 2 batches submitted	
5.	Fill volume in BMR is 08ml and in stability 05ml mentioned. Clarification is required	There was a typographical error in the stability data (i.e 5ml mentioned instead of 8ml) So please consider correct pack size of Brinza Ophthalmic Suspension as 8ml. Correct reports along with 24th month stability interval result are attached.
Decision: Approved with Innovator's specifications. • **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		

219	Name, address of Applicant / Marketing Authorization Holder	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial triangle, kahuta road, Islamabad-44000
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial triangle, kahuta road, Islamabad-44000
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32069 dated 23-09-2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 9264939862
	The proposed proprietary name / brand name	Omarigliptin 12.5mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Omarigliptin…..…12.5mg
	Pharmaceutical form of applied drug	Green color, round shaped, film coated tablet
	Pharmacotherapeutic Group of (API)	Dipeptidyl-Peptidase IV Inhibitors (Antidiabetic)
	Reference to Finished product specifications	Innovator Specs
	Proposed Pack size	4's

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Marizev 12.5mg Tablet by M/s MSD K.K, PMDA Approved.
	For generic drugs (me-too status)	OMARIL 12.5mg Tablet by M/s Genix Pharma Pvt. Ltd**., Registration Letter not issued**
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 11-02-2019, was valid till 09-05-2022 after extension for 3 months. Request for GMP inspection R&1 date: 22-12-2021 is provided.
	Name and address of API manufacturer.	M/s Chifeng Arker Pharmaceutical Technology Co., Ltd. No.8 Mysun street, hongshan Economic development Zone, chifeng, Inner Mongolia, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubility's, physical form(Crystalline form I), manufacturers, description of manufacturing process and controls, tests for impurities & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (D85-160101, D85-160102, D85-160201)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Marizev 12.5mg tablets by MSD company limited Tokyo Japan, by

		performing quality tests (Physical Appearance, identification, Average weight, Disintegration Time, Assay). CDP has been performed against the same brand that is Marizev 12.5mg tablets by MSD company limited Tokyo Japan, in Acid media (pH 1.0-1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Chifeng Arker Pharmaceutical Technology Co., Ltd. No.8 Mysun street, hongshan Economic development Zone, chifeng, Inner Mongolia, China		
API Lot No.	D85-201101		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (4's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)		
Batch No.	NPD 229 T-01	NPD 229 T-02	NPD 229 T-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	25-06-2021	25-06-2021	25-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 286th meeting decided to approve registration of Sofovir-V 400mg/100mg Tablet. Inspection date: 5 & 15 October, 2018 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of Drug Manufacturing License no. 20160053 issued by Inner Mongolia Drug Administration valid till 28-12-20256.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of, invoice (invoice# PSPW-201105) dated 05-11-2020 cleared by DRAP

		Islamabad office dated 01-12-2020 specifying import of Omarigliptin 1Kg (Batch# D85-201101).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.No	Shortcomings Communicated	Reply
1.	Differential fee for New Drug Product.	Differential fee of Rs.45,000/- has submitted vide slip no.980938052 dated 14-10-2022.
2.	Justify the finished product specification without the test for content uniformity..	Firm submitted the drug product analysis in which test for content uniformity results are included.
3.	Scientific justification for dissolution parameters including type of apparatus, speed and dissolution medium is required.	Firm replied that "For dissolution test we followed the USP general chapter 1092. In reference to minutes of registration board DRAP 291 meeting (2-4th sept 2019) Since the pKa value of the drug is 8.1 and as per pH pKa relationship, the drug is more soluble at high pH. So by this we take the idea that phosphate buffer 6.8 should be used. Secondly the release time of the product was also checked during comparative dissolution and more than 90% of drug was released in the medium. So we followed the above method".
4.	Dissolution medium in section 3.2.P.5.2 phosphate buffer (pH 6.8) while stability studies protocol 0.01N HCl is used as dissolution medium. Clarify	Firm replied that Dissolution medium used for the tablets is 6.8 phosphate buffer. While 0.01N HCl is a typo mistake in stability study protocol. Our testing method have pH 6.8 buffer.
5.	Submit 6th month data for stability studies.	Submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

220	Name, address of Applicant / Marketing Authorization Holder	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial triangle, kahuta road,

		Islamabad-44000
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial triangle, kahuta road, Islamabad-44000
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32070. dated 23-09-2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 85642565
	The proposed proprietary name / brand name	Omarigliptin 25mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Omarigliptin…..…25mg
	Pharmaceutical form of applied drug	Green color, round shaped, film coated tablet
	Pharmacotherapeutic Group of (API)	Dipeptidyl-Peptidase IV Inhibitors (Antidiabetic)
	Reference to Finished product specifications	Innovator Specs
	Proposed Pack size	4’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Marizev 25mg Tablet by M/s MSD K.K, PMDA Approved.
	For generic drugs (me-too status)	OMARIL 25mg Tablet by M/s Genix Pharma Pvt. Ltd.,
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 11-02-2019, was valid till 09-05-2022 after extension for 3 months. Request for GMP inspection R&1 date: 22-12-2021 is provided.
	Name and address of API manufacturer.	M/s Chifeng Arker Pharmaceutical Technology Co., Ltd. No.8 Mysun street, hongshan Economic development Zone, chifeng, Inner Mongolia, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility’s, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure

		system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubility's, physical form(Crystalline form I), manufacturers, description of manufacturing process and controls, tests for impurities & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 36 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (D85-160101, D85-160102, D85-160201)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Marizev 25mg tablets by MSD company limited Tokyo Japan, by performing quality tests (Physical Appearance, identification, Average weight, Disintegration Time, Assay). CDP has been performed against the same brand that is Marizev 25mg tablets by MSD company limited Tokyo Japan, in Acid media (pH 1.0-1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Chifeng Arker Pharmaceutical Technology Co., Ltd. No.8 Mysun street, hongshan Economic development Zone, chifeng, Inner Mongolia, China
API Lot No.	D85-201101
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (4's)
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12 (Months)		
Batch No.	NPD 230 T-01	NPD 230 T-01	NPD 230 T-01
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	25-06-2021	25-06-2021	25-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 286th meeting decided to approve registration of Sofovir-V 400mg/100mg Tablet. Inspection date: 5 & 15 October, 2018 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of Drug Manufacturing License no. 20160053 issued by Inner Mongolia Drug Administration valid till 28-12-20256.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of, invoice (invoice# PSPW-201105) dated 05-11-2020 cleared by DRAP Islamabad office dated 01-12-2020 specifying import of Omarigliptin 1Kg (Batch# D85-201101).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Shortcomings Communicated	Reply
1.	Differential fee for New Drug Product.	Differential fee of Rs.45,000/- has submitted vide slip no. 5269077782 dated 14-10-2022.
2.	Justify the finished product specification without the test for content uniformity..	Firm submitted the drug product analysis in which test for content uniformity results are included.
3.	Scientific justification for dissolution parameters including type of	Firm replied that "For dissolution test we followed the USP general chapter 1092.

	apparatus, speed and dissolution medium is required.	In reference to minutes of registration board DRAP 291 meeting (2-4th sept 2019) Since the pKa value of the drug is 8.1 and as per pH pKa relationship, the drug is more soluble at high pH. So by this we take the idea that phosphate buffer 6.8 should be used. Secondly the release time of the product was also checked during comparative dissolution and more than 90% of drug was released in the medium. So we followed the above method".
4.	Dissolution medium in section 3.2.P.5.2 phosphate buffer (pH 6.8) while stability studies protocol 0.01N HCl is used as dissolution medium. Clarify	Firm replied that Dissolution medium used for the tablets is 6.8 phosphate buffer. While 0.01N HCl is a typo mistake in stability study protocol. Our testing method have pH 6.8 buffer.
5.	Submit 6th month data for stability studies.	Submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

221	Name, address of Applicant / Marketing Authorization Holder	M/s Himark Laboratories Private Limited Lahore
	Name, address of Manufacturing site.	M/s Himark Laboratories Private Limited Plot 37-A, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13910 dated 02-06-2022
	Details of fee submitted	PKR 30000 /-: Deposit slip # 647957126
	The proposed proprietary name / brand name	Himox 400 mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Moxifloxacin as hydrochloride .... 400 mg
	Pharmaceutical form of applied drug	White to off-white color oblong shaped film coated tablet
	Pharmacotherapeutic Group of (API)	Fluoroquinolones

	Reference to Finished product specifications	BP Specs.
	Proposed Pack size	1 ×5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	AVELOX 400mg tablet M/S Bayer Health Care Inc. (USFDA Approved).
	For generic drugs (me-too status)	Mofest 400 mg tablet by M/s Sami Pharmaceuticals (Pvt.) Ltd. Reg. No. 050745
	GMP status of the Finished product manufacturer	New license granted on 26/09/2019 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability
	Module III (Drug Substance)	Official monograph of Fexofenadine Hydrochloride is present in BP. Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months. Batches:(LE000510711/001/2018, LE000510711/002/2018, LE000510711/003/2018)

	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted pharmaceutical equivalence study of trial formulation (B # T-70) with comparator product MOXIGET 400mg Tablet (B # 205F31) of M/s GETZ pharma. The results of the quality tests of both products fall within the specifications and are comparable. The firm has performed comparative dissolution profile in pH 1.2, acetate buffer pH 4.5 and phosphate buffer 6.8. The results showed that similarity factor f2 was above 50 in three media.
	Analytical method validation/verification of product	Firm has submitted report of verification studies of analytical method for the drug substance. Firm has submitted report of validation of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited Lahore, Pakistan		
API Lot No.	00510711/002/2021		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×5's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-70	T-71	T-72
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	20-06-2021	20-06-2021	20-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 129/2020-DRAP (AD/1998630-530) issued by DRAP on the basis of evaluation conducted on 22-06-2022 and valid for 2 years.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	API had been locally procured from Pharmagen Ltd.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Shortcomings Communicated	Reply
1.	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3	Firm submitted the Batch manufacturing record for all the trial batches of drug product.
2.	Details of analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	Submitted
3.	(CoA) of the same batch for Drug Substance / /Active Pharmaceutical Ingredient by drug product manufacturer shall be submitted.	Submitted
4.	COA of primary / secondary reference standard including source and lot number shall be provided.	Submitted
5.	Pharmaceutical Equivalence and CDP not performed with Innovator. Clarification is required	Firm submitted the Pharmaceutical equivalence report and CDP performed against Avelox tablet 400mg. However the Manufacturer name of innovator brand, batch no. and expiry date of brand was not mentioned on the submitted reports.
6.	A brief description of process validation including the proposed protocol shall be submitted.	Submitted
7.	• Specifications claimed are USP while in section 1.5.6 claimed as BP.	Firm claimed that their drug product complies USP specification. Further, submitted the revised specification of dissolution in accordance with USP.

	• Justify your acceptance criteria for dissolution test as NLT 80% of the labeled amount of Moxifloxacin is dissolved in 30 min; USP has specified as NLT 80% (Q) of the labeled amount of Moxifloxacin dissolved in 30 min.	
8.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has stated that Audit trail is maintained manually.
9.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Decision: Approved with USP specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

222	**Name, address of Applicant / Importer**	M/s Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi
	Details of Drug Sale License of importer	**License No:** 565 **Address:** Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi. **Address of Godown:** (a) 1st floor, Plot no. 211, Sector 23 Korangi Industrial Area, Karachi (b) Plot No 32, Sector 16, Korangi Industrial Area, Karachi **Validity:** 16-06-2024 **Status:** License to sell Drugs by way of Wholesale **Renewal:** Yes Submitted valid till 16-06-2022
	Name and address of marketing authorization holder (abroad)	ANFARM HELLAS S.A. 61st km NAT.RD. ATHENS-LAMIA, Schimatari Viotias 32009, Greece.
	Name, address of manufacturer(s)	ANFARM HELLAS S.A. 61st km NAT.RD. ATHENS-LAMIA, Schimatari Viotias 32009, Greece. **Local repacking by:** Global Pharmaceuticals Private Limited. Plot No. 204 – 205, Industrial Triangle, Kahuta Road, Islamabad, Pakistan
	Name of exporting country	Greece

	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized CoPP (**certificate no. 72204**) dated **11-08-2021** issued by National Organization for Medicines (EOF), 284 Mesogeion Ave. 155 62 Holargos Attica, Greece. The CoPP confirms status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every 3 years. The name of importing country on CoPP is mentioned as Pakistan. **Free sale in country of origin:** Yes
	Details of letter of authorization / sole agency agreement	Firm has submitted original, legalized sole agency agreement (letter of authorization) as product registration holder. The letter specifies that the manufacturer **ANFARM HELLAS S.A., located at 4 Achaias Str. & Trizinias, 14564, Kifisia Attiki Greece** (administration office as per COPP) appoints M/s Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi to register their products in Pakistan. The authorization letter is issued on 28-06-2021
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☐ Finished Pharmaceutical product import ☒ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 28326 dated: 14-10-2021
	Details of fee submitted	PKR 100,000/- Deposit slip # 97617572626
	The proposed proprietary name / brand name	DOWPENEM INJECTION 500g IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	**Each vial of Powder contains:** Meropenem trihydrate equivalent to Meropenem…….500mg (with sodium carbonate) **Diluent:** **Each ampoule contains:** Sterilized water for injection……10ml
	Pharmaceutical form of applied drug	Powder for Injection/ Infusion
	Pharmacotherapeutic Group of (API)	Carbapenem Antibiotic

	Reference to Finished product specifications	In House
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Merrem (Meropenem) Injection 500mg IV **(USFDA** Approved).
	For generic drugs (me-too status)	Meroget Injection of Getz Pharma Pvt. Ltd. (Reg # 083174)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Name, address of drug substance manufacturer	ACS DOBFAR SpA 2: Addetta Site, Viale Addetta, 2a/12-3/5 20067 Tribiano, Milano - Italy
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API. Stability study conditions: Real time: 25^{o}C ± 2^{o}C and 60% RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Accelerated Batches: (330772 023 0, 330772 025 0, 330772 027 0) Real time Batches: (330772 8001 8, 330772 8001 0, 330772 8038 1)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted Pharmaceutical Equivalence against the innovator product Meronem 500mg by

		AstraZeneca Batch no # 14047 C
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Colourless glass Vial type III sealed with rubber stopper and aluminium cap with Plastic flip-off seal
	Stability study data of drug product, shelf life and storage conditions	Accelerated stability studies have been conducted at 40°C ±2°C / 75%±5% RH for 06 months. Real time stability studies conducted at 30 °C±2°C / 65% ± 5% RH for one batch for 36 months ((24410) and two batches 24 months (36474, 33994) Batches of stability studies : (24410, 36474, 33994)

Evaluation by PEC:

Sr.no.	Obseravtions/Shortcoming	Reply of the Firm
1.	Letter of Authorization by ANFARM HELLAS S.A does not mentioned that label vials will be imported.	Firm replied that the letter for Authorization provided in the submitted dossier states that Martin Dow Limited has expreseed its willingness to import the products Dowpenem Injection 500mg &1g in full compliance with the relevant local and international guidelines and cGMP standards which actually corresponds to the labelled vials. We, hereby clarify that we are importing the product in the form of labelled vials and final packaging along with diluents will be done by Global Pharmaceuticals.
2.	Product is available in USP pharmacopeia while applied formulation is claimed in house specifications. Clarify. Firm claimed that in-house specifications are more stringent than USP specifications.	
3.	Certificate of analysis by both drug substance manufacturer	Firm submitted a declaration letter from ANFARM HELLAS S.A in which it is stated

Controls	USP monograph of Meropenem Injection	Anafarm's Release specification
Assay	90%-120%	95%-105%
Content of sodium	80%-120%	…
Sodium carbonate content	….	14.7%-16.1%
Bacterial Endotoxin	NMT 0.12 EU/mg	NMT 0.12 EU/mg
Loss on Drying	9.0%-12.0%	9.0%-12.0%
pH	7.3-8.3	7.3-8.3
Sterility test	Sterile	Sterile
Particulate contaminants	Meets the requirements for SVP injections	Meets the requirements for SVP injections
Uniformity of dosage unit	Meets the requirement	Meets the requirement

Further firm stated that Anafarm do not test sodium content ,however the percentage of sodium carbonate is calculated to be equal to 15.4% i.e. equal to 6.7% (w/w) sodium, so the limits are between 6.7-7.0%.

	and drug product manufacturer not submitted.	that we,Anafarm S.A. receives Meropenem sterile bulk and not the API Meropenem trihydrate.Thus no analysis on the API is performed and thus no method verification is performed.
4.	Manufacturing process does not show blending of Sodium carbonate with meropenem trihydrate neither by API manufacturer nor by ANFARM HELLAS S.A	Firm submitted the reply in which it is stated that the mixing of the excipient Sodium carbonate lyophilized sterile with the API meropenem trihydrate sterile is considered as the first step of the manufacturing process of the sterile bulk.
5.	Data of compatibility studies has been submitted with ANFARM HELLAS S.A diluent while in this case diluent will be locally purchased and no compatibility studies conducted. Justify.	Firm submit commitment that they perform compatibility studies of the product with the locally purchased diluent before marketing of the product.
6.	Stability studies provided by drug product manufacturer ANFARM HELLAS S.A while product will be imported as labelled vials and final packaging will be done by Global Pharmaceuticals. Justify.	Firm submit commitment that stability studies for the final product packaged by Global Pharmaceuticals will be performed for the first three consecutive batches of commercial scale.
7.	Please specify final quality control release site.	Firm claimed that final quality release site will be Global Pharmaceuticals and the finished product specification are according to USP.
8.	Steps of packaging not mentioned performed in the global pharmaceuticals.	Submitted

Decision: Deferred for following:

- **Justification of not performing test of Sodium content test by M/s Anfarm as recommended by USP monograph.**
- **Analytical method verification studies of drug substance performed by M/s Anfarm.**
- **Details regarding Packaging, Quality control analysis and batch release activities to be conducted by M/s Global pharmaceuticals.**

223	**Name, address of Applicant / Importer**	M/s Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi
	Details of Drug Sale License of importer	**License No:** 565 **Address:** Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi. **Address of Godown:** (a) 1st floor, Plot no. 211, Sector 23 Korangi Industrial Area, Karachi (b) Plot No 32, Sector 16, Korangi Industrial Area, Karachi **Validity:** 16-06-2024 **Status:** License to sell Drugs by way of Wholesale **Renewal:** Yes Submitted valid till 16-06-2022

	Name and address of marketing authorization holder (abroad)	ANFARM HELLAS S.A. 61st km NAT.RD. ATHENS-LAMIA, Schimatari Viotias 32009, Greece.
	Name, address of manufacturer(s)	ANFARM HELLAS S.A. 61st km NAT.RD. ATHENS-LAMIA, Schimatari Viotias 32009, Greece. **Local repacking by:** Global Pharmaceuticals Private Limited. Plot No. 204 – 205, Industrial Triangle, Kahuta Road, Islamabad, Pakistan
	Name of exporting country	Greece
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original, legalized CoPP (**certificate no. 72204**) dated **11-08-2021** issued by National Organization for Medicines (EOF), 284 Mesogeion Ave. 155 62 Holargos Attica, Greece. The CoPP confirms status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every 3 years. The name of importing country on COPP is mentioned as Pakistan. **Free sale in country of origin:** Yes
	Details of letter of authorization / sole agency agreement	Firm has submitted original, legalized sole agency agreement (letter of authorization) as product registration holder. The letter specifies that the manufacturer **ANFARM HELLAS S.A., located at 4 Achaias Str. & Trizinias, 14564, Kifisia Attiki Greece** (administration office as per COPP) appoints M/s Martin Dow Limited, Plot no. 37, Sector 19, Korangi Industrial Area, Karachi to register their products in Pakistan. The authorization letter is issued on 28-06-2021
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☐ Finished Pharmaceutical product import ☒ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 29009 dated: 25-10-2021
	Details of fee submitted	PKR 150,000/- deposit Slip # 5765002081
	The proposed proprietary name / brand name	DOWPENEM INJECTION 1g IV

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	**Each vial of Powder contains:** Meropenem trihydrate equivalent to Meropenem…….1000mg (with sodium carbonate) **Diluent:** **Each ampoule contains:** Sterilized water for injection…….20ml
	Pharmaceutical form of applied drug	Powder for Injection/ Infusion
	Pharmacotherapeutic Group of (API)	Carbapenem Antibiotic
	Reference to Finished product specifications	In House
	Proposed Pack size	1's
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	Merrem (Meropenem) Injection 1000mg IV **(USFDA** Approved).
	For generic drugs (me-too status)	Meroget Injection of Getz Pharma Pvt. Ltd. (Reg # 083175)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Name, address of drug substance manufacturer	ACS DOBFAR SpA 2: Addetta Site, Viale Addetta, 2a/12-3/5 20067 Tribiano, Milano - Italy
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API. Stability study conditions: Real time: 25^{o}C ± 2^{o}C and 60% RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Accelerated Batches: (330772 023 0, 330772 025 0, 330772 027 0) Real time Batches: (330772 8001 8, 330772 8001 0, 330772 8038 1)

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted Pharmaceutical Equivalence against the innovator product Meronem 500mg by AstraZeneca Batch no # 14047 C. **Firm submitted justification** "The manufacturer of Meropenem injection 500mg and 1g ha performed the pharmaceutical Equivalence on the same Powder of Merpenem trihydrate that is filled in the vials of both 500mg and 1g. Hence, Pharmaceutical equivalence of one strength (500mg) with the Innovator brand shall be considered as as pharmaceutical equivalence of the other strength (1g) That is why the manufacturer has covered the same pharmaceutical equivalence under the heading of both strengths. Moreover, the parameters covering in pharmaceutical equivalence of Meropenm injection 500mg are general and can be used for bulk powder testing. Hence confirming the point of equivalence for meropenem injection"
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Colourless glass Vial type III sealed with rubber stopper and aluminium cap with Plastic flip-off seal
	Stability study data of drug product, shelf life and storage conditions	Accelerated stability studies have been conducted at 40^{o}C ±2^{o}C / 75%±5% RH for 06 months. Real time stability studies conducted at 30 ^{o}C±2^{o}C / 65% ± 5% RH for one batch for 36 months (317121) and two batches 24 months (31523, 31813) Batches of stability studies : (317121, 31523, 31813)

Evaluation by PEC:

Sr.no.	Obseravtions/Shortcoming	Reply of the Firm
1.	Letter of Authorization by ANFARM HELLAS S.A does not mentioned that label vials will be imported.	Firm replied that the letter for Authorization provided in the submitted dossier states that Martin Dow Limited has expreseed its willingness to import the products Dowpenem Injection 500mg &1g in full compliance with the relevant local and international guidelines and cGMP standards which actually corresponds to the labelled vials.

<table>
<tr><td></td><td></td><td>We, hereby clarify that we are importing the product in the form of labelled vials and final packaging along with diluents will be done by Global Pharmaceuticals.</td></tr>
<tr><td>2.</td><td colspan="2">Product is available in USP pharmacopeia while applied formulation is claimed in house specifications. Clarify.
Firm claimed that in-house specifications are more stringent than USP specifications.
<table>
<tr><th>Controls</th><th>USP monograph of Meropenem Injection</th><th>Anafarm's Release specification</th></tr>
<tr><td>Assay</td><td>90%-120%</td><td>95%-105%</td></tr>
<tr><td>Content of sodium</td><td>80%-120%</td><td>…</td></tr>
<tr><td>Sodium carbonate content</td><td>….</td><td>14.7%-16.1%</td></tr>
<tr><td>Bacterial Endotoxin</td><td>NMT 0.12 EU/mg</td><td>NMT 0.12 EU/mg</td></tr>
<tr><td>Loss on Drying</td><td>9.0%-12.0%</td><td>9.0%-12.0%</td></tr>
<tr><td>pH</td><td>7.3-8.3</td><td>7.3-8.3</td></tr>
<tr><td>Sterility test</td><td>Sterile</td><td>Sterile</td></tr>
<tr><td>Particulate contaminants</td><td>Meets the requirements for SVP injections</td><td>Meets the requirements for SVP injections</td></tr>
<tr><td>Uniformity of dosage unit</td><td>Meets the requirement</td><td>Meets the requirement</td></tr>
</table>
Further firm stated that Anafarm do not test sodium content ,however the percentage of sodium carbonate is calculated to be equal to 15.4% i.e. equal to 6.7% (w/w) sodium, so the limits are between 6.7-7.0%.</td></tr>
<tr><td>3.</td><td>Certificate of analysis by both drug substance manufacturer and drug product manufacturer not submitted.</td><td>Firm submitted a declaration letter from ANFARM HELLAS S.A in which it is stated that we,Anafarm S.A. receives Meropenem sterile bulk and not the API Meropenem trihydrate.Thus no analysis on the API is performed and thus no method verification is performed.</td></tr>
<tr><td>4.</td><td>Manufacturing process does not show blending of Sodium carbonate with meropenem trihydrate neither by API manufacturer nor by ANFARM HELLAS S.A</td><td>Firm submitted the reply in which it is stated that the mixing of the excipient Sodium carbonate lyophilized sterile with the API meropenem trihydrate sterile is considered as the first step of the manufacturing process of the sterile bulk.</td></tr>
<tr><td>5.</td><td>Data of compatibility studies has been submitted with ANFARM HELLAS S.A diluent while in this case diluent will be locally purchased and no compatibility studies conducted. Justify.</td><td>Firm submit commitment that they perform compatibility studies of the product with the locally purchased diluent before marketing of the product.</td></tr>
<tr><td>6.</td><td>Stability studies provided by drug product manufacturer ANFARM HELLAS S.A while product will be imported as labelled vials and final packaging will be done by</td><td>Firm submit commitment that stability studies for the final product packaged by Global Pharmaceuticals will be performed for the first three consecutive batches of commercial scale.</td></tr>
</table>

	Global Pharmaceuticals. Justify.	
7.	Please specify final quality control release site.	Firm claimed that final quality release site will be Global Pharmaceuticals and the finished product specification are according to USP.
8.	Steps of packaging not mentioned performed in the global pharmaceuticals.	Submitted

Decision: Deferred for following:

- **Justification of not performing test of Sodium content test by M/s Anfarm as recommended by USP monograph.**
- **Analytical method verification studies of drug substance performed by M/s Anfarm.**
- **Details regarding Packaging, Quality control analysis and batch release activities to be conducted by M/s Global pharmaceuticals.**

224	Name, address of Applicant / Marketing Authorization Holder	M/s Dyson Research Laboratories PVT. LTD. 28-km, Ferozepur Road, Lahore.
	Name, address of Manufacturing site.	M/s Dyson Research Laboratories Private Limited 28-km, Ferozepur Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28328 dated 14-10-2021
	Details of fee submitted	PKR 30,000/-: Deposit slip # 913035788506
	The proposed proprietary name / brand name	Valatine Tablet 25mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Agomelatine……..25mg
	Pharmaceutical form of applied drug	Light yellow colored, oblong film coated tablet with cut line on one side and Dyson engraved on other side.
	Pharmacotherapeutic Group of (API)	Psychoanaleptic
	Reference to Finished product specifications	Innovator
	Proposed Pack size	5’s, 10’s, 14’s, 20’s, 28’s, 30’s, 50’s & 100’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Valdoxan 25 mg film-coated tablets by M/s Les Laboratoires Servier, France.
	For generic drugs (me-too status)	Valdoxan tablet 25mg of M/s. Servier (Reg. # 078160)

	GMP status of the Finished product manufacturer	Last inspection was conducted on 13-07-2020 for renewal of DML. Tablet (General, Hormonal) Liquid syrup (General), Oral dry powder suspension (General), and Capsule (general) section approved.
	Name and address of API manufacturer.	M/s. Changzhou Pharmaceutical Factory No.518 Laodong East Road, Changzhou, Jiangsu Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's,, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Agomelatine is not available in any official pharmacopoeia. The firm has submitted detail of nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (120301, 120302, 120401)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Valdoxan 25mg tablet by Servier Research and Pharmaceuticals by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Valdoxan 25mg Tablet by Servier Research and Pharmaceuticals in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8) & acetate buffer (pH 4.5). The values for f1 and f2 are in the acceptable range.

	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s. Changzhou Pharmaceutical Factory No.518 Laodong East Road, Changzhou, Jiangsu Province, China.		
API Lot No.	AG190601		
Description of Pack (Container closure system)	PVC-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	02-11-2019	02-11-2019	02-11-2019
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML # Su20160138 certificate issued Food and Drug Administration Jiangsu Province valid till 24-09-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of, invoice (invoice# CYI19233) dated 16-07-2019 cleared by DRAP Lahore office dated 01-08-2019 specifying import of Agomelatine Citric acid co- crystal 150g (Batch# AG190601).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks of Evaluator:		

S.No	Shortcomings Communicated	Reply
1.	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted	**Submitted**
2.	As per Commercial Invoice Agomelatine Citric acid co- crystal was imported, while submitted documents for drug substance and applied formulation mentions only Agomelaine. Clarify.	Firm replied that "we have imported only agomelatine, while agomelatine citric acid co-crystal mentioned on invoice is merely a human error/typing error. Valdoxan 25 mg film-coated tablets (innovator brand approve in MHRA have agomelatine as an active ingredient.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Frim shall ensure import of drug substance in form of "Agomelatine" base only as per innovator product, for commercial manufacturing of applied drug product**

225	Name, address of Applicant / Marketing Authorization Holder	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Name, address of Manufacturing site.	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24370 dated 29-08-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 810399800
	The proposed proprietary name / brand name	Flemicillin 250 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin capsule contains: Ampicillin …… 250 mg (as Ampicillin trihydrate)
	Pharmaceutical form of applied drug	Black cap and red body Capsule shell #2 filled with white to off white powder.
	Pharmacotherapeutic Group of (API)	Penicillin antibiotic
	Reference to Finished product specifications	BP Specifications

	Proposed Pack size	20 x 5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ampicillin 250mg Capsules by M/s Cresecent Pharma Limited, MHRA Approved.
	For generic drugs (me-too status)	Penbritin Capsules by M/s GSK, Reg. No. 000188
	GMP status of the Finished product manufacturer	New DML letter issued dated; 14-09-2021
	Name and address of API manufacturer.	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ampicillin is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Ampicillin Batches: 00003/001/2015, 00003/002/2015, 00003/003/2015)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Penbritin 250mg Capsule by GSK Pakistan Limited (Batch WV7H) by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand by in Acid media (pH 1.2) & Acetate buffer 4.5 pH and Phosphate Buffer (pH 6.8) and water . The values

		for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA			
Manufacturer of API	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.		
API Lot No.	00003/054/2021		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (10×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-001	T-001
Batch Size	2000 Capsules	2000 Capsules	2000 Capsules
Manufacturing Date	12-2021	12-2021	12-2021
Date of Initiation	27-12-2021	27-12-2021	27-12-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	
7.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 129/2020-DRAP (AD/1998630-530) issued by DRAP on the basis of evaluation conducted on 22-06-2022 and valid for 2 years.
8.	Documents for the procurement of API with approval from DRAP (in case of import).	• API had been locally procured from Pharmagen Ltd. • Copy of commercial invoice attached.
9.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
10.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
11.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks of Evaluator:		

S.No	Shortcomings Communicated	Reply
1.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is required.	**Submitted**
2.	Specificity and Precision(Repeatability) data of drug substance not submitted.	**Submitted**
3.	Justification is required for not performing the identification test, pH and determination of optical rotation during the stability study of drug substance	Stability studies by the API manufacturer of recent batches including all these parameters is submitted.
4.	Submitted Process validation protocol are general not product related. Clarification is required.	Revised process validation protocol is submitted.
5.	Time for Q not mentioned	Revised internal specifications are submitted.
6.	Q mentioned in Specifications is NLT 80% (Q+ 5%) while in analytical testing method is NLT 75% (Q+ 5%). Clarification is required.	Firm submitted the revised drug product specification data in which the dissolution acceptance criteria is NLT 80% (Q), time limit has not mentioned in the acceptance criteria.
7.	• Purchase documents for Ampicilline. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

226	Name, address of Applicant / Marketing Authorization Holder	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Name, address of Manufacturing site.	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24371 dated 29-08-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 227656312265
	The proposed proprietary name / brand name	Flemicillin 500 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each hard gelatin capsule contains: Ampicillin ……. 500 mg (as Ampicillin trihydrate)
	Pharmaceutical form of applied drug	Black cap and red body Capsule shell #2 filled with white to off white powder.
	Pharmacotherapeutic Group of (API)	Penicillin antibiotic
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	20 x 5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ampicillin 500mg Capsules by M/s Cresecent Pharma Limited, MHRA Approved.
	For generic drugs (me-too status)	Penbritin Capsules by M/s GSK, Reg. No. 000189
	GMP status of the Finished product manufacturer	New DML letter issued dated; 14-09-2021
	Name and address of API manufacturer.	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ampicillin is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months

		Ampicillin Batches: 00003/001/2015, 00003/002/2015, 00003/003/2015)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Penbritin 500mg Capsule by GSK Pakistan Limited (Batch RY9X) by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand by in Acid media (pH 1.2) & Acetate buffer 4.5 pH and Phosphate Buffer (pH 6.8) and water . The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA			
Manufacturer of API	M/s Pharmagen Limited Kot Nabi Bukshwala 34 Km- Ferozpur Road, Lahore, Pakistan.		
API Lot No.	00003/054/2021		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (10×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 Capsules	2000 Capsules	2000 Capsules
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	15-02-2022	15-02-2022	15-02-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	
12.	Approval of API/ DML/GMP certificate of API manufacturer issued by	Copy of GMP certificate No. 129/2020-DRAP (AD/1998630-530) issued by DRAP on the basis of

	concerned regulatory authority of country of origin.	evaluation conducted on 22-06-2022 and valid for 2 years.
13.	Documents for the procurement of API with approval from DRAP (in case of import).	• API had been locally procured from Pharmagen Ltd. • Copy of commercial invoice attached.
14.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
15.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
16.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Shortcomings Communicated	Reply
1.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance manufacturer is required.	Submitted
2.	Specificity and Precision(Repeatability) data of drug substance not submitted.	Submitted
3.	Justification is required for not performing the identification test, pH and determination of optical rotation during the stability study of drug substance	Stability studies by the API manufacturer of recent batches including all these parameters is submitted.
4.	Submitted Process validation protocol are general not product related. Clarification is required.	Revised process validation protocol is submitted.
5.	Time for Q not mentioned	Revised internal specifications are submitted.
6.	Q mentioned in Specifications is NLT 80% (Q+ 5%) while in analytical testing method is NLT 75% (Q+ 5%). Clarification is required.	Firm submitted the revised drug product specification data in which the dissolution acceptance criteria is NLT 80% (Q), time limit has not mentioned in the acceptance criteria.
7.	• Purchase documents for Ampicilline. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing • Record of Digital data logger for temperature and humidity	Submitted

	monitoring of stability chambers (real time and accelerated)	

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

227	Name and address of manufacturer / Applicant	M/s Ameer & Adnan Pharmaceutical Pvt Ltd. Plot No.47, Sundar Industrial Estate, Lahore
	Brand Name +Dosage Form + Strength	Zolid 100mg Capsule
	Composition	Each Capsule Contains: Itraconazole…100mg
	Diary No. Date of R& I & fee	Dy.No 7898 dated 22-02-2019 Rs.20,000/- Dated 22-02-2019
	Pharmacological Group	Antifungal
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specifications
	Pack size & Demanded Price	4' s, 10's ,As per SRO
	Approval status of product in Reference Regulatory Authorities	Itraconazole 100 mg capsules of(MHRA approved)
	Me-too status	Itrax Capsule by M/s Ferozsons Labs
	GMP status	Last GMP inspection conducted on 05-01-2018 and report concludes that firm had maintained conformance to cGMP.
	Remarks of the Evaluator	The reference product contains pellets of itraconazole while applied formulation contains powder. Justify your formulation in line with the reference product.
	Response of firm	Firm submitted the reference of MHRA approved product, which is also the yellowish beige color micro granules filled in hard capsule.
	Decision: Approved with USP specifications. • **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications of each strength as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Registration letter will be issued upon submission of requisite documents i.e., COA, GMP, and stability studies for the source of pellets.**	
228	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals B-64, KDA, Scheme No. 1, Main Karsaz Road, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Levixa XR 500mg Tablet
	Composition	Each extended release tablet contains: Levetiracetam……500mg
	Diary No. Date of R& I & fee	Dy.No. 40498 dated 06-12-2018 Rs.20,000/- Dated 05-12-2018
	Pharmacological Group	Antiepileptic
	Type of Form	Form-5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, 30's: As per SRO
	Approval status of product in Reference Regulatory Authorities	Levetiracetam of (MHRA Approved)

	Me-too status	Letrawin Tablets 500mg of M/s Opal Laboratory
	GMP status	Last GMP inspection conducted on 10-04-18, and the report concludes that the firm was considered to be operating at an acceptable level of compliance with good manufacturing practices
	Remarks of the Evaluator	Applied formulation is extended release so which polymer is used to make extended release tablet
	Response of the Firm	Firm submitted the revised formulation without any polymer used for extended release profile.
	Decision: Approved. Registration letter will be issued upon submission of master formulation declaring the excipients for extended release profile along with fee of Rs. 7500/- for correction/pre-approval change in master formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
229	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals B-64, KDA, Scheme No. 1, Main Karsaz Road, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Pequit XR 150mg Tablet
	Composition	Each extended release tablet contains: Quetiapine as fumarate eq to Questiapine…150mg
	Diary No. Date of R& I & fee	Dy.No. 40519 dated 06-12-2018 Rs.20,000/- Dated 05-12-2018
	Pharmacological Group	Antipsychotic Drugs
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, 20's, 30's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Seroquel XR of USFDA approved.
	Me-too status	Qusel XR 150mg Tablet of M/s Hilton Pharma
	GMP status	Last GMP inspection conducted on 10-04-18, and the report concludes that the firm was considered to be operating at an acceptable level of compliance with good manufacturing practices
	Remarks of the Evaluator	Master formulation do not contain any polymer for extended release tablet. Submit master formulation and manufacturing method in line with reference product.
	Response of the Firm	Firm submitted the revised formulation without any polymer used for extended release profile.
	Decision: Approved. Registration letter will be issued upon submission of master formulation declaring the excipients for extended release profile along with fee of Rs. 7500/- for correction/pre-approval change in master formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
230	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals B-64, KDA, Scheme No. 1, Main Karsaz Road, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Pequit XR 200mg Tablet
	Composition	Each extended release tablet contains: Quetiapine as fumarate eq to Questiapine…200mg
	Diary No. Date of R& I & fee	Dy.No. 40520 dated 06-12-2018 Rs.20,000/- Dated 05-12-2018

	Pharmacological Group	Antipsychotic Drugs
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, 20's, 30's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Seroquel XR of USFDA approved.
	Me-too status	Qusel XR 200mg Tablet of M/s Hilton Pharma
	GMP status	Last GMP inspection conducted on 10-04-18, and the report concludes that the firm was considered to be operating at an acceptable level of compliance with good manufacturing practices
	Remarks of the Evaluator	Master formulation do not contain any polymer for extended release tablet. Submit master formulation and manufacturing method in line with reference product.
	Response of the Firm	Firm submitted the revised formulation without any polymer used for extended release profile.
	Decision: Approved. Registration letter will be issued upon submission of master formulation declaring the excipients for extended release profile along with fee of Rs. 7500/- for correction/pre-approval change in master formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
23	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals B-64, KDA, Scheme No. 1, Main Karsaz Road, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Pequit XR 300mg Tablet
	Composition	Each extended release tablet contains: Quetiapine as fumarate eq to Questiapine…300mg
	Diary No. Date of R& I & fee	Dy.No. 40521 dated 06-12-2018 Rs.20,000/- Dated 05-12-2018
	Pharmacological Group	Antipsychotic Drugs
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, 20's, 30's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Seroquel XR of USFDA approved.
	Me-too status	Qusel XR 300mg Tablet of M/s Hilton Pharma
	GMP status	Last GMP inspection conducted on 10-04-18, and the report concludes that the firm was considered to be operating at an acceptable level of compliance with good manufacturing practices
	Remarks of the Evaluator	Master formulation do not contain any polymer for extended release tablet. Submit master formulation and manufacturing method in line with reference product.
	Response of the Firm	Firm submitted the revised formulation without any polymer used for extended release profile.
	Decision: Approved. Registration letter will be issued upon submission of master formulation declaring the excipients for extended release profile along with fee of Rs. 7500/- for correction/pre-approval change in master formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	

232	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals B-64, KDA, Scheme No. 1, Main Karsaz Road, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Pequit XR 400mg Tablet
	Composition	Each extended release tablet contains: Quetiapine as fumarate eq to Questiapine…400mg
	Diary No. Date of R& I & fee	Dy.No. 40522 dated 06-12-2018 Rs.20,000/- Dated 05-12-2018
	Pharmacological Group	Antipsychotic Drugs
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	10's, 20's, 30's ; As per SRO
	Approval status of product in Reference Regulatory Authorities	Seroquel XR of USFDA approved.
	Me-too status	Qusel XR 400mg Tablet of M/s Hilton Pharma
	GMP status	Last GMP inspection conducted on 10-04-18, and the report concludes that the firm was considered to be operating at an acceptable level of compliance with good manufacturing practices
	Remarks of the Evaluator	Master formulation do not contain any polymer for extended release tablet. Submit master formulation and manufacturing method in line with reference product.
	Response of the Firm	Firm submitted the revised formulation without any polymer used for extended release profile.
	Decision: Approved. Registration letter will be issued upon submission of master formulation declaring the excipients for extended release profile along with fee of Rs. 7500/- for correction/pre-approval change in master formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
233	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals B-64, KDA, Scheme No. 1, Main Karsaz Road, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Tramax 100mg SR Capsule
	Composition	Each Sustained Release Capsule Contains: Tramadol Hcl…100mg
	Diary No. Date of R& I & fee	Dy.No. 41495 dated 07-12-2018 Rs.20,000/- Dated 07-12-2018
	Pharmacological Group	Narcotic analgesic
	Type of Form	Form 5
	Finished product Specification	BP
	Pack size & Demanded Price	10's, 20's, 30's: As per SRO
	Approval status of product in Reference Regulatory Authorities	CONZIP 100mg Capsules of (USFDA approved)
	Me-too status	Zultra SR 100mg of M/s. Wilshire Laboratories
	GMP status	Last GMP inspection conducted on 10-04-18, and the report concludes that the firm was considered to be operating at an acceptable level of compliance with good manufacturing practices
	Remarks of the Evaluator	Submit Master formula, manufacturing method, analytical method

		CIP-TRAMADOL ER (tramadol hydrochloride) extended-release) capsules are a new formulation of tramadol HCl for analgesia. The drug product consists of extended release film coated white beads and an immediate release tablet encapsulated in white opaque, size 1, 0 and 00, hard gelatin capsules Dosage | Immediate release | Extended release 100 mg | 25 mg | 75 mg
	Decision: Deferred for review of formulation against the innovator product.	
234	Name and address of manufacturer / Applicant	M/s High-Q Pharmaceuticals B-64, KDA, Scheme No. 1, Main Karsaz Road, Karachi, Pakistan
	Brand Name +Dosage Form + Strength	Flunar 5mg Capsule
	Composition	Each Capsule Contains: Flunarizine Hcl Eq. to Flunarizine Base…5mg
	Diary No. Date of R& I & fee	Dy.No. 41493 dated 07-12-2018 Rs.20,000/- Dated 07-12-2018
	Pharmacological Group	Narcotic analgesic
	Type of Form	Form 5
	Finished product Specification	Manufacturer specification
	Pack size & Demanded Price	3's, 6's, 10's, 12: As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved by Health Canada
	Me-too status	Migram 5mg Capsule of M/S Wilshire Laboratories
	GMP status	Last GMP inspection conducted on 10-04-18, and the report concludes that the firm was considered to be operating at an acceptable level of compliance with good manufacturing practices
	Remarks of the Evaluator	Firm submitted the evidence of approval of applied formulation in Health Canada along with revised manufacturing method, formulation.
	Decision: Approved with Innovator's specifications. • **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications and correction of pharmacological group as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
235	Name and address of manufacturer / Applicant	M/s Sante Pvt Ltd. 245/2-Z, Block 6, PECHS, Karachi 75400"
	Brand Name +Dosage Form + Strength	Xenase 2.5mg Tablet
	Composition	Each tablet contains: Olopatadine as Hydrochloride eq to Olopatadine……..2.5mg
	Diary No. Date of R& I & fee	Dy.No (Duplicate Dossier) dated 27-02-2014 Rs.15,000/- (Copy)
	Pharmacological Group	Decongestants And Antiallergics
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	3 x 10's

	Approval status of product in Reference Regulator Authorities	PMDA japan approved
	Me-too status	
	GMP status	02-07-2019 Conclusion: Based on the current practices and keeping in view the attitude of the management towards better compliance of GMP their overall compliance level for the said dosage form is rated as Good
	Remarks of the Evaluator.	

STABILITY STUDY DATA

Drug	Xenase 2.5mg Tablet		
Name of Manufacturer	M/s Sante Pvt Ltd. 245/2-Z, Block 6, PECHS, Karachi 75400"		
Manufacturer of API	M/S Crystal Pharma, S.A.U., a subsidiary of AMRI Parque technologico de Boecillo, Parcela 105. 47151 Boecillo, Valladolid spain		
API Lot No.	V0673/0 16010 V0673/0 19040		
Description of Pack (Container closure system)	PVDC Alu blister		
Stability Storage Condition	Real time : 30°C ± 2° C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: Batch # 01T: 24 months Batch # 02T and 03T :09 months Accelerated: 6 months		
Frequency	Accelerated:0,3,6 (month) Real Time: Batch # 01T: 0,3,6,9,12,18,24 (month) Batch # 02T and 03T : 0,3,6,9 (month)		
Batch No.	01T	02T	03T
Batch Size	8000 Tablets	8000 Tablets	8000 Tablets
Manufacturing Date	11-2017	12-2019	12-2019
Date of Initiation	20-12-2017	30-01-2020	30-01-2020
No. of Batches	03		
Date of Submission	11-02-20221(4705)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm (if available)	Firm has referred to onsite inspection report of their product "Zithrosan 1% eye drops" which was presented in 289th meeting of Registration Board wherein the Board decided to approve registration of this product

		Date of inspection: 14th March, 2019. According to inspection report, following points were confirmed. • The firm has 21CFR compliant HPLC software. • The firm has audit trail reports available. Adequate monitoring and control are available for stability chamber
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Copy of COA of Olopatadine HCl (Batch# V0673/0 16010 and V0673/0 19040) from M/S Crystal Pharma, S.A.U., a subsidiary of AMRI Parque technologico de Boecillo, Parcela 105. 47151 Boecillo, Valladolid spain is submitted. Copy of COA (Batch# V0673/0 16010 and V0673/0 19040) from M/S Sante (Pvt) Ltd is submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	
4.	Stability study data of API from API manufacturer	The firm has submitted copy of **accelerated, 06 Months** (40°C ± 2°C & 75±5%RH) & **long term, 60 Months** (25°C ± 2°C & 60±5%RH) stability study reports of 03 batches
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP Certificate No # ES/057/20 for M/s Crystal Pharma, S.A.U., Planta API no esteroides site address Parque technologico de Boecillo, Parcela 105. 47151 Boecillo, Valladolid Spain issued by Agencia Espanola de Medicamentos y productos Sanitarious, is submitted. Based on inspection conducted on 13-03-2020 valid for 3 years
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of form3, form 7 and Commercial Invoice No: 20190001 Dated: 10-01-2019 from M/S Crystal Pharma, S.A.U., is submitted attested by AD(Karachi) dated ; 15-01-2019 for Oloptadine HCl quantity 2KG Batch # V0673/0 16010 Copy of Commercial Invoice No: 20190001 Dated: 10-01-2019 from M/S Crystal Pharma, S.A.U., a subsidiary of AMRI is submitted attested by AD(Karachi) dated ; 15-01-2019 for Oloptadine HCl quantity 2KG Batch # V0673/0 19040
7.	Protocols followed for conduction of stability study	Yes
8.	Method used for analysis of FPP	In house specifications but available in japnease pharmacopiea
9.	Drug-excipients compatibility studies (where applicable)	Same excipients used as used by innovator. Excipients are different

<table>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted copy of Trial batch manufacturing record.
Details are as under:<table><tr><td colspan="3">Xenase 2.5mg Tablet</td></tr><tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr><tr><td>01T</td><td>8000 Tablets</td><td>14-11-2017</td></tr><tr><td>02T</td><td>8000 Tablets</td><td>16-12-2019</td></tr><tr><td>03T</td><td>8000 Tablets</td><td>16-12-2019</td></tr></table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td></td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td></td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td></td></tr>
<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td></td></tr>
<tr><td colspan="3">REMARKS OF EVALUATOR</td></tr>
<tr><td colspan="3">• Differential fee of RS: 35000/- for new molecule.
• Reference of previous approval of applications with stability study data of the firm (if available)
• Method used for analysis of API from both API Manufacturer and Finished Product manufacturer.
• Stability study data of API from API manufacturer.
• Documents for the procurement of Olopatadine HCl batch no # V0673/0 16010 with approval from DRAP
• Method used for analysis of FPP inhouse while product is available in Japanese pharmacopeia. Clarification is required for inhouse specifications.
• Drug-excipients compatibility studies
• Record of comparative dissolution data.
• Content uniformity is not included in initial certificate of analysis. Clarification is required.
• Raw data sheets for calculations of assay, dissolution and content uniformity for all time point of finished products.
• Compliance Record of HPLC software 21CFR & audit trail reports on product testing.
• Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).</td></tr>
<tr><td colspan="3">Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.</td></tr>
<tr><td>236</td><td>Name and address of manufacturer / Applicant</td><td>M/s Sante Pvt Ltd. 245/2-Z, Block 6, PECHS, Karachi 75400"</td></tr>
</table>

	Brand Name +Dosage Form + Strength	Xenase 5mg Tablet
	Composition	Each tablet contains: Olopatadine Hydrochloride ……..5mg
	Diary No. Date of R& I & fee	Dy.No 378 dated 23-11-2011 Rs.15,000/- 21-11-2011
	Pharmacological Group	Decongestants And Antiallergics
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	3 x 10's
	Approval status of product in Reference Regulator Authorities	PMDA japan approved
	Me-too status	
	GMP status	02-07-2019 Conclusion: Based on the current practices and keeping in view the attitude of the management towards better compliance of GMP their overall compliance level for the said dosage form is rated as Good
	Remarks of the Evaluator.	

STABILITY STUDY DATA

Drug	Xenase 5mg Tablet		
Name of Manufacturer	M/s Sante Pvt Ltd. 245/2-Z, Block 6, PECHS, Karachi 75400"		
Manufacturer of API	M/S Crystal Pharma, S.A.U., a subsidiary of AMRI Parque technologico de Boecillo, Parcela 105. 47151 Boecillo, Valladolid spain		
API Lot No.	V0673/0 16010 V0673/0 19040		
Description of Pack (Container closure system)	PVDC Alu blister		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: Batch # 01T: 24 months Batch # 02T and 03T :09 months Accelerated: 6 months		
Frequency	Accelerated:0,3,6 (month) Real Time: Batch # 01T: 0,3,6,9,12,18,24 (month) Batch # 02T and 03T : 0,3,6,9 (month)		
Batch No.	01T	02T	03T
Batch Size	6667 Tablets	6667 Tablets	6667 Tablets
Manufacturing Date	11-2017	12-2019	12-2019

Date of Initiation	20-12-2017	30-01-2020	30-01-2020
No. of Batches	03		
Date of Submission	11-02-20221(4706)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm (if available)	Firm has referred to onsite inspection report of their product "Zithrosan 1% eye drops" which was presented in 289th meeting of Registration Board wherein the Board decided to approve registration of this product Date of inspection: 14th March, 2019. According to inspection report, following points were confirmed. • The firm has 21CFR compliant HPLC software. • The firm has audit trail reports available. Adequate monitoring and control are available for stability chamber
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Copy of COA of Olopatadine HCl (Batch# V0673/0 16010 and V0673/0 19040) from M/S Crystal Pharma, S.A.U., a subsidiary of AMRI Parque technologico de Boecillo, Parcela 105. 47151 Boecillo, Valladolid spain is submitted. Copy of COA (Batch# V0673/0 16010 and V0673/0 19040) from M/S Sante (Pvt) Ltd is submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	
4.	Stability study data of API from API manufacturer	The firm has submitted copy of **accelerated, 06 Months** (40°C ± 2°C & 75±5%RH) & **long term, 60 Months** (25°C ± 2°C & 60±5%RH) stability study reports of 03 batches
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP Certificate No # ES/057/20 for M/s Crystal Pharma, S.A.U., Planta API no esteroides site address Parque technologico de Boecillo, Parcela 105. 47151 Boecillo, Valladolid Spain issued by Agencia Espanola de Medicamentos y productos Sanitarious, is submitted. Based on inspection conducted on 13-03-2020 valid for 3 years
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of form3, form 7 and Commercial Invoice No: 20190001 Dated: 10-01-2019 from M/S Crystal Pharma, S.A.U., is submitted attested by AD(Karachi) dated ; 15-01-2019 for Oloptadine HCl quantity 2KG Batch # V0673/0 16010

<table>
<tr><td></td><td></td><td>Copy of Commercial Invoice No: 20190001 Dated: 10-01-2019 from M/S Crystal Pharma, S.A.U., a subsidiary of AMRI is submitted attested by AD(Karachi) dated ; 15-01-2019 for Oloptadine HCl quantity 2KG Batch # V0673/0 19040</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>In house specifications but available in japnease pharmacopiea</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Same excipients used as used by innovator. Excipients are different</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted copy of Trial batch manufacturing record.
Details are as under:
<table>
<tr><td colspan="3">Xenase 5mg Tablet</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr>
<tr><td>01T</td><td>6667 Tablets</td><td>14-11-2017</td></tr>
<tr><td>02T</td><td>6667 Tablets</td><td>16-12-2019</td></tr>
<tr><td>03T</td><td>6667 Tablets</td><td>16-12-2019</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td></td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td></td></tr>
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<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td></td></tr>
<tr><td colspan="3">REMARKS OF EVALUATOR</td></tr>
<tr><td colspan="3">

Differential fee of RS: 35000/- for new molecule.
Reference of previous approval of applications with stability study data of the firm (if available)
Method used for analysis of API from both API Manufacturer and Finished Product manufacturer.
Stability study data of API from API manufacturer.
Documents for the procurement of Olopatadine HCl batch no # V0673/0 16010 with approval from DRAP
Method used for analysis of FPP inhouse while product is available in Japanese pharmacopeia. Clarification is required for inhouse specifications.
Drug-excipients compatibility studies
Record of comparative dissolution data.
Content uniformity is not included in initial certificate of analysis. Clarification is required.

</td></tr>
</table>

• Raw data sheets for calculations of assay, dissolution and content uniformity for all time point of finished products. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).		
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		
237.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Zovir 250mg/10ml Injection
	Composition	Each 10ml Vial Contains: Acyclovir…250mg
	Diary No. Date of R& I & fee	Dy.No. 14299 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antiviral
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	1's (10ml); As per SRO
	Approval status of product in Reference Regulatory Authorities	Zovirax I.V. 250 mg of MHRA approved
	Me-too status (with strength and dosage form)	Aclovir 250mg Powder for infusion of Genix pharma Reg# 073690
	GMP status	cGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision of 320th meeting of Reg. Board	Deferred for confirmation of required manufacturing facility / section (lyophilized vial General)
	Response of the Firm	Firm replied that they had applied for liquid injection and in RRA both liquid and powder injection are available.
	Decision: Deferred for submission of detail of applied formulation in line with product available in approved reference regulatory agencies and confirmation of generic status of liquid injection along with registration number, brand name and name of firm.	
238.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Zovir 500mg/20ml Injection
	Composition	Each 20ml vial Contains: Acyclovir…500mg
	Diary No. Date of R& I & fee	Dy.No. 14298 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antiviral
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	1's (20ml) ; As per SRO

	Approval status of product in Reference Regulatory Authorities	Zovirax I.V. 500 mg of MHRA approved
	Me-too status (with strength and dosage form)	Aclovir 500mg Powder for infusion of Genix pharma Reg# 073691
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	• Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision of 320th meeting of Reg. Board	Deferred for confirmation of required manufacturing facility / section (lyophilized vial General)
	Response of the Firm	Firm replied that they had applied for liquid injection and in RRA both liquid and powder injection are available.
	Decision: Deferred for submission of detail of applied formulation in line with product available in approved reference regulatory agencies and confirmation of generic status of liquid injection along with registration number, brand name and name of firm.	
239.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Irofit Tablet 20mg/2.5mg
	Composition	Each Film Coated Tablet Contains: Iron protein succinylate 400mg eq to elemental iron …20mg Folic Acid……..2.5mg
	Diary No. Date of R& I & fee	Dy.No. 17427 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Antianemic preparations
	Type of Form	Form-5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's, 14's, 20's , :As per SRO
	Approval status of product in Reference Regulatory Authorities	Not found
	Me-too status (with strength and dosage form)	Eisen Tablets of Genome Pharmaceuticals
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	

	Decision of 320th meeting	The Board deferred the case for submission of detail of specifications and complete analytical method for the applied product.
	Response of the Firm	Firm submitted the detailed specification and complete analytical procedure of applied formulation.
	Decision: Approved.	
240.	Name and address of manufacturer / Applicant	M/s Rotex Pharma Pvt Ltd. Plot No. 206 & 207. Industrial Triangle, Kahuta Road, Islamabad
	Brand Name +Dosage Form + Strength	Methane 1% w/v Lotion
	Composition	Each ml Contains: Permethrin…10mg
	Diary No. Date of R& I & fee	Dy.No. 14296 dated 07-03-2019 Rs.20,000/- Dated 06-03-2019
	Pharmacological Group	Pyrethroid insecticide
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	30ml: As per SRO
	Approval status of product in Reference Regulatory Authorities	Nix lotion of USFDA approved
	Me-too status (with strength and dosage form)	Not found
	GMP status	CGMP certificate on the basis of Evaluation conducted on 11-08-2022
	Previous remarks of the Evaluator.	• Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Previous decision(s)	**Deferred for following reasons:** Deferred for consideration on its turn. **(M-296)**
	Remarks of the Evaluator.	
	Decision of 320th meeting	Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Remarks of the Firm	Firm submitted the evidence of Me-too product Z-X Lotion of M/s. Martin Dow Limited Reg. no. 067937
	Decision: Approved.	
241.	Name and address of manufacturer / Applicant	M/S Fredmann Pharmaceuticals Plot # 82-83 B, Old Industrial Area Mirpur, Azad Kashmir
	Brand Name +Dosage Form + Strength	Bresco 5mg Chewable Tablet
	Composition	Each chewable tablet contains: Montelukast as (sodium)……5mg
	Diary No. Date of R& I & fee	Dy.No.2471; 23-02-2017; Rs.20,000/- (23-02-2017)
	Pharmacological Group	Leukotriene receptor antagonist
	Type of Form	Form 5
	Finished product Specifications	USP
	Pack size & Demanded Price	2 x 7's ; As per SRO

	Approval status of product in Reference Regulatory Authorities	Singulair 5mg chewable of (USFDA approved)
	Me-too status (with strength and dosage form)	Lontuka 5mg Chewable Tablet M/s Linz Pharmaceuticals.
	GMP status	Last GMP inspection conducted on 24-11-2017 ,and the report concludes that firm was at fair level of GMP
	Remarks of the Evaluator	changed the formulation from film coated to chewable tablet.
	Decision of 281st meeting of Registration Board	Deferred for submission of fee for revision of formulation
	Response of the Firm	Firm submitted the fee of Rs.30,000/- vide slip no. 05725608 dated 24-10-2022
	Decision: Approved	

Deferred Cases of Previous Meetings:

242.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10562 dated: 27-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 5820244638
	The proposed proprietary name / brand name	Newfate 1 g / 10 mL Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 10 mL contains: Sucralfate ……..1 g
	Pharmaceutical form of applied drug	Liquid suspension filled in amber glass bo sealed with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	Cytoprotective agent (Drugs for Peptic Ulcer and Gastro-Oesophageal Reflux Disease - GORD) ATC Code: A02BX02
	Reference to Finished product specifications	Innovator's Specs.

	Proposed Pack size	60 mL , 120 mL, 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Carafate 1 g / 10 mL Suspension by M/s Allergan Pharmaceuticals Approved by USFDA
	For generic drugs (me-too status)	Ulsanic 500 mg/5 ml Suspension M/s Highnoon Laboratories, Reg. No. 032072
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	M/S Northeast Pharmaceutical group Co. Ltd. No. 29 Shenxiliu dong road, Economic Technological Development District SHENGYANG. P.R. CHINA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system an stability studies of drug substance.
	Stability studies	Stability study conditions: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DY0011500185, DY0011500186 & DY0011500187)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of their developed formulation New-fate Suspension with comparator product Ulsanic Suspension of Highnoon Laboratories.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/S Northeast Pharmaceutical group Co. Ltd. No. 29 Shenxiliu dong road, Economic Technological Development District SHENGYANG. P.R. CHINA.		
API Lot No.	DY0011900195		
Description of Pack (Container closure system)	Oral Suspension filled in amber glass bottle sealed with pilfer pr aluminium caps.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	15-09-2021	15-09-2021	15-09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate No # LN20190041 for M/S Northeast Pharmaceutical group Co. Ltd. No. 29 Shenxiliu dong road, Economic Technological Development District SHENGYANG. P.R. CHINA issued by China Food and Drug administration. It is valid till 15-07-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs including Sucralfate USP for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3,form 7 & invoice (invoice# EXP/71221(20-21) dated: 06-09-2021 specifying import 400g Sucralfate

		USP (Batch# DY0011900195) however not attested by DRAP. Copy of DHL provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	UV method was used.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	3.2.S.4.2	• Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance is required. • Specification claimed USP while Submitted analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug product manufacturer are according to B.P. Clarify which monograph have been used among USP or B.P Pharmacopeia monograph for drug substance.	• Analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by Drug substance are attached. • It is clarified that USP monograph has been used for routine testing of drug substance.
2.	3.2.S.4.3	If USP Pharmacopeia followed than Analytical verification of sucrose octasulfate by drug product manufacturer should be submitted. If B.P pharmacopeia followed than Analytical verification of sucrose octasulfate and aluminium by drug product manufacturer should be submitted	Analytical verification of Sucrose Octasulfate by drug product manufacture is attached.
3.	3.2.S.5	Reference standard according to USP and B.P is Potassium sucrose octasulfate while submitted COA of working standard of Sucralfate USP. Clarification is required.	COA of Potassium Sucrose Octasulfate i attached.
4.	3.2.P.2.2.1	• Pharmaceutical equivalence of the applied drug shall be	• Pharmaceutical Equivalence had bee performed with market brand leader

		established with the innovator product and results of all the quality tests of the developed formulation and the innovator product shall be submitted and discussed. • B.P specification mentioned in Pharmaceutical equivalence. Clarification is required**.**	as Innovator product is not available in the country. I had be done according to ***WHO_TRS_902_ANNEX11*** report which is attached • Actual Specification is Innovator, BP mentioned mistakenly.
5.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia) shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia) is provided.
6.	3.2.P.5.2	• In assay Content of Aluminium and sucrose octasulfate separate are not detected. Clarification should be submitted in this regard. • In Monograph of Drug substance assay is conducted by HPLC while drug product assay was conducted by U.V. Clarification is required from where you have adopted U.V method for assay.	• Revised method is attached • Due to non-Pharmacopeial product, in-house method had been developed on UV. Method validation is provided in 3.2. P.5.3.
7.	3.2.P.5.3	Analytical method validation of sucrose octasulfate not conducted. Clarification is required	Analytical method validation of sucrose octasulfate is attached.
8.	3.2.P.8	Commercial invoice with approval from DRAP.	Copy of DHL provided.

Decision of 320th meeting of Registration Board:
Registration Board deferred the case for following:

- Justification of assay of drug product conducted by UV method while drug substance assay is conducted by HPLC as per USP monograph.
- Performance of assay of drug product as per Revised method.

Reply of the Firm:
Firm submitted the revised analytical procedure of drug product along with verification report in which assay has been performed on HPLC.
Batch analysis reports of drug product in accordance with revised analytical procedure has also been submitted by the firm.

Decision: Approved. Firm shall submit analytical performance of long term stability studies of next time point based upon the revised HPLC method, before issuance of registration letter.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

243.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore

	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10883 dated: 29-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 52967004840
	The proposed proprietary name / brand name	Newfer Syrup 50 mg/5mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Iron (III) Hydroxide Polymaltose Complex Eq. to Elemental Iron -----50 mg Folic Acid …….. 0.35mg
	Pharmaceutical form of applied drug	Liquid Syrup filled in amber glass bottle sealed with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	Iron Supplement
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	60 mL , 120 mL, 400 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	……
	For generic drugs (me-too status)	Ferosoft-FA Syrup by M/S Hilton Pharma , Reg. No. 045110
	GMP status of the Finished product manufacturer	New additional section of Oral Liquid general section approved on : 28-10-2021 letter issued on: 12-11-2021 and inspection conducted on: 28-07-2021
	Name and address of API manufacturer.	**Iron Polymaltose Complex:** Chemiworld Pvt. Ltd. Plot No. 97, J- Industrial Estate Jamrud Peshawar Pakistan. **Folic Acid:** Hebei Jiheng Pharmaceutical Co., Ltd, 1 Weiwu Street, Hengshui City, Hebei Province, P.R. China 053000
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures

		and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of both drug substances (i.e. Iron Polymaltose Complex and Folic acid).
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **Batches of Iron Polymaltose Complex :** (BPS-0405118, BPS-0405119, BPS-0405120) **Folic acid :** (021702001, 021702002, 021702003)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of the developed formulation Newfer Syrup 50 mg/5mL with comparator product ***Ferosoft-FA Syrup*** by ***Hilton Pharma.***
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	**Iron Polymaltose Complex:** Chemiworld Pvt. Ltd. Plot No. 97, J-Industrial Estate Jamrud Peshawar Pakistan. **Folic Acid:** Hebei Jiheng Pharmaceutical Co., Ltd, 1 Weiwu Street, Hengshui City, Hebei Province, P.R. China 053000
API Lot No.	**Iron Polymaltose Complex:** K20-IPC-420

		Folic Acid: 022004010		
Description of Pack (Container closure system)		Oral Suspension filled in Amber glass bottle sealed with pilfer pr aluminium caps.		
Stability Storage Condition		Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		T-01	T-02	T-03
Batch Size		45 Bottles	45 Bottles	45 Bottles
Manufacturing Date		09-2021	09-2021	09-2021
Date of Initiation		21-09-2021	21-09-2021	21-09-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**IPC:** The firm has submitted copy of GMP Certificate # F.3-20/2017-DRAP-90 on the basis of inspection conducted on 29-11-2016 for M/S Chemiworld Pvt. Ltd. issued by DRAP. The firm has submitted application for issuance of new GMP certificate. **Folic Acid :** Copy of GMP certificate No. HE20170030 issued by China Food and Drug Administration valid till 26/05/2022.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs Folic acid for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3, form 7 & invoice (invoice# HJG/EXP/0124) dated: 07-09-2021 specifying import 100g Folic acid (Batch# 022004010) however not attested by DRAP. Copy of DHL provided.		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	UV method used		
6.	Record of Digital data logger for temperature and humidity monitoring of	Submitted		

	stability chambers (real time and accelerated)		

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	1.6.5	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin for Iron Polymaltose Complex.	Firm submitted copy of request to federal inspector of Drugs, Peshawar for issuance of GMP certificate.
2.	3.2.S.4.1	Drug substance manufacturer and Drug product manufacturer did not mentioned Which specifications followed for Iron Polymaltose Complex. Please clarify.	It is clarified that Iron Polymaltose Complex is not present in any Pharmacopeia and manufacturer has developed an in-house method. Drug Product manufacturer also followed the Drug Substance manufacturer's method for testing
3.	3.2.S.4.2	Analytical procedures used for routine testing of the both Drug substance /Active Pharmaceutical Ingredient (Iron Polymaltose Complex &Folic Acid) by Drug substance is required	Analytical Procedures used for routine testing of the drug substance / Active Pharmaceutical Ingredient by Drug Substance is attached.
4.	3.2.S.4.3	• In analytical method verification of Iron polymaltose complex Sodium nitrile mentioned . clarification is required. • Submit analytical method verification according to analytical testing method of Iron polymaltose complex • Analytical verification is done by titration while analytical testing method of folic acid is by HPLC. Clarification is required.	• It is clarified that sodium nitrile is a clerical mistake. • Analytical verification according to analytical testing method of Iron Polymaltose Complex. Is attached. • Revised Verification by HPLC is attached.
5.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia) is provided.
6.	3.2.P.5.1	Specifications claimed are B.P. provide evidence.	Revised specification with in-house specs is attached.
7.	3.2.P.5.2	• Clarification is required that how drug product analytical testing method developed. • In Drug substance Iron polymaltose complex assay of iron contents and polymaltose contents are separately conducted. While in your analytical testing method assay	• The Product is not available in any Pharmacopeia we have test the product with in-house testing method. The standard & sample solutions scan on UV Spectrophotometer pick absorbance on maximum nm. After scanning this solution we have

		of Iron polymaltose is conducted. Justify how quantity of elemental Iron is equivalent to 50mg deducted.	scan sample solution placebo for the conformation of method absorbance and wavelength. • In Drug substance iron Polymaltose complex assay of iron contents and Polymaltose contents are separately conducted but in syrup have many other excipients which disturbed in testing so that we use factor calculation for the equivalence of Iron Polymaltose complex to iron. 1mg of Iron is equivalent to 1.1243mg of Iron Polymaltose complex
8.	3.2.P.8	• Purchase documents for iron hydroxide polymaltose • Commercial invoice with approval from DRAP.	• Iron Polymaltose Complex was purchased locally. • Copy of DHL is provided.

Decision of M-320:
The Board deferred the case for scientific justification of performance of assay testing by using UV-spectrophotometer instead of using potentiometric titration or atomic absorption spectrophotometer.

Firm submitted the revised assay procedure in which atomic absorption spectrophotometer has been used for quantification of iron content.

Decision: Approved. Firm shall submit analytical performance of long term stability studies of next time point based upon the revised Atomic absorption spectrophotometric method before issuance of registration letter.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

244.	Name, address of Applicant / Marketing Authorization Holder	M/s News Pharma Lahore Plot 42, Sundar Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s News Pharma Plot 42, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10882 dated: 29-04-2022
	Details of fee submitted	PKR 30,000/-: Deposit slip # 4481928067

	The proposed proprietary name / brand name	New-Deslor Syrup 2.5 mg / 5 mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Desloratadine .... 0.5 mg
	Pharmaceutical form of applied drug	Oral solution filled in amber glass bottle sealed with pilfer proof aluminium caps.
	Pharmacotherapeutic Group of (API)	Anti-histamine
	Reference to Finished product specifications	Inhouse
	Proposed Pack size	60 mL / 120 mL
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	New-Clarityn by Merck Sharp and Dhome Ltd. Approved by AEPMS (Spanish Agency for Medicine and Health Products.)
	For generic drugs (me-too status)	Desora 0.5 mg/mL M/s Continental Pharma, Reg. No. 055192
	GMP status of the Finished product manufacturer	New Section granted on 12/11/2021 Oral Liquid General Section approved.
	Name and address of API manufacturer.	M/s Morepen Laboratories Ltd. Address: Village-Masulkhana, Parwanoo, District, Solan, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DH-1501, DH-1502, DH-1503)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of their developed formulation New-Deslor Syrup with comparator product Clarinex Syrup of M/s Merck & Co.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s M/s Morepen Laboratories Ltd. Village-Masulkhana, Parwanoo, Distt. Solan India.		
API Lot No.	DH-0106		
Description of Pack (Container closure system)	Oral solution filled in amber glass bottle sealed with pilfer proof alumini caps.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	45 Bottles	45 Bottles	45 Bottles
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	24-09-2021	24-09-2021	24-09-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New section

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate for M/s Morepen Laboratories Ltd, India issued by State Drugs Controller, Controlling cum Licensing Authority, Baddi, District Solan. It is valid till 30-04-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.14901/2021/DRAP-AD-CD(I&E) dated 04/10/2021 is submitted wherein the permission to import different APIs Folic acid for the purpose of test/analysis and stability studies is granted. Firm has submitted copy of Form 3, form 7 & invoice (invoice# MME202100508) dated: 14-09-2021 specifying import 0.5Kg Desloratadine (Batch# DH-0106).
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Manual audit trail report submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.No	Section	Shortcomings Communicated	Reply
1.	2.3.R.1.1	Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2. P.3.5. Clarification is required.	Short method was mentioned in BMR. Now Revise BMR (s) are submitted as with detailed method as mentioned in 3.2.P.2.3 and 3.2.P.3.5.
2.	2.3.R.1.2	Manufacturing method mentioned in BMR's is not same as mentioned in section 3.2.P.2.3 and 3.2. P.3.5. Clarification is required	Short method was mentioned in BMR. Now Revise BMR (s) are submitted as with detailed method as mentioned in 3.2.P.2.3 and 3.2.P.3.5
3.	3.2.S.4.3	Testing method of desloratadine is by HPLC while verification is done by U.V method. Clarification is required.	Revised verification by HPLC method is submitted
4.	3.2.S.7	Accelerated stability studies of drug substance not submitted.	Accelerated stability studies of drug substance submitted.
5.	3.2.P.2.5	Preservative effectiveness studies to be performed as per recommendations of pharmacopoeia shall be provided	Preservative effectiveness studies performed as per recommendations of pharmacopoeia are provided

6.	3.2.P.5.1	Specifications claimed for drug product are B.P. provide evidence.	Revised Specification are attached (Inhouse)
7.	3.2.P.5.2	Justification is required for performing assay testing by UV method	The Product is not available in any pharmacopeia so we have test from inhouse testing method. The validation of testing method is attached in dossier
8.	3.2.P.8	Commercial invoice with approval from DRAP.	Copy of DHL provided.

Decision of M-320:
Registration Board deferred the case for Justification of assay of drug product conducted by UV method while drug substance assay is conducted by HPLC as per BP monograph.

Reply: Firm submitted the revised assay procedure in which HPLC method has adopted for quantification of active along with performance report of drug product an revised verification report.

Decision: Approved with innovator's specifications. Firm shall submit analytical performance of long term stability studies of next time point based upon the revised HPLC method along with submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021 , before issuance of registration letter

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

245.	Name, address of Applicant / Importer	M/s INAYA TRADERS Flat no. 1, 1st floor, Plot no. A-152 Block-8, KAECHS, Karachi.
	Details of Drug Sale License of importer	**License No:** 0238 **Address:** Flat no. 1, 1st floor, Plot no. A-152 Block-8, KAECHS, Karachi. **Validity:** 21-June-2024
	Name and address of marketing authorization holder (abroad)	Shouguang Fukang Pharmaceuticals Co., Ltd Address: No.666 Donghuan Road, Shounguang City Shandong Province, P.R. China.
	Name, address of manufacturer(s)	Shouguang Fukang Pharmaceuticals Co., Ltd Address: No.999 Wensheng East road, Shouguang City Country: P.R. China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)** • Original legalized COPP (Certificate# ShanDong20222004) issued by Shandong Provincial Drug Adminstration issued on May,16th , 2022 • Free Sale status: The COPP endorses the free sale status of the applied product in China GMP status: COPP Specified that certifying

		authority arrange Periodic inspection of manufacturing plant and facility and operations confirms to GMP requirements. Drug manufacturing License: legalized copy of DML No# Lu 20160126 submitted and valid till October ,26,2025
	Details of letter of authorization / sole agency agreement	Sole agency agreement has been submitted with M/s Shouguang Fukang Pharmaceuticals Co., Ltd Dated:30-05-2022 (Copy)
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 26228 dated: 16-11-2022
	Details of fee submitted	PKR 150,000/- Deposit slip # 2179283144
	The proposed proprietary name / brand name	**PARACETAMOL 500MG Tablet B.P**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet Contains: Paracetamol…….500mg
	Pharmaceutical form of applied drug	Uncoated Tablet
	Pharmacotherapeutic Group of (API)	Non-steroidal anti-inflammatory drug (NSAID)
	Reference to Finished product specifications	B.P
	Proposed Pack size	20 x 10’s & 1000’s
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	Paracetamol 500mg Tablets of Fourrts (UK) Pharmacare Ltd MHRA Approved Actavis Paracetamol 500mg Tablets of Fourrts (UK) Pharmacare Ltd MHRA Approved
	For generic drugs (me-too status)	Panadol 500mg of M/ GSK
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure,

		general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.
	Name, address of drug substance manufacturer	Hebei Jiheng Pharmaceuticals Co., LTD Address: No. 1Weiwu Street, Hengshui Industrial Park, Hebei Province, China.
	Module-III Drug Substance:	Firm has submitted detailed data for drug substance data related to nomenclature, structure, general properties, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted long term stability study data of 3 batches of drug substance at 25°C ± 2°C / 60 ± 5% RH for 48 months. The accelerated stability data is conducted at 40°C ± 2°C / 75 ± 5% RH for 6 months. Batches: (011608001, 011608002, 011608003)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against Paracetamol 500mg Tablet by GSK (190312) by performing quality tests (Identification, Average weight, related substances, microbial limit, Assay, Dissolution, Uniformity of weight). CDP has been performed against the same brand by in Acid media (pH 1.2) & Acetate buffer 4.5 pH and Phosphate Buffer (pH 6.8) . The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted analytical method verification studies of the drug product.

	Container closure system of the drug product	PVC and Aluminium foil
	Stability study data of drug product, shelf life and storage conditions	Accelerated stability studies have been conducted at 40 °C ±2 °C and 75%±5% RH for 06 months. Real time stability studies conducted at 30 °C±2 °C and 65% ± 5% RH for 36months. Batches: (180611, 180612, 180613)

Evaluation by PEC:

S.No	Section	Shortcoming communicated	
1.	1.3.1	Name and address of marketing authorization holder (abroad)	Submitted
2.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for drug substance(s) shall be submitted.	Firm submitted analytical verification studies of drug substance.
3.	3.2.S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture	Firm submitted Certificate of analysis by both drug substance manufacturer and drug product manufacturer.
4.	3.2.P.2.2.1	• Submit details of manufacturer, marketing authorization including country of origin of product against which pharmaceutical equivalence and Comparative dissolution profile conducted.	Paracetamol 500mg tablet manufactured by Accord Healthcare Ireland Ltd Batch No# 190312 Mfg date: 2019/04 Exp date: 2022/04 (In initial dossier firm submitted that pharmaceutical equivalence and CDP was conducted against Product of GSK in reply they submitted that pharmaceutical equivalence and CDP was conducted against Paracetamol 500mg tablet

		• F1 or F2 calculation for comparative dissolution not submitted.	manufactured by Accord Healthcare Ireland Ltd) • F2 calculations submitted.
Decision of M-321: The Board deferred the case for clarification since in initial dossier firm submitted that pharmaceutical equivalence and CDP was conducted against Product of GSK in reply they submitted that pharmaceutical equivalence and CDP was conducted against Paracetamol 500mg tablet manufactured by Accord Healthcare Ireland Ltd.			
Firm submitted a clarification letter from the QC manager (name of manager was not written) of M/s. Shouguang Fukang Pharmaceuticals in which it was stated that " I, on behalf of Shouguang Fukang Pharmaceuticals would like to inform you here that the pharmaceutical equivalence and comparative dissolution profile which we have submitted has initially mentioned sample of GSK Ireland as the product against which our product paracetamol 500mg tablet has been tested, but it was subsequently corrected as paracetamol 500mg tablet manufactured by Accord Healthcare Ireland ,Batch no. 190312 we would like to confirm here that GSK Ireland was a typographical error which was subsequently corrected.			
Decision: Deferred for submission of evidence of procurement of innovator drug product alongwith complete details regarding manufacturer and batch no of the innovator product for performance of Pharmaceutical equivalence studies.			

Item No. V: Agenda of Evaluator-XV (Mst.Saima Hussain)

Cases of Finished Import received on Form 5-F

246	Name, address of Applicant / Importer	M/s Himmel Pharmaceuticals (Pvt.) Ltd. 793-D, Block ''C'', Faisal Town Lahore.
	Details of Drug Sale License of importer	License No: 05-352-0065-016174-D Address:793-D, Block-C, Faisal Town Lahore Address of Godown: NA Validity: 06. Feb.2022 Status: License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s Beacon Pharmaceuticals Limited Plant address: Kathali, Bhaluka, Mymensingh Bangladesh Office address: 9/B/2, Toyenbee Circular Road, Motijheel Dhaka, Bangladesh
	Name, address of manufacturer(s)	M/s Beacon Pharmaceuticals Limited Plant address: Kathali, Bhaluka, Mymensingh Bangladesh Office address: 9/B/2, Toyenbee Circular Road, Motijheel Dhaka, Bangladesh
	Name of exporting country	Bangladesh

	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: Original legalized COPP (Certificate# DA/6-110/2016/3303 issued on 01-06-2020 by Government of the people's republic of Bangladesh, Ministry of Health & Family welfare, Directorate General of Drug Administration, Oushad Bhaban, Mohkhali Dhaka-1212, Bangladesh. GMP: Firm has submitted Legalized GMP certificate (Certificate No. DA/6-110/06/10002) issued by M/s Beacon Pharmaceuticals limited. Also Renewal certificate is submitted (Certificate No. DA/6-110/06/4950).
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of distribution certificate from Beacon Pharmaceuticals limited. The letter specifies that the manufacturer appoints M/s Himmel Pharmaceuticals Pvt. Ltd. to register their products in Pakistan. The authorization letter is valid till June, 2025.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy.No. 16109 :Date10.06.2021
	Details of fee submitted	PKR.100,030/- Date: 29-01-2021
	The proposed proprietary name / brand name	Sunitix 12.5mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains Sunitinib Malate INN…….12.5mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specifications	In house
	Proposed Pack size	28's
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	Sutent 12.5mg capsule USFDA approved
	For generic drugs (me-too status)	Sutent capsule 12.5mg (Pfizer Laboratories) Reg.no.052225
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Nanjing First Pharmaceuticals Co. Ltd. China Room No.2303,Technical Garden B Place Industrial University No.5 Xinmofang Road, Nanjing, China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted long term stability study data of 3 batches of drug substance at 25°C ± 2°C / 60 ± 5% RH for 36 months. The accelerated stability data is conducted at 40°C ± 2°C / 75 ± 5% RH for 6 months
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Comparative analysis Studies against the reference product Sutent 12.5mg capsule (Pfizer Laboratories) has been submitted
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	HDPE bottle (each contains 28 capsules)
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. Accelerated stability studies have been conducted at $40^{o}C \pm 2^{o}C$ and 75%±5% RH for 6 months. Real time stability studies conducted at $30^{o}C \pm 2^{o}C$ and 65% ± 5% for 24 months
Evaluation by PEC:		

Sr. no.	Observations/Deficiencies/ Short-comings	Response of the Firm
1.	Submit data of analytical Method verification studies under section 3.2.S.4 including specificity, accuracy and repeatability (method precision) since you have submitted validation studies GC method for determination of residual solvent of Sunitinib Malate.	Firm has submitted the reply of this query.
2.	Scientific justification is required that how the applied product will be pharmaceutically equivalent to the innovator product i.e. sutent in which the granules are filled in capsules, while in the applied product dry powder mixture of active material and excipient are filled in capsules.	Firm has not submitted the reply of this query.
3.	All quality test which have been included in the finished product specification was not performed during pharmaceutical equivalence studies, clarification is required in this regard.	Firm has not submitted the reply of this query.
4.	Assay limits mentioned in the pharmaceutical equivalence data is in percentage without the clarification that either it is the quantification of salt or its base form. While the acceptance criteria specified in the finished product specification was content of sunitinib per capsule :22.50mg to 27. 50mg.Justification is required regarding the disparity in acceptance criteria of assay of drug product.	Firm has not submitted the reply of this query.
5.	As per the chromatographic condition specified in the procedure of dissolution testing under section 3.2.P.2: wavelength of UV detector was 230nm, column temperature 25°C and retention time is 2 min (as per chromatograms) while the chromatographic condition specified under section 3.2.P.5.2: wavelength of UV detector is 430nm, column temperature 30°C and retention time is approx.6.0 minutes. Justification is required regarding the variation in chromatographic condition despite using the same dissolution medium i.e.0.1M HCl +0.5% sodium lauryl sulphate.	Firm has not submitted the reply of this query.
6.	According to the FDA's Dissolution guidance document 2018 (same document has been referred for innovator product) the standard dissolution testing condition for sunitinib malate capsule should be	Firm has not submitted the reply of this query.

	"Paddle Method (USP apparatus 2) • Stirring rate = 50 RPM • 500 mL of 0.1N HCl in aqueous medium • No surfactant in medium • 37±0.5°C". While the dissolution condition specified by the drug product manufacturer under section 3.2.P.2 and 3.2.P.5.2 was different from the said FDA's guidance document. Scientific justification is required in this regard.	
7.	Justify the dissolution specification NLT 70% of the labelled amount of sunitinib is dissolved in 60 minutes since the acceptance criteria as per the FDA dissolution database for the innovator product is "*for immediate release solid oral drug products containing a high solubility drug substance the dissolution criterion is Q=80% in 30 minutes".*	Firm has not submitted the reply of this query.
8.	Same comparative dissolution profile data has been submitted for sunitix 25 capsule and sunitix 12.5 capsule, clarification is required in this regard.	Firm has not submitted the reply of this query.
9.	• Detailed analytical method validation report is required mentioning the concentration of test solutions and their individual results along with the results of mean value. • Analytical method validation protocol specified assay method for capsule containing granules while the manufacturing process of drug product evident that capsule containing dry powder mixture of active material and excipient has been prepared. Justification is required that how the validation studies performed on assay method of capsule containing granules be applied on capsule containing dry powder mixture of active and excipients.	Firm has submitted the revised analytical method validation for drug product.
10.	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product under section 2.3.R.1.1, for which stability studies data is provided in Module 3 section 3.2. P.8.	Firm submitted BMR, according to which 269.19 gm of sunitinib Malate having potency of 99.3% has been for manufacturing of 8,000 capsule.
11.	Firm has already had registration of sunitinib Malate Capsule imported from Germany and details are as follows: Product License Holder: Aqvida GmbH Kaiser-Wilhelm-Strabe 89 20355 Hamburg Germany. Manufacturer: M/s Combino Pharm (Malta) Ltd. HF 60, Hal Far Industrial Estate, Hal Far, Birzebbugia, BBG3000, Malta. Sunitinib Aqvida 12.5mg hard capsule (Reg.no.103778) Sunitinib Aqvida 25mg hard capsule (Reg.no.103779)	

	Sunitinib Aqvida 50mg hard capsule (Reg.no.103780)

Decision: Deferred for submission of following:

- **Scientific justification is required that how the applied product will be pharmaceutically equivalent to the innovator product i.e. sutent in which the granules are filled in capsules, while in the applied product dry powder mixture of active material and excipient were filled in capsules.**
- **Submission of pharmaceutical equivalence report in which all the quality parameters of drug product specification should be included.**
- **Justification is required regarding the disparity in acceptance criteria of assay of drug product, assay limits mentioned in the pharmaceutical equivalence data is in percentage without the clarification that either it is the quantification of salt or its base form. While the acceptance criteria specified in the finished product specification was content of sunitinib per capsule :22.50mg to 27. 50mg.**
- **Scientific justification is required for using dissolution condition different from the dissolution parameters recommended in USFDA's innovator brand review report.**
- **Justify the dissolution specification NLT 70% of the labelled amount of sunitinib is dissolved in 60 minutes since the acceptance criteria as per the FDA dissolution database for the innovator product is "*for immediate release solid oral drug products containing a high solubility drug substance the dissolution criterion is Q=80% in 30 minutes".***
- **Same comparative dissolution profile data has been submitted for sunitix 25 capsule and sunitix 12.5 capsule, clarification is required in this regard.**

247.	Name, address of Applicant / Importer	M/s Himmel Pharmaceuticals (Pvt.) Ltd. 793-D, Block ''C'', Faisal Town Lahore.
	Details of Drug Sale License of importer	License No: 05-352-0065-016174-D Address:793-D, Block-C,Faisal Town Lahore Address of Godown: NA Validity: 06. Feb.2022 Status: License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s BEACON Pharmaceuticals Limited Plant address: Kathali, Bhaluka, Mymensingh Bangladesh Office address: 9/B/2, Toynbee Circular Road, Motijheel Dhaka, Bangladesh
	Name, address of manufacturer(s)	M/s BEACON Pharmaceuticals Limited Plant address: Kathali, Bhaluka, Mymensingh Bangladesh Office address: 9/B/2, Toynbee Circular Road, Motijheel Dhaka, Bangladesh
	Name of exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: Original legalized COPP (Certificate# DA/6-110/2016/3304 issued on 01-06-2020 by Government of the people's republic of Bangladesh, Ministry of Health & Family welfare, Directorate General of Drug Administration, Oushad Bhaban, Mohkhali Dhaka-1212, Bangladesh. GMP: Firm has submitted Legalized GMP certificate (Certificate No. DA/6-110/06/10002) issued by M/s Beacon Pharmaceuticals limited. Also Renewal certificate is submitted (Certificate No. DA/6-110/06/4950).

	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of distribution certificate from Beacon Pharmaceuticals limited. The letter specifies that the manufacturer appoints M/s Himmel Pharmaceuticals Pvt. Ltd. to register their products in Pakistan. The authorization letter is valid till June, 2025.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No.16108 , Date: 10.06.2021
	Details of fee submitted	PKR.100,030/- Date: 29-01-2021
	The proposed proprietary name / brand name	Sunitix 25mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains Sunitinib Malate INN …….25mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specifications	In house
	Proposed Pack size	28’s
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	Sutent 25mg capsule USFDA approved
	For generic drugs (me-too status)	Sutent (Pfizer Laboratories) Reg.no. 052226
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Nanjing First Pharmaceuticals Co. Ltd. China Room No.2303,Technical Garden B Place Industrial University No.5 Xinmofang Road, Nanjing, China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data

		for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted long term stability study data of 3 batches of drug substance at 25°C ± 2°C / 60 ± 5% RH for 36 months. The accelerated stability data is conducted at 40°C ± 2°C / 75 ± 5% RH for 6 months
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Comparative analysis Studies against the reference product Sutent 25mg capsule (Pfizer Laboratories) has been submitted
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	HDPE bottle (each contains 28 capsules)
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. Accelerated stability studies have been conducted at 40°C±2°C and 75%±5% RH for 6 months. Real time stability studies conducted at 30°C±2°C and 65% ± 5% for 24 months

Evaluation by PEC:

Sr. no.	Observations/Deficiencies/ Short-comings	Response of the Firm
1.	Submit data of analytical Method verification studies under section 3.2.S.4 including specificity, accuracy and repeatability (method precision) since you have submitted validation studies GC method for determination of residual solvent of Sunitinib Malate.	Firm has submitted the reply of this query.
2.	Scientific justification is required that how the applied product will be pharmaceutically equivalent to the innovator product i.e. sutent in which the granules are filled in capsules, while in the applied product dry powder mixture of	Firm has not submitted the reply of this query.

	active material and excipient are filled in capsules.	
3.	All quality test which have been included in the finished product specification was not performed during pharmaceutical equivalence studies, clarification is required in this regard.	Firm has not submitted the reply of this query.
4.	Assay limits mentioned in the pharmaceutical equivalence data is in percentage without the clarification that either it is the quantification of salt or its base form. While the acceptance criteria specified in the finished product specification was content of sunitinib per capsule :22.50mg to 27. 50mg.Justification is required regarding the disparity in acceptance criteria of assay of drug product.	Firm has not submitted the reply of this query.
5.	As per the chromatographic condition specified in the procedure of dissolution testing under section 3.2.P.2: wavelength of UV detector was 230nm, column temperature 25℃ and retention time is 2 min (as per chromatograms) while the chromatographic condition specified under section 3.2.P.5.2: wavelength of UV detector is 430nm, column temperature 30℃ and retention time is approx.6.0 minutes. Justification is required regarding the variation in chromatographic condition despite using the same dissolution medium i.e.0.1M HCl +0.5% sodium lauryl sulphate.	Firm has not submitted the reply of this query.
6.	According to the FDA's Dissolution guidance document 2018 (same document has been referred for innovator product) the standard dissolution testing condition for sunitinib malate capsule should be *"Paddle Method (USP apparatus 2) • Stirring rate = 50 RPM • 500 mL of 0.1N HCl in aqueous medium • No surfactant in medium • 37±0.5°C"*. While the dissolution condition specified by the drug product manufacturer under section 3.2.P.2 and 3.2.P.5.2 was different from the said FDA's guidance document. Scientific justification is required in this regard.	Firm has not submitted the reply of this query.
7.	Justify the dissolution specification NLT 70% of the labelled amount of sunitinib is dissolved in 60 minutes since the acceptance criteria as per the FDA dissolution database for the innovator	Firm has not submitted the reply of this query.

	product is "*for immediate release solid oral drug products containing a high solubility drug substance the dissolution criterion is Q=80% in 30 minutes".*	
8.	Same comparative dissolution profile data has been submitted for sunitix 25 capsule and sunitix 12.5 capsule, clarification is required in this regard.	Firm has not submitted the reply of this query.
9.	• Detailed analytical method validation report is required mentioning the concentration of test solutions and their individual results along with the results of mean value. • Analytical method validation protocol specified assay method for capsule containing granules while the manufacturing process of drug product evident that capsule containing dry powder mixture of active material and excipient has been prepared. Justification is required that how the validation studies performed on assay method of capsule containing granules be applied on capsule containing dry powder mixture of active and excipients.	Firm has submitted the revised analytical method validation for drug product.
10.	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product under section 2.3.R.1.1, for which stability studies data is provided in Module 3 section 3.2. P.8.	Firm submitted BMR, according to which 269.19 gm of sunitinib Malate having potency of 99.3% has been for manufacturing of 8,000 capsule.
11.	Firm has already had registration of sunitinib Malate Capsule imported from Germany and details are as follows: Product License Holder: Aqvida GmbH Kaiser-Wilhelm-Strabe 89 20355 Hamburg Germany. Manufacturer: M/s Combino Pharm (Malta) Ltd. HF 60, Hal Far Industrial Estate, Hal Far, Birzebbugia, BBG3000, Malta. Sunitinib Aqvida 12.5mg hard capsule (Reg.no.103778) Sunitinib Aqvida 25mg hard capsule (Reg.no.103779) Sunitinib Aqvida 50mg hard capsule (Reg.no.103780)	

Decision: Deferred for submission of following:

- **Scientific justification is required that how the applied product will be pharmaceutically equivalent to the innovator product i.e. sutent in which the granules are filled in capsules, while in the applied product dry powder mixture of active material and excipient were filled in capsules.**
- **Submission of pharmaceutical equivalence report in which all the quality parameters of drug product specification should be included.**
- **Justification is required regarding the disparity in acceptance criteria of assay of drug product, assay limits mentioned in the pharmaceutical equivalence data is in percentage without the clarification that either it is the quantification of salt or its base form. While the acceptance criteria specified in the finished product specification was content of sunitinib per capsule :22.50mg to 27. 50mg.**

	• **Scientific justification is required for using dissolution condition different from the dissolution parameters recommended in USFDA's innovator brand review report.** • **Justify the dissolution specification NLT 70% of the labelled amount of sunitinib is dissolved in 60 minutes since the acceptance criteria as per the FDA dissolution database for the innovator product is "*for immediate release solid oral drug products containing a high solubility drug substance the dissolution criterion is Q=80% in 30 minutes*".** • **Same comparative dissolution profile data has been submitted for sunitix 25 capsule and sunitix 12.5 capsule, clarification is required in this regard.**	
248.	Name, address of Applicant / Importer	M/s Hakimsons Private Limited., Hakimsons House, A-58/B, S.I.T.E, Manghopir Road, Karachi-75700, Pakistan
	Details of Drug Sale License of importer	Address: A-58/B, S.I.T.E, Karachi Validity: 21-08-2022 Status: Drug license by the way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Eugia Pharma Specialities Limited. Survey No. 550, 551 & 552, Kolthur Village, Shamirpet Mandal, Medchal-Malkajgiri, District Medchal, Telangana, 500101, India.
	Name, address of manufacturer(s)	M/s Eugia Pharma Specialities Limited. Survey No. 550, 551 & 552, Kolthur Village, Shamirpet Mandal, Medchal-Malkajgiri, District Medchal, Telangana, 500101, India
	Name of exporting country	INDIA
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted Original Legalized CoPP (Certificate#2850/STORES/2020-06) issued by Drugs Control Administration, Government of Telangana, India for IRNIZET 100 (Irinotecan Hydrochloride 20mg/ml) Concentrate for Solution for Infusion 100mg/5ml. CoPP confirms facilities and operations conforming to GMP as recommended by the World Health Organization. The certificate is valid till 19-03-2023. GMP certificate: The firm has submitted copy of GMP certificate for M/s Eugia Pharma Specialities Ltd. India issued by Drugs control Administration, Government of Telangana, India. The certificate is valid till 19-03-2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted a copy of letter of authorization from M/s Aurobindo Pharma Limited, plot No.2, Maitri Vihar, Ameerpet, Hyderabad. According to the letter, the firm has appointed "M/s Hakimsons Pvt. Ltd," with principal place of business at A-58/B, S.I.T.E, Manghopir Road, Karachi as its Exclusive Distributor for the territory of Islamic Republic of Pakistan. The letter was issued on 10-12-2020 and it is valid for a period of five years. The applicant has submitted notarized copy of letter clarifying the relationship between Eugia pharma specialities Limited and Aurobindo Pharma Ltd.

	Eugia pharma specialities Limited is wholly owned subsidiary company of Aurobindo Pharma Limited with registered office address "Plot No.2, Maitrivihar, Ameerpet, Hyderabad, Telanagana State, India. Eugia pharma specialities Limited, with manufacturing site address "survey no. 550, 551 & 552, kolthur village, shamirpet Mandal, Medchal - Malkagiri District, Telangana, Indi, manufactures oncology & Hormonal products and is one of the manufacturing facilities associated with Aurobindo Pharma Limited.
Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
Dy. No. and date of submission	Form-5F ; Dy. No. 23872 dated : 31/08/2021
Details of fee submitted	PKR 100,000/-: 23-02-2021 Balanced Fee PKR 50,000/- ; 16/03/2022
Proposed proprietary name / brand name	IRNIZET 40 (Irinotecan Hydrochloride) Concentrate for Solution for Infusion 40mg/2ml
Strength/concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each mL contains Irinotecan Hydrochloride ……20 mg
Pharmaceutical form of applied drug	Concentrate for Solution for Infusion
Pharmacotherapeutic Group of (API)	Antineoplastic agents, other antineoplastic agents (ATC code: L01XX19)
Reference to Finished product specifications	USP Specifications
Proposed Pack size	1's vial
Proposed unit price	As per PRC
The status in reference regulatory authorities	CAMPTOSAR Injection for Infusion 40mg/2ml by PFIZER INC (USFDA approved)
For generic drugs (me-too status)	Campto Injection 40mg/2ml of M/s Pfizer (Reg # 021127) Irinotecan Injection 40mg/2ml of M/s Novartis (Reg#066186)
Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Name, address of drug substance manufacturer	M/s Laurus Labs Limited, Plot No. 21, Jawaharlal Nehru Pharma City, Parawada, Visakhapatnam-531021 Andhra Pradesh, India Tel: +91-891-3061222 Fax: +91-891-3061270
Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated and real time conditions. It was concluded that Irinotecan HCl Trihydrate is stable up to 6 months under accelerated conditions (40 ^{o}C ±2 ^{o}C/75%± 5% RH) & 60 months under long term conditions (25^{o}C ±2^{o}C / 60% ± 5% RH)
Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has submitted physicochemical evaluation of CAMPTO 20 mg/mL concentrate for solution for infusion., (batch # M86531) of M/s Pfizer Limited and also submitted finished product evaluation of Irinotecan 20 mg/ml concentrate for solution for infusion. [40 mg/2 mL] (batch # EIH1810F) of Eugia Pharma Specialities Limited.
Analytical method validation/verification of product	Firm has submitted Assay Method Validation Protocols along with Reports of Irinotecan 20 mg/ml concentrate for solution for infusion. [40 mg/2 mL] Finished product as well as for Active substance. In-house analytical test methods were developed to determine the identification (By HPLC), Assay (By HPLC), Related substance (By HPLC), R-Enantiomer content (by HPLC), and color absorbance (By UV) in

		drug product and methods have been validated as per the ICH.
	Container closure system of the drug product	Vial size and type: Glass Vial Tubular Type-I, 6R Amber BB vial with 13 mm Neck Rubber stopper: Dark Grey bromo butyl rubber stopper, 13mm Flip off seal: Al. Seal with PP disc, 13 mm red color.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches of Irinotecan HCl 20mg/ml, concentrate for solution for Infusion (40mg/2ml) The accelerated stability study data is conducted at 40 ^{o}C ±2 ^{o}C/ 75%± 5% RH for 06 months. The real time stability study data is conducted at 30^{o}C ±2^{o}C / 65% ± 5% RH for 24months. (Invert)

Batch No.	Batch size	Mfg. Date	Initiation date
EIH1810-A	10 L	04-2018	28-08-2018
EIH1811-A	30 L	04-2018	19-06-2018
EIH1812-A	30 L	05-2018	19-06-2018

Evaluation by PEC:

S. no.	Observations/Deficiencies/ Short-comings	Response of the Firm
1.	Clarify the marketing status of applied product in the exporting country, since the submitted free sale certificate and CoPP evident that the applied product has not been freely available in the market of country of origin and according to the free sale certificate, market status of applied product is in export only.	Firm submitted the approval status of applied formulation in the reference regulatory authorities and inform that the applied formulation is available in the market of Belgium & USA, instead of inform about the marketing status of applied product in the exporting country.
2.	Provide the valid free sale certificate, since the validity of submitted certificate was up till 25/06/2021.	Firm submitted the free sale certificate that is valid uptill 02/02/2025, in which marketing status of applied product is for export only.

Decision: Deferred for clarification of marketing status of applied finished product in the exporting country, since the submitted free sale certificate and CoPP evident that the applied product has not been freely available in the market of country of origin.

249.	Name, address of Applicant / Importer	Name: The Searle Company Limited Address: Head Office: Section-D, 2nd Floor One IBL Centre, Plot # 1, Block 7 & 8, (DMCHS), Tipu Sultan Road, Off, Shahrah-e-Faisal, Karachi. Factory: The Searle Company Limited, F-319 SITE Karachi, Pakistan.
	Details of Drug Sale License of importer	License No: 1001 Address: Section-D, 2nd Floor One IBL Centre, Plot # 1, Block 7 & 8, (DMCHS), Tipu Sultan Road, Off, Shahrah-e-Faisal, Karachi. Address of Godown:

		1) Plot No Section 1 F-2/Q Site Karachi. Validity: 15-05-2021. Status: License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	LABORATORIOS LEÓN FARMA, SA C/ La Vallina, s/n, Polígono Industrial Navatejera, Villaquilambre 24008 (León) SPAIN
	Name, address of manufacturer(s)	LABORATORIOS LEÓN FARMA, SA C/ La Vallina, s/n, Polígono Industrial Navatejera, Villaquilambre 24008 (León) SPAIN
	Name of exporting country	SPAIN
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted original, legalized copy of CoPP certificate (No.2020/02446) dated 11/27/2018 issued by Spanish Agency for Medicines and Health Products. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every 3 years. The name of importing country on CoPP is mentioned as Spain.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of Authorization from LABORATORIOS LEÓN FARMA, SA. The letter species that the manufacturer appoints The Searle Company Limited to register their products in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical Product Import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 23845: 31-08-2021
	Details of fee submitted	PKR 100,000/-: 28-07-2020
	The proposed proprietary name / brand name	Urisolin Plus Capsules 0.5mg + 0.4mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Dutasteride …… 0.5mg Tamsulosin Hydrochloride… 0.4mg
	Pharmaceutical form of applied drug	Capsule, Hard
	Pharmacotherapeutic Group of (API)	Alpha-adrenoreceptor antagonists (ATC code: G04CA52)

	Reference to Finished product specifications	Ph Eur
	Proposed Pack size	As per DPC
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	JALYN® Capsules (Approved by USFDA)
	For generic drugs (me-too status)	Getz Pharma Pakistan (Pvt.) Ltd Tamsolin Plus Dutasteride 0.5mg + Tamsulosin hydrochloride 0.4mg
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Dutasteride: Aurobindo Pharma Tamsulosin hydrochloride: Zentiva
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Dutasteride: Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 25°C ± 2ºC & RH 60%+/-5% and Accelerated time stability study is conducted at 40°C ± 2ºC & RH 75%+/- 5%. The stability study data is till 24 months. Tamsulosin hydrochloride: Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 25°C ± 2ºC & RH 60%+/-5% and 40°C ± 2ºC & RH 75%+/- 5%. The stability study data is till 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of

		specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence and CDP has been performed against the reference product Name: Duodart® 0.5/0.4 mg hard capsules Batch nº: 13692073B Manufacturer: Glaxo Smith Kline Laboratories Expiry date: July 2017
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	white HDPE bottle with silica gel desiccant contained in a white cap
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches The accelerated stability study data is conducted at 40ºC ±2ºC / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30ºC ±2ºC / 75% ± 5% RH for 12 months.
Evaluation by PEC: Firm submitted the differential fee of Rs.50,000/- deposit slip no. 41090716 dated 22-06-2022.		
Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.		
250	Name, address of Applicant / Importer	M/s Highnoon Laboratories Ltd. 17.5km, Multan Road, Lahore-53700, Pakistan.
	Details of Drug Sale License of importer	License No: 05-352-0066-027583D Address: Address of Godown: 1. Situated at 18km Multan Road, Lahore (Behind Highnoon Laboratories Limited, Opposite Star Food Cold Storage). 251. Situated at 19km Multan Road (Din Muhammad Town, Chung) Lahore Validity: 12-Sep-2022 Status: License to sell drugs as distributor Renewal: Firm has submitted a receipt of renewal, but it does not contain any date
	Name and address of marketing authorization holder (abroad)	M/s Highnoon Laboratories Ltd. 17.5km, Multan Road, Lahore-53700, Pakistan.
	Name, address of manufacturer(s)	Cipla Limited, Maharashtra India. Plot D-7, D-22, D-27 MIDC Industrial Area, Kurkumbh Village, Taluka-Daund, Pune, Maharashtra 413802, India
	Name of exporting country	India

	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted an original, legalized copy of CoPP certificate (No. COPP/CERT/PD/110147/2022/11/39010/190011) dated 30-01-2022 issued by Food and Drug Administration, M.S. Bandra-kurla complex, Bandra (E), Mumbai-400 051. Mahrashtra, India for Cipmolnu 200mg Capsule. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. The name of importing country on CoPP is mentioned as Pakistan. Furthermore, the CoPP was valid till 21-05-2022.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of Originally Notarized letter of Authorization from Cipla Limited, Maharashtra India. The letter species that the manufacturer appoints M/s Highnoon Laboratories Ltd. to register their products in Pakistan. The authorization letter is valid till 03-03-2023.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 11466 12-05-2022
	Details of fee submitted	PKR 75,000/-: 09-02-2022
	The proposed proprietary name / brand name	Cipmolnu 200mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Molnupiravir…….200 mg
	Pharmaceutical form of applied drug	White to off- white powder filled in size ‘0’ capsule with light blue opaque cap and body.
	Pharmacotherapeutic Group of (API)	Antiviral
	Reference to Finished product specifications	Innovator
	Proposed Pack size	1’s, 5’s, 7’s, 10’s, 12’s, 28’s, 30’s, 40’s, 50’s, 60’s, 100’s, 120’s
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Lagevrio 200 mg hard capsules MHRA approved
	For generic drugs (me-too status)	N/A
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Name, address of drug substance manufacturer	M/s Cipla Limited-Kurkumbh Plot No. D-7, D-27, D-22 MIDC Industrial Area, Kurkumbh Village, Taluka-Daund, District-Pune (Maharashtra)-413 802, India.
	Module-III Drug Substance:	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (impurity A, MOL-Hydroxylamine & unspecified), specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 1 year Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (LDX210049, LDX210055, LDX210056)
	Module-III Drug Product:	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence have been established against the brand leader that is Molnupiravir Capsules 200 mg by Merck Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Molnupiravir Capsules 200 mg by Merck Pharma in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

	Container closure system of the drug product	40's bottle pack
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 75% ± 5% RH for 1 year.

Batch No.	KA12304	KA12305	KA123 6
Batch Size	30,000	30,000	30,00
Manufacturing Date	07-2021	07-2021	07-202
Date of Initiation	13-08-2021	13-08-2021	13-08 2021

Evaluation by PEC:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide readable copy of valid Drug sale license.	Submitted
2.	Provide stability data of drug substance performed at accelerated and long term stability condition till the claimed shelf life/retest date.	Firm submitted the 6th month accelerated and 1 year real time stability data of drug substance.
3.	Provide the stability data of three trial batches/commercial batches till the claimed shelf life, since you have submitted only three months stability data of drug product.	Firm submitted the 6th month accelerated and 1 year real time stability data of drug substance.

Decision: Deferred for following:

- **Submission of complete stability data of drug substance and drug product till the claimed shelf life/retest date as per zone IV conditions.**
- **Regulatory status of approval of applied formulation by reference regulatory authority by way of routine procedure of market authorisation.**

252.	Name, address of Applicant / Importer	Biocare Pharmaceutica. Address:- 807 Shadman-1, Lahore
	Details of Drug Sale License of importer	License No: 05-352-0063-032069D Address: 807 Shadman-1, District Lahore. Address of Godown: First floor B-C, Street No. 3, Near LGS School, Shah Jamal District Lahore. Validity: 17-04-2022. Status: License to sell drugs as distributor Renewed/New DSL: Drug sales License is renewed. New Drug sales License is attached for DRAP reference. (New License No. 05-352-0063-032069D) , Validity:- 17.04.2027.
	Name and address of marketing authorization holder (abroad)	License Holder/Supplier: PT DEXA MEDICA. Address:- Jalan Jenderal Bambang Utoyo No. 138, Palembang 30115, Indonesia, Tel:- (+62-21) 7454 111. Telephone : (+62-21) 7454 111

	Name, address of manufacturer(s)	Manufactured By:- PT Ferron Par Pharmaceuticals. Address Manufacturing site Jababeka Industrial Estate I, Jl. Jababeka VI Blok J-3 Cikarang Bekasi 17520, Indonesia, Telephone: +62 21 898 33333
	Name of exporting country	Indonesia
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted original, legalized copy of CoPP with certificate No. RG.01.05.32.321.07.21.2976, dated July 6, 2021 issued by National Agency of Drug and Food Control, Indonesia. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. CoPP validity is July 6, 2023 based upon its 2 year validity. The name of importing country on CoPP is mentioned as Pakistan. Embassy Attested/Legalized GMP is also attached. GMP Validity is March, 13, 2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of legalized distribution agreement signed by both parties Biocare Pharmaceutica & PT Dexa Medica. Agreement clearly mention Aboard License Holder Dexa Medica (Indinesia) appoints M/s Biocare Pharmaceutica to register/market/sell/Distribute their product Granon (Granisetron HCL) 1 mg/1ml Inj. in Pakistan. Agreement validity is 10 years with additional 5 year renewal clause.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 31639 : 17-11-2021
	Details of fee submitted	PKR 150,000 /-: Slip # 9327411064, Date:- 13-11-2021
	The proposed proprietary name / brand name	GRANON

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each mL of contains Granisetron Hydrochloride equivalent to Granisetron 1 mg.
	Pharmaceutical form of applied drug	Solution for injection Clear, colorless solution.
	Pharmacotherapeutic Group of (API)	Alimentary Tract and Metabolism, Antiemetics and Antinauseants
	Reference to Finished product specifications	USP
	Proposed Pack size	5 Ampoules per Pack (Box 5 Ampoules)
	Proposed unit price	Rs 554/Ampoule. Rs. 2770 for 5 ampoules Box
	The status in reference regulatory authorities	Granisetron HCl 1 mg/1ml (1mg/ml) is UKMHRA, TGA (Australia) and EMA (European Medicine Agency) approved 5-HT3 receptor antagonist used as an antiemetic to prevent/treat nausea and vomiting caused by chemotherapy and radiation therapy and to prevent and treat nausea and vomiting after surgery in adults. It is currently actively market in United Kingdom (UK), Australia and in European countries like Germany, France Finland, Estonia, Greece, Ireland, Latvia and Italy etc.
	For generic drugs (me-too status)	Mfr. Name/Importer/Local:- A.J Mirza Pharma (PVT) LTD, Brand:- Granicip, Strength:- 1mg/1ml, Composition:- Granisetron Hydrochloride, Reg. No. 052261, Dosage Form:- Solution in Ampoule for injection & Price (MRP):- Register but not launch in Pakistan market.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Hubei Haosun Pharmaceutical Co., Ltd. Address No. 20, Juxian Road, Gedian Economic & Technology Development Area, Hubei, 436070, P. R. China

	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The 6 months accelerated study is complete for 3 batches at 40±2 °C/75±5%RH. The real time 3 batches stability data is conducted at 25±2°C/60±5%RH. The real time stability study data is till 48 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established by conducting all the quality tests against the reference original brand Kytril (Granisetron) 1mg/1ml injection, batch number F0024F71, produced by Roche, Switzerland.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Granon (GranisetronHcl) 1 mg/1ml solution for injection is filled into Type I clear glass ampoule 1 mL.
	Stability study data of drug product, shelf life and storage conditions	• 24 months real time stability data at 30°C ± 2°C / 75% ± 5%RH of 03 batches (Zone IVB) is Submitted. • 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 03 batches is submitted.

Evaluation by PEC:

Sr.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide specification and detailed analytical procedure used for testing of drug substance by drug product manufacturer, since the submitted details were of drug product manufacturer.	Firm submitted the specification and detailed analytical procedure used for testing of drug substance by drug substance manufacturer and drug product manufacturer.

2.	Pharmaceutical equivalence of granon 3mg/3ml injection has been performed against Kytril Injection 0.1% as evident from the submitted document, justify to perform equivalence study with the reference product that is different in strength and volume from that of applied product.	Firm replied that kyril injection 0.1% is a product containing granisetron hydrochloride equivalent to 3mg of granisetron free base in 3 ml or equivalent to equivalent to 1mg of granisetron free base in 1ml where it is the same concentration with Granon 1mg/ml and Granon 3mg/3ml Injection, only different in filling volume.
3.	Clarification is required either the product comply USP specification or in-house specification.	Firm clarified that product comply USP specification, sone additional test were performed in accordance with in-house specification.

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

253.	Name, address of Applicant / Importer	Biocare Pharmaceutica. Address:- 807 Shadman-1, Lahore
	Details of Drug Sale License of importer	License No: 05-352-0063-032069D Address: 807 Shadman-1, District Lahore. Address of Godown: First floor B-C, Street No. 3, Near LGS School, Shah Jamal District Lahore. Validity: 17-04-2022. Status: License to sell drugs as distributor Renewed/New DSL: Drug sales License is renewed. New Drug Sales License is attached for DRAP reference. (New License No. 05-352-0063-032069D) , Validity:- 17.04.2027.
	Name and address of marketing authorization holder (abroad)	License Holder/Supplier: PT DEXA MEDICA. Address: - Jalan Jenderal Bambang Utoyo No. 138, Palembang 30115, Indonesia, Tel: - (+62-21) 7454 111. Telephone : (+62-21) 7454 111
	Name, address of manufacturer(s)	Manufactured By:- PT Ferron Par Pharmaceuticals. Address Manufacturing site Jababeka Industrial Estate I, Jl. Jababeka VI Blok J-3 Cikarang Bekasi 17520, Indonesia, Telephone: +62 21 898 33333
	Name of exporting country	Indonesia
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted original, legalized copy of CoPP with certificate No. RG.01.05.32.321.05.21.2848, dated May 20, 2021 issued by National Agency of Drug and Food Control, Indonesia. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. CoPP validity is May 20, 2023 based upon its 2-year validity. <u>The name of importing country on CoPP is mentioned as Pakistan.</u>

		Embassy Attested/Legalized GMP is also attached. GMP Validity is March, 13, 2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of legalized distribution agreement signed by both parties Biocare Pharmaceutica & PT Dexa Medica. Agreement clearly mention Aboard License Holder Dexa Medica (Indinesia) appoints M/s Biocare Pharmaceutica to register/market/sell/Distribute their product Granon (Granisetron HCL) 1 mg/1ml Inj. in Pakistan. Agreement validity is 10 years with additional 5 year renewal clause.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 31640 : 17-11-2021
	Details of fee submitted	PKR 150,000 /-: Slip # 17375816, Date:- 13-11-2021
	The proposed proprietary name / brand name	GRANON
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 3 ml ampoule contains a total content of 3 mg granisetron as the hydrochloride in 3 ml of a sterile solution.
	Pharmaceutical form of applied drug	Solution for injection Clear, colorless solution.
	Pharmacotherapeutic Group of (API)	Alimentary Tract and Metabolism, Antiemetics and Antinauseants
	Reference to Finished product specifications	USP
	Proposed Pack size	5 Ampoules per Pack (Box 5 Ampoules)
	Proposed unit price	Rs 850/Ampoule. Rs. 4250 for 5 ampoules Box

	The status in reference regulatory authorities	Granisetron HCl 3 mg/3ml (1mg/ml) is UKMHRA, TGA (Australia) and EMA (European Medicine Agency) approved 5-HT3 receptor antagonist used as an antiemetic to prevent/treat nausea and vomiting caused by chemotherapy and radiation therapy and to prevent and treat nausea and vomiting after surgery in adults. It is currently actively market in United Kingdom (UK), Australia and in European countries like Germany, France Finland, Estonia, Greece, Ireland, Latvia and Italy etc. (Evidences Attached/along with approved Leaf Inserts: - Please refer to Module 1. Page # 271-323 of CTD dossier).
	For generic drugs (me-too status)	Mfr. Name/Importer/Local: - CCL Pharmaceuticals (Pvt)., Ltd, Brand: - Graniset, Strength: - 3mg/3ml, Composition: - Granisetron Hydrochloride, Reg. No. 048027, Dosage Form:- Solution in Ampoule for injection
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Hubei Haosun Pharmaceutical Co., Ltd. Address No. 20, Juxian Road, Gedian Economic & Technology Development Area, Hubei, 436070, P. R. China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The 6 months accelerated study is complete for 3 batches at 40±2 °C/75±5%RH. The real time 3 batches stability data is conducted at 25±2°C/60±5%RH. The real time stability study data is till 48 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical

		development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established by conducting all the quality tests against the reference original brand Kytril (Granisetron) 3mg/3ml injection, batch number F0024F71, produced by Roche, Switzerland, Roche, imported by PT Boehringer Ingelheim
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Granon (Granisetron Hcl) 3 mg/3ml solution for injection is filled into Type I clear glass ampoule 5 mL.
	Stability study data of drug product, shelf life and storage conditions	• 4 batches Accelerated and Long-term stability data is submitted. • 36 months real time long term stability data at 30°C ± 2°C / 75% ± 5%RH (ZONE IVB) of 2 batches and 24 months long term real time stability data 02 batches at 30°C ± 2°C / 75% ± 5%RH (Zone IVB) is Submitted. Overall 4 batches long term stability data is submitted. Firm has claim 24 months shelf life based upon its Long term real time 4 batches ZONE IVB stability data. • 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 04 batches is submitted.

Evaluation by PEC:

Sr.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide specification and detailed analytical procedure used for testing of drug substance by drug product manufacturer, since the submitted details were of drug product manufacturer.	Firm submitted the specification and detailed analytical procedure used for testing of drug substance by drug substance manufacturer and drug product manufacturer.
2.	Pharmaceutical equivalence of granon 3mg/3ml injection has been performed against Kytril Injection 0.1% as evident from the submitted document, justify to perform equivalence study with the reference product that is different in strength and volume from that of applied product.	Firm replied that kyril injection 0.1% is a product containing granisetron hydrochloride equivalent to 3mg of granisetron free base in 3 ml or equivalent to equivalent to 1mg of granisetron free base in 1ml where it is the same concentration with Granon 1mg/ml and Granon 3mg/3ml Injection, only different in filling volume.

3.	Clarification is required either the product comply USP specification or in-house specification.	Firm clarified that product comply USP specification, some additional test were performed in accordance with in-house specification.

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

254.	Name, address of Applicant / Importer	Biocare Pharmaceutica. Address:- 807 Shadman-1, Lahore
	Details of Drug Sale License of importer	License No: 05-352-0063-032069D Address: 807 Shadman-1, District Lahore. Address of Godown: First floor B-C, Street No. 3, Near LGS School, Shah Jamal District Lahore. Validity: 17-04-2022. Status: License to sell drugs as distributor Renewed/New DSL: Drug sales License is renewed. New Drug sales License is attached for DRAP reference. (New License No. 05-352-0063-032069D) , Validity:- 17.04.2027.
	Name and address of marketing authorization holder (abroad)	License Holder/Supplier: PT DEXA MEDICA. Address:- Jalan Jenderal Bambang Utoyo No. 138, Palembang 30115, Indonesia, Tel:- (+62-21) 7454 111. Telephone : (+62-21) 7454 111
	Name, address of manufacturer(s)	Manufacturer: PT DEXA MEDICA. Address:- Jalan Jenderal Bambang Utoyo No. 138, Palembang 30115, Indonesia, Tel:- (+62-21) 7454 111. Telephone : (+62-21) 7454 111
	Name of exporting country	Indonesia
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Firm has submitted original, legalized copy of CoPP with certificate No. RG.01.05.32.321.05.21.2849, dated May 20, 2021 issued by National Agency of Drug and Food Control, Indonesia. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every year. CoPP validity is May 20, 2023 based upon its 2 year validity. <u>The name of importing country on CoPP is mentioned as Pakistan.</u> Embassy Attested/Legalized GMP is also attached. GMP Validity is April 5, 2023.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of legalized distribution agreement signed by both parties Biocare Pharmaceutica & PT Dexa Medica. Agreement clearly mention Aboard License Holder Dexa Medica (Indonesia) appoints M/s Biocare Pharmaceutical to register/market/sell/Distribute their product Granon (Granisetron HCL) 1 mg/1ml Inj. in Pakistan. Agreement validity is 10 years with additional 5 year renewal clause.
	Status of the applicant	☐ Manufacturer

		☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 31638 : 17-11-2021
	Details of fee submitted	PKR 150,000 /-: Slip # 474738766,Date:- 13-11-2021
	The proposed proprietary name / brand name	GRANON
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains granisetron hydrochloride equivalent to granisetron 1 mg.
	Pharmaceutical form of applied drug	Film-coated tablet White, round and shallow convex tablet, diameter 6 mm. Side I DEXA and side II unmarked
	Pharmacotherapeutic Group of (API)	Alimentary Tract and Metabolism, Antiemetics and Antinauseants
	Reference to Finished product specifications	USP
	Proposed Pack size	10 Tablets per Pack (10'S)
	Proposed unit price	Rs 250 per Tablet. Rs. 2500 for 10'S Pack.
	The status in reference regulatory authorities	Granisetron HCl 1 mg film coated Tablet is UKMHRA, TGA (Australia) and EMA (European Medicine Agency) approved 5-HT3 receptor antagonist used as an antiemetic to prevent/treat nausea and vomiting caused by chemotherapy and radiation therapy and to prevent and treat nausea and vomiting after surgery in adults. It is currently actively market in United Kingdom (UK), Australia and in European countries like Germany, France Finland, Estonia, Greece, Ireland, Latvia and Italy etc. (Evidences Attached/along with approved Leaf Inserts: - Please refer to Module 1. Page # 181-232 of CTD dossier).
	For generic drugs (me-too status)	Mfr. Name/Local: - CCL Pharmaceuticals (Pvt)., Ltd, Brand: - Graniset, Strength: - 1 mg, Composition: - Granisetron Hydrochloride, Reg. No. 048026, Dosage Form: - Film Coated Tablet &

		Price (MRP): - Rs. 2650/pack 10 Tablets (10'S) .
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Qilu Pharmaceutical Co., Ltd. Address:- No. 243 Gong Ye Bei Road, Jinan, Shandong Province 250100, P. R. China
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The 6 months accelerated study is complete for 3 batches at 40±2 °C/75±5%RH. The real time 3 batches Zone IVA stability data is conducted at 30±2°C/65±5%RH. The real time stability study data is till 24 months. Overall firm has provided 6 batches Zone IVA (30±2°C/65±5%RH) 24 months real time long-term API Stability data along with 6 months 4 batches Accelerated stability data at 40±2 °C/75±5%RH.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established by conducting all the quality tests against the reference original brand Kytril (Granisetron) 1 mg film coated tablet, batch number M1000B71, produced by Roche,

		Nederland, B.V. Detail Comparative Dissolution Profile is also provided by manufacturer Dexa Medica.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Granon (Granisetron Hcl) 1 mg tablet is Packed in polycellonium strip.
	Stability study data of drug product, shelf life and storage conditions	4 batches Accelerated and Long term stability data is submitted. • 36 months real time long term stability data at 30°C ± 2°C / 75% ± 5%RH (ZONE IVB) of 2 batches and 24 months long term real time stability data 01 batches at 30°C ± 2°C / 75% ± 5%RH (Zone IVB) is Submitted. Overall 4 batches long term stability data is submitted. One ongoing real time Zone IVB stability data of 12 months is also submitted by firm. Firm has claim 24 months shelf life based upon its complete Long term real time 3 batches ZONE IVB stability data. • 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 04 batches is submitted.

Evaluation by PEC:

Sr. no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide specification and detailed analytical procedure used for testing of drug substance by drug product manufacturer, since the submitted details were of drug product manufacturer.	Firm submitted the specification and detailed analytical procedure used for testing of drug substance by drug substance manufacturer and drug product manufacturer.
2.	Clarification is required either the product comply USP specification or the or the applied product claimed in-house specification.	Firm clarified that product comply USP specification, some additional test were performed in accordance with in-house specification.
3.	Scientific justification is required for setting the widened time point window i.e. till 30 minutes, when the drug release more than 85% within 15 minutes as evident from the CDP report and the submitted stability data also revealed that more than 95% drug release in 30 minutes.	Firm replied that Granon film coated tablet is refer to USP monograph with a limit of T 30minutes≥75%(Q).The purpose of specifying dissolution limits is to ensure batch-to- batch consistency within arrange which gurantess acceptable biopharmaceutical performance in vivo.

Decision: Approved as per Policy for inspection of Manufacturer abroad and verification of local storage facility.

Cases of Local Manufacturing received on Form 5-F

255.	Name, address of Applicant / Marketing Authorization Holder	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan.

		Telephone: + (21) 32213886, 32633590, UAN 111-742-762
	Name, address of Manufacturing site.	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 12652 dated 24-05-2022
	Details of fee submitted	PKR 30,000/-: dated 20/04/2022
	The proposed proprietary name / brand name	Roviros Eze Tablets 5mg + 10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Rosuvastatin USP……..…5mg Ezetimibe USP……..10mg (Innovator's Specs.)
	Pharmaceutical form of applied drug	Pink color round shape film coated tablet, one side engraved NQ and other side engraved bisect line.
	Pharmacotherapeutic Group of (API)	HMG-CoA reductase inhibitors in combination with other lipid modifying agents
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Roszet Tablets (Rosuvastatin + Ezetimibe) is registered and being marketed by Althera Pharmaceuticals LLC (Approved by US FDA, United States of America).
	For generic drugs (me-too status)	Rovista Eze Tablets 5/10mg by M/s Getz Pharma (Pvt.) Ltd., (Reg. No. 073716) Each film-coated tablet contains: Rosuvastatin Calcium eq. to Rosuvastatin…5mg Ezetimibe……10mg (Innovator's Specs.)
	GMP status of the Finished product manufacturer	New GMP Certificate granted on 28/05/2022.

		Tablet (General & Antibiotic), Capsule (General & Cephalosporin), Dry Powder for Suspension (General Antibiotic &Cephalosporin), Oral Liquid (Syrup) (Non-Antibiotic & Antibiotic), Cream / Ointment / Lotion (Non-Antibiotic & Antibiotic & Steroids), Eye & Ear Drops (Non-Antibiotic & Antibiotic & Steroids), Liquid Enema (General), Sachet (General), Small Volume Lyophilized Injectable (Non-Antibiotic, Antibiotic), Gel & Tablet (Hormones) sections approved.
	Name and address of API manufacturer.	Rosuvastatin Calcium: RUYUAN HEC PHARM CP., LTD. Xiaba Development Zone, RUtuan Country, Shaoguan City, Guangdong Province, P.R.China. Ezetimibe: Saptagir Laboratories Pvt. Ltd. Sy.No. Parts of 27, 46 & 50 to 56, Ananthasagar (Vill), Chegunta (Mandal), Medak (Dist.), Telangana, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Rosuvastatin Calcium: Monograph of Rosuvastatin Calcium is present is as per USP specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related compunds (Rosuvastatin related compound A, Rosuvastatin diastereomers, Rosuvastatin ketone, Rosuvastatin lactone, Rosuvastatin dehydro analog, Enantiomeric purity, Any unspecifies impurity, total Impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

		Ezetimibe: Monograph of Ezetimibe is present is as per USP specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances ({Desfluoroaniline analog, o-Fluorobenzene isomer, m-Fluoroaniline, Ezetimibe ketone, Unspecified Impurity, Total Impurities}, {Organic Impurities [Procedure-2 by HPLC*] S,S,S- Ezetimibe, R,R,R-Ezetimibe, R,R,S-Ezetimibe, S,S,R-Ezetimibe, R,S,R-Ezetimibe, Total chiral impurities, Total Impurities} specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Rosuvastatin Calcium: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Batches: RSV-201704101, RSV-201704102, RSV-201705101 Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: RSV-201704101, RSV-201704102, RSV-201705101 Ezetimibe: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Batches: EI0011117, EI0021217, EI0031217 Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: EI0011117, EI0021217, EI0031217
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader Rolip Eze Tablet 5/10mg is registered and being marketed by Hilton Pharma (Pvt.) Ltd., by performing quality tests (Description, Identification, Dissolution and Assay) CDP has been performed against the same brand that is Rolip-Eze Tablet 5/10mg (Rosuvastatin Calcium 5mg + Ezetimibe 10mg) by Hilton Pharma (Pvt.) Ltd., in Acid media (pH 1.2), Acetate Buffer (pH 4.5 & pH 4.5 with 0.45% SLS {QC release media for Ezetimibe}) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Rosuvastatin Calcium: RUYUAN HEC PHARM CP., LTD. Xiaba Development Zone, RUtuan Country, Shaoguan City, Guangdong Province, P.R.China. Ezetimibe: Saptagir Laboratories Pvt. Ltd. Sy.No. Parts of 27, 46 & 50 to 56, Ananthasagar (Vill), Chegunta (Mandal), Medak (Dist.), Telangana, India		
API Lot No.	Rosuvastatin Calcium RSV-(RD)202104602 Ezetimibe: EZ0160621		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's).		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	485DS01	485DS02	485DS03
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	13-10-2021	13-10-2021	13-10-2021
No. of Batches	03		
Administrative Portion			

7.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Rosuvastatin Calcium: Copy of GMP certificate no DE_BE_01_GMP_2019_0042 issued by State Office for Health and Social Affairs, Germany valid till 29/11/2022. Ezetimibe: Copy of GMP certificate no. 82079/TS/2022 issued by Drugs Control Administration, Government of Telangana valid till 22/02/2023.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Rosuvastatin Calcium: Copy of invoice no WIS210069 dated 16-06-2021 duly attested by Assistant Director, DRAP, Karachi on 30-06-2021 was provided. Ezetimibe: Copy of Invoice No. 2122/SL/031 dated 20-07-2021 duly attested by Assistant Director, DRAP, Karachi on 17-08-2021 was provided.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S. no.	Sections	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	3.2. S.4.4	COA of Rosuvastatin calcium by drug substance manufacturer evident that the drug substance meet the requirements of A-SPC-RSV-A instead of USP specification, justify, how the drug product manufacturer use USP specifications for quality testing of drug substance as mentioned on their submitted raw material analysis report, when the drug substance did not conform to USP specification.	Firm submitted the reply that the COA of drug substance also complies USP specification and the analytical procedure by drug substance also complied USP monograph. However the chloride content is not included in the COA of drug substance by drug substance manufacturer.

2. **According to the formulation development data, the applied product is bilayer film coated tablet, while the review report of innovator brand specifies that the roszet tablet is film coated pink color biconvex shaped tablet. Justify, how the applied product will be pharmaceutically equivalent to the innovator brand.**

Firm submitted the patent document of innovator brand according to which the solid dosage form is bilayer tablet, document was extracted from the link https://ppubs.uspto.gov/pubwebapp/. However, the review report of innovator brand present on USFDA official website claim that the Roszet tablet is film coated tablet. Further, previously Registered all brands of Rosuvastatin and Ezetimibe in Pakistan are film coated tablet.

FDA	TGA	MHRA
Orange book share patent of ROSZET which is US9763885 indicate product is bilayer film coated	Australian Public Assessment Report for Rosuzet, Ezalo The Advisory Committee on Prescription Medicines (ACPM), having considered the evaluations and the Delegate's overview, as well as the sponsor's response to these documents, advised the following: The ACPM resolved to recommend to the TGA delegate of the Minister and Secretary that: The ACPM, taking into account the submitted evidence of efficacy, safety and quality, agreed with the Delegate and considered Rosuzet/Ezalo bilayer tablets, containing ezetimibe and rosuvastatin (as calcium) as a new combination of active ingredients in the doses of 10 mg/5 mg, 10 mg/10 mg, 10 mg/20 mg and 10 mg/40 mg. **All of these stregnths are uncoated bilayer tablet according to the product description available on the official website of TGA Australia.**	Reference of product from "Public Assessment Report (NL/H/3647/001/DC) Twicor 10 mg/10 mg, film-coated tablets (rosuvastatin calcium/ezetimibe) As mention above, reference of Public Assessment report in section II Quality Aspects Introduction i.e.: "Twicor is a pink colored round shaped bilayer film-coated tablet embossed with "AL" on one side." Moreover in manufacturing process it is stated that The manufacturing process of the drug product can be divided in three steps: manufacture of rosuvastatin granules; manufacture of ezetimibe granules; compression into bi-layer tablets and film coating of tablets. The process is a standard manufacturing process." (Enclose for reference) Reference of product from MHRA (Summary Of Product Characteristics): NAME OF THE MEDICINAL PRODUCT: Twicor 20 mg/10 mg film-coated tablets QUALITATIVE AND QUANTITATIVE COMPOSITION:

				Each film-coated tablet contains 20 mg of rosuvastatin (as calcium) and 10 mg of ezetimibe. For the full list of excipients, see section 6.1.In section 6 of "Summary of Product Characteristics" it is clearly evident that product is bilayer tablet as separate core formulation for Rosuvastatin layer and separate core formulation for Ezetimibe layer is mention **Summary of product characteristic available on the official website of MHRA, describe the product as film coated tablet and the word bilayer is not mentioned in the document.Further,only the applied two stregnths i.e. 10/10 and 20/10 mg of Rosuvastatin/Ezetimibe is available in this brand.**
3.	3.2.P.5.2	Justify for using same dissolution medium for both active substances when the release behavior of both substance has varied across all three physiological mediums as evident from the submitted CDP report, similarly the innovator brand also recommended two different dissolution medium for both active substances.	Firm submitted the revised dissolution testing method in accordance with innovator brand Roszet tablet and performed 6th month stability studies as per revised finished product specification.	
4.	3.2.P.8.2	Provide the valid GMP certificate of API manufacturer Rosuvastatin calcium ,since the submitted certificate was of year 2019.	Firm submitted the valid Drug manufacturing licence of M/s. Ruyuan HEC Pharm Co. Ltd.,China,expiry date of license is 07th October,2026.	

Decision: Regisration Board deliberated the above cited references from MHRA wherein composition for core of each drug substance has been mentioned separately making it evident that the reference product is approved as bi-layer tablet. Hence Regsitration Board approved the "Roviros Eze 5/10 mg Tablet".

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

256.	Name, address of Applicant / Marketing Authorization Holder	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762
	Name, address of Manufacturing site.	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 12653 dated 24-05-2022
	Details of fee submitted	PKR 30,000/-: dated 20/04/2022
	The proposed proprietary name / brand name	Roviros Eze Tablets 10mg + 10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Rosuvastatin Calcium eq. to Rosuv USP……...…10mg Ezetimibe USP……..10mg (Innovator's Specs.)
	Pharmaceutical form of applied drug	Light yellow color round shape film coated tablet, one side engraved NQ and other side engraved bisect line.
	Pharmacotherapeutic Group of (API)	HMG-CoA reductase inhibitors in combination with other lipid modifying agents
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Roszet Tablets (Rosuvastatin + Ezetimibe) is registered and being marketed by Althera Pharmaceuticals LLC (Approved by US FDA, United States of America).
	For generic drugs (me-too status)	Rovista Eze Tablets 10/10mg by M/s Getz Pharma (Pvt.) Ltd., (Reg. No. 073718) Each film-coated tablet contains:

		Rosuvastatin Calcium eq. to Rosuvastatin……10mg Ezetimibe……10mg (Innovator's Specs.)
	GMP status of the Finished product manufacturer	New GMP Certificate granted on 28/05/2022. Tablet (General & Antibiotic), Capsule (General & Cephalosporin), Dry Powder for Suspension (General Antibiotic &Cephalosporin), Oral Liquid (Syrup) (Non-Antibiotic & Antibiotic), Cream / Ointment / Lotion (Non-Antibiotic & Antibiotic & Steroids), Eye & Ear Drops (Non-Antibiotic & Antibiotic & Steroids), Liquid Enema (General), Sachet (General), Small Volume Lyophilized Injectable (Non-Antibiotic, Antibiotic), Gel & Tablet (Hormones) sections approved.
	Name and address of API manufacturer.	Rosuvastatin Calcium: RUYUAN HEC PHARM CP., LTD. Xiaba Development Zone, RUtuan Country, Shaoguan City, Guangdong Province, P.R.China. Ezetimibe: Saptagir Laboratories Pvt. Ltd. Sy.No. Parts of 27, 46 & 50 to 56, Ananthasagar (Vill), Chegunta (Mandal), Medak (Dist.), Telangana, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Rosuvastatin Calcium: Monograph of Rosuvastatin Calcium is present is as per USP specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related compunds (Rosuvastatin related compound A, Rosuvastatin diastereomers,

		Rosuvastatin ketone, Rosuvastatin lactone, Rosuvastatin dehydro analog, Enantiomeric purity, Any unspecifies impurity, total Impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Ezetimibe: Monograph of Ezetimibe is present is as per USP specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances ({Desfluoroaniline analog, o-Fluorobenzene isomer, m-Fluoroaniline, Ezetimibe ketone, Unspecified Impurity, Total Impurities}, {Organic Impurities [Procedure-2 by HPLC*] S,S,S- Ezetimibe, R,R,R-Ezetimibe, R,R,S-Ezetimibe, S,S,R-Ezetimibe, R,S,R-Ezetimibe, Total chiral impurities, Total Impurities} specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Rosuvastatin Calcium: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Batches: RSV-201704101, RSV-201704102, RSV-201705101 Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: RSV-201704101, RSV-201704102, RSV-201705101 Ezetimibe: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Batches: EI0011117, EI0021217, EI0031217 Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: EI0011117, EI0021217, EI0031217
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities,

		specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader Rolip Eze Tablet 10/10mg is registered and being marketed by Hilton Pharma (Pvt.) Ltd., by performing quality tests (Description, Identification, Dissolution and Assay) CDP has been performed against the same brand that is Rolip-Eze Tablet 10/10mg (Rosuvastatin Calcium 10mg + Ezetimibe 10mg) by Hilton Pharma (Pvt.) Ltd., in Acid media (pH 1.2), Acetate Buffer (pH 4.5 & pH 4.5 with 0.45% SLS {QC release media for Ezetimibe}), Citrate Buffer (pH 6.6) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Rosuvastatin Calcium: RUYUAN HEC PHARM CP., LTD. Xiaba Development Zone, RUtuan Country, Shaoguan City, Guangdong Province, P.R. China. Ezetimibe: Saptagir Laboratories Pvt. Ltd. Sy.No. Parts of 27, 46 & 50 to 56, Ananthasagar (Vill), Chegunta (Mandal), Medak (Dist.), Telangana, India		
API Lot No.	Rosuvastatin Calcium RSV-(RD)202104602 Ezetimibe: EZ0160621		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's).		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	486DS01	486DS02	486DS03

Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	13-10-2021	13-10-2021	13-10-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Rosuvastatin Calcium: Copy of GMP certificate no DE_BE_01_GMP_2019_0042 issued by State Office for Health and Social Affairs, Germany valid till 29/11/2022. Ezetimibe: Copy of GMP certificate no. 82079/TS/2022 issued by Drugs Control Administration, Government of Telangana valid till 22/02/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Rosuvastatin Calcium: Copy of invoice no WIS210069 dated 16-06-2021 duly attested by Assistant Director, DRAP, Karachi on 30-06-2021 was provided. Ezetimibe: Copy of Invoice No. 2122/SL/031 dated 20-07-2021 duly attested by Assistant Director, DRAP, Karachi on 17-08-2021 was provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S. no.	Sections	Observations/Deficiencies/ Short-comings	Reply of the Firm

<table>
<tr><td>1.</td><td>3.2. S.4.4</td><td>COA of Rosuvastatin calcium by drug substance manufacturer evident that the drug substance meet the requirements of A-SPC-RSV-A instead of USP specification, justify, how the drug product manufacturer use USP specifications for quality testing of drug substance as mentioned on their submitted raw material analysis report, when the drug substance did not conform to USP specification.</td><td>Firm submitted the reply that the COA of drug substance also complies USP specification and the analytical procedure by drug substance also complied USP monograph. However the chloride content is not included in the COA of drug substance by drug substance manufacturer.</td></tr>
<tr><td>2.</td><td colspan="3">According to the formulation development data, the applied product is bilayer film coated tablet, while the review report of innovator brand specifies that the roszet tablet is film coated pink color biconvex shaped tablet. Justify, how the applied product will be pharmaceutically equivalent to the innovator brand.
Firm submitted the patent document of innovator brand according to which the solid dosage form is bilayer tablet, document was extracted from the link https://ppubs.uspto.gov/pubwebapp/. However, the review report of innovator brand present on USFDA official website claim that the Roszet tablet is film coated tablet. Further, previously Registered all brands of Rosuvastatin and ezetimibe in Pakistan are film coated tablet.
<table>
<tr><th>FDA</th><th>TGA</th><th>MHRA</th></tr>
<tr><td>Orange book share patent of ROSZET which is US9763885 indicate product is bilayer film coated</td><td>Australian Public Assessment Report for Rosuzet, Ezalo
The Advisory Committee on Prescription Medicines (ACPM), having considered the evaluations and the Delegate’s overview, as well as the sponsor’s response to these documents, advised the following:
The ACPM resolved to recommend to the TGA delegate of the Minister and Secretary that:
The ACPM, taking into account the submitted evidence of efficacy, safety and quality, agreed with the Delegate and considered Rosuzet/Ezalo bilayer tablets, containing ezetimibe and rosuvastatin (as calcium) as a new combination of active ingredients in the doses of 10 mg/5 mg, 10 mg/10 mg, 10 mg/20 mg and 10 mg/40 mg.

All of these stregnths are uncoated bilayer tablet according to the product</td><td>Reference of product from “Public Assessment Report (NL/H/3647/001/DC)
Twicor 10 mg/10 mg, film-coated tablets (rosuvastatin calcium/ezetimibe)
As mention above, reference of Public Assessment report in section II Quality Aspects Introduction i.e.:
“Twicor is a pink colored round shaped bilayer film-coated tablet embossed with “AL” on one side.”
Moreover in manufacturing process it is stated that
The manufacturing process of the drug product can be divided in three steps: manufacture of rosuvastatin granules; manufacture of ezetimibe granules; compression into bi-layer tablets and film coating of tablets. The process is a standard manufacturing process.”
(Enclose for reference)</td></tr>
</table></td></tr>
</table>

			description available on the official website of TGA Australia.	Reference of product from MHRA (Summary Of Product Characteristics): NAME OF THE MEDICINAL PRODUCT: Twicor 20 mg/10 mg film-coated tablets QUALITATIVE AND QUANTITATIVE COMPOSITION: Each film-coated tablet contains 20 mg of rosuvastatin (as calcium) and 10 mg of ezetimibe. For the full list of excipients, see section 6.1.In section 6 of "Summary of Product Characteristics" it is clearly evident that product is bilayer tablet as separate core formulation for Rosuvastatin layer and separate core formulation for Ezetimibe layer is mention **Summary of product characteristic available on the official website of MHRA, describe the product as film coated tablet and the word bilayer is not mentioned in the document.Further,only the applied two stregnths i.e. 10/10 and 20/10 mg of Rosuvastatin/Ezetimibe is available in this brand.**
3.	3.2.P.5.2	Justify for using same dissolution medium for both active substances when the release behavior of both substance has varied across all three physiological mediums as evident from the submitted CDP report, similarly the innovator brand also recommended two different dissolution medium for both active substances.		Firm submitted the revised dissolution testing method in accordance with innovator brand Roszet tablet and performed 6th month stability studies as per revised finished product specification.
4.	3.2.P.8.2	Provide the valid GMP certificate of API manufacturer Rosuvastatin		Firm submitted the valid Drug manufacturing licence of M/s. Ruyuan HEC Pharm Co.

		calcium ,since the submitted certificate was of year 2019.	Ltd.,China,expiry date of license is 07th October,2026.

Decision: Regisration Board deliberated the above cited references from MHRA wherein composition for core of each drug substance has been mentioned separately making it evident that the reference product is approved as bi-layer tablet. Hence Regsitration Board approved the "Roviros Eze 10/10 mg Tablet".

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

257.	Name, address of Applicant / Marketing Authorization Holder	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762
	Name, address of Manufacturing site.	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 12654 dated 24-05-2022
	Details of fee submitted	PKR 30,000/-: dated 09/05/2022
	The proposed proprietary name / brand name	Roviros Eze tablets 20mg/10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Rosuvastatin Calcium eq. to Rosuvastatin ….20mg Ezetimibe USP…….. 10mg (Innovator's Specs.)
	Pharmaceutical form of applied drug	Pink colored, round shaped, film coated tablet, both sides plain
	Pharmacotherapeutic Group of (API)	HMG-CoA reductase inhibitors in combination with other liquids modifying agents.
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	10's tablets

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Product Roszet tablets (Rosuvastatin + Ezetimibe) is Registered and being marketed Althera Pharmaceuticals LLC (Approved by US FDA, United states of America)
	For generic drugs (me-too status)	Getz Pharma. Rovista Eze tablet 20mg/10mg (Reg. No.073717) Each film coated tablet contains: Rosuvastatin Calcium eq. to Rosuvastatin ….20mg Ezetimibe…. 10mg (Innovator' s Specification)
	GMP status of the Finished product manufacturer	New GMP Certificate granted on 28/05/2022. Tablet (General & Antibiotic), Capsule (General & Cephalosporin), Dry Powder for Suspension (General Antibiotic &Cephalosporin), Oral Liquid (Syrup) (Non-Antibiotic & Antibiotic), Cream / Ointment / Lotion (Non-Antibiotic & Antibiotic & Steroids), Eye & Ear Drops (Non-Antibiotic & Antibiotic & Steroids), Liquid Enema (General), Sachet (General), Small Volume Lyophilized Injectable (Non-Antibiotic, Antibiotic), Gel & Tablet (Hormones) sections approved.
	Name and address of API manufacturer.	<u>Rosuvastatin Calcium:</u> Ruyan HEC PHARMA CO., LTD. Xiaba development zone, Ruyan Country, Shaoguan City, Guongdong Province, PR China Saptagir Laboratories Pvt. Ltd: Sy. No. Parts of 27, 46, 50 to 56 Ananthasagar (Vill), Chegunta (Mandal), Medak District, telagana , India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.

	Module III (Drug Substance)	Rosuvastatin Calcium: Monograph of Rosuvastatin Calcium is present is as per USP specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related compunds (Rosuvastatin related compound A, Rosuvastatin diastereomers, Rosuvastatin ketone, Rosuvastatin lactone, Rosuvastatin dehydro analog, Enantiomeric purity, Any unspecifies impurity, total Impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Ezetimibe: Monograph of Ezetimibe is present is as per USP specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances ({Desfluoroaniline analog, o-Fluorobenzene isomer, m-Fluoroaniline, Ezetimibe ketone, Unspecified Impurity, Total Impurities}, {Organic Impurities [Procedure-2 by HPLC*] S,S,S- Ezetimibe, R,R,R-Ezetimibe, R,R,S-Ezetimibe, S,S,R-Ezetimibe, R,S,R-Ezetimibe, Total chiral impurities, Total Impurities} specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Rosuvastatin Calcium: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Batches: RSV-201704101, RSV-201704102, RSV-201705101 Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: RSV-201704101, RSV-201704102, RSV-201705101 Ezetimibe: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months

		Batches: EI0011117, EI0021217, EI0031217 Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: EI0011117, EI0021217, EI0031217
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, eference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader Rolip Eze Tablet 20/10mg is registered and being marketed by Hilton Pharma (Pvt.) Ltd., by performing quality tests (Description, Identification, Dissolution and Assay) CDP has been performed against the same brand that is Rolip-Eze Tablet 20/10mg (Rosuvastatin Calcium 20mg + Ezetimibe 10mg) by Hilton Pharma (Pvt.) Ltd., in Acid media (pH 1.2), Acetate Buffer (pH 4.5 & pH 4.5 with 0.45% SLS {QC release media for Ezetimibe}) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Rosuvastatin Calcium Ruyan HEC PHARMA CO., LTD. Xiaba development zone, Ruyan Country, Shaoguan City, Guongdong Province, PR China Ezetimibe: Saptagir Laboratories Pvt. Ltd: Sy. No. Parts of 27, 46, 50 to 56 Ananthasagar (Vill), Chegunta (Mandal), Medak District, telagana , India Tel: 91-7815934034
API Lot No.	Rosuvastatin Calcium RSV-(RD)202104602 Ezetimibe: EZ0160621
Description of Pack (Container closure	Alu-Alu blister 10's tablets packed in unit carton.

system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6(Months)		
Batch No.	487DS01	487DS02	487DS03
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	13-10-2021	13-10-2021	13-10-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Rosuvastatin Calcium : Copy of GMP certificate no DE_BE_01_GMP_2019_0042 issued by State Office for Health and Social Affairs, Germany valid till 29/11/2022. Ezetimibe: Copy of GMP certificate no. 82079/TS/2022 issued by Drugs Control Administration, Government of Telangana valid till 22/02/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Rosuvastatin Calcium Copy of invoice no WIS210069 dated 16-06-2021 duly attested by Assistant Director, DRAP, Karachi on 30-06-2021 was provide. Ezetimibe : Copy of Invoice No. 2122/SL/031 dated 20-07-2021 duly attested by Assistant Director, DRAP, Karachi on 17-08-2021 was provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks OF Evaluator:		

<table>
<tr><th>S. no.</th><th>Sections</th><th>Observations/Deficiencies/ Short-comings</th><th>Reply of the Firm</th></tr>
<tr><td>1.</td><td>3.2. S.4.4</td><td>COA of Rosuvastatin calcium by drug substance manufacturer evident that the drug substance meet the requirements of A-SPC-RSV-A instead of USP specification, justify, how the drug product manufacturer use USP specifications for quality testing of drug substance as mentioned on their submitted raw material analysis report, when the drug substance did not conform to USP specification.</td><td>Firm submitted the reply that the COA of drug substance also complies USP specification and the analytical procedure by drug substance also complied USP monograph. However the chloride content is not included in the COA of drug substance by drug substance manufacturer.</td></tr>
<tr><td>2.</td><td colspan="3">According to the formulation development data, the applied product is bilayer film coated tablet, while the review report of innovator brand specifies that the roszet tablet is film coated pink color biconvex shaped tablet. Justify, how the applied product will be pharmaceutically equivalent to the innovator brand.
Firm submitted the patent document of innovator brand according to which the solid dosage form is bilayer tablet, document was extracted from the link https://ppubs.uspto.gov/pubwebapp/. However, the review report of innovator brand present on USFDA official website claim that the Roszet tablet is film coated tablet. Further, previously Registered all brands of Rosuvastatin and ezetimibe in Pakistan are film coated tablet.
<table>
<tr><th>FDA</th><th>TGA</th><th>MHRA</th></tr>
<tr><td>Orange book share patent of ROSZET which is US9763885 indicate product is bilayer film coated</td><td>Australian Public Assessment Report for Rosuzet, Ezalo
The Advisory Committee on Prescription Medicines (ACPM), having considered the evaluations and the Delegate’s overview, as well as the sponsor’s response to these documents, advised the following:
The ACPM resolved to recommend to the TGA delegate of the Minister and Secretary that:
The ACPM, taking into account the submitted evidence of efficacy, safety and quality, agreed with the Delegate and considered Rosuzet/Ezalo bilayer tablets, containing ezetimibe and rosuvastatin (as calcium) as a new combination of active ingredients in the doses of 10 mg/5 mg, 10 mg/10 mg, 10 mg/20 mg and 10 mg/40 mg.</td><td>Reference of product from “Public Assessment Report (NL/H/3647/001/DC)
Twicor 10 mg/10 mg, film-coated tablets (rosuvastatin calcium/ezetimibe)
As mention above, reference of Public Assessment report in section II Quality Aspects Introduction i.e.:
“Twicor is a pink colored round shaped bilayer film-coated tablet embossed with “AL” on one side.”
Moreover in manufacturing process it is stated that
The manufacturing process of the drug product can be divided in three steps: manufacture of rosuvastatin granules; manufacture of ezetimibe granules; compression into bi-layer tablets and film coating of tablets. The process is a</td></tr>
</table></td></tr>
</table>

			All of these stregnths are uncoated bilayer tablet according to the product description available on the official website of TGA Australia.	standard manufacturing process." (Enclose for reference) Reference of product from MHRA (Summary Of Product Characteristics): NAME OF THE MEDICINAL PRODUCT: Twicor 20 mg/10 mg film-coated tablets QUALITATIVE AND QUANTITATIVE COMPOSITION: Each film-coated tablet contains 20 mg of rosuvastatin (as calcium) and 10 mg of ezetimibe. For the full list of excipients, see section 6.1.In section 6 of "Summary of Product Characteristics" it is clearly evident that product is bilayer tablet as separate core formulation for Rosuvastatin layer and separate core formulation for Ezetimibe layer is mention **Summary of product characteristic available on the official website of MHRA, describe the product as film coated tablet and the word bilayer is not mentioned in the document.Further,only the applied two stregnths i.e. 10/10 and 20/10 mg of Rosuvastatin/Ezetimibe is available in this brand.**
3.	3.2.P.5.2	Justify for using same dissolution medium for both active substances when the release behavior of both substance has varied across all three physiological mediums as evident from the submitted CDP report, similarly the innovator brand also recommended two different dissolution medium for both active substances.	Firm submitted the revised dissolution testing method in accordance with innovator brand Roszet tablet and performed 6th month stability studies as per revised finished product specification.	

4.	3.2.P.8.2	Provide the valid GMP certificate of API manufacturer Rosuvastatin calcium ,since the submitted certificate was of year 2019.	Firm submitted the valid Drug manufacturing licence of M/s. Ruyuan HEC Pharm Co. Ltd.,China,expiry date of license is 07th October,2026.

Decision: Regisration Board deliberated the above cited references from MHRA wherein composition for core of each drug substance has been mentioned separately making it evident that the reference product is approved as bi-layer tablet. Hence Regsitration Board approved the "Roviros Eze 20/10 mg Tablet".

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

258.	Name, address of Applicant / Marketing Authorization Holder	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762 E-mail address: info@nabiqasim.com
	Name, address of Manufacturing site.	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762 E-mail address: info@nabiqasim.com
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 12636 dated 24-05-2022
	Details of fee submitted	PKR 75,000/-: dated 12/05/2022
	The proposed proprietary name / brand name	Roviros Eze tablets 40mg/10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Rosuvastatin Calcium eq. to Rosuvastatin ….40mg Ezetimibe USP…….. 10mg (Innovator's Specs.)

	Pharmaceutical form of applied drug	Light yellow, round shaped, one side engraved NQ while other side is plain.
	Pharmacotherapeutic Group of (API)	HMG-CoA reductase inhibitors in combination with other liquids modifying agents.
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	10's tablets
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Product Roszet tablets (Rosuvastatin + Ezetimibe) is Registered and being marketed Althera Pharmaceuticals LLC (Approved by US FDA, United states of America)
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	New GMP Certificate granted on 28/05/2022. Tablet (General & Antibiotic), Capsule (General & Cephalosporin), Dry Powder for Suspension (General Antibiotic &Cephalosporin), Oral Liquid (Syrup) (Non-Antibiotic & Antibiotic), Cream / Ointment / Lotion (Non-Antibiotic & Antibiotic & Steroids), Eye & Ear Drops (Non-Antibiotic & Antibiotic & Steroids), Liquid Enema (General), Sachet (General), Small Volume Lyophilized Injectable (Non-Antibiotic, Antibiotic), Gel & Tablet (Hormones) sections approved.
	Name and address of API manufacturer.	<u>Rosuvastatin Calcium:</u> Ruyan HEC PHARMA CO., LTD. Xiaba development zone, Ruyan Country, Shaoguan City, Guongdong Province, PR China Saptagir Laboratories Pvt. Ltd: Sy. No. Parts of 27, 46, 50 to 56 Ananthasagar (Vill), Chegunta (Mandal), Medak District, telagana , India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Rosuvastatin Calcium:

		Monograph of Rosuvastatin Calcium is present is as per USP specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related compunds (Rosuvastatin related compound A, Rosuvastatin diastereomers, Rosuvastatin ketone, Rosuvastatin lactone, Rosuvastatin dehydro analog, Enantiomeric purity, Any unspecifies impurity, total Impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Ezetimibe: Monograph of Ezetimibe is present is as per USP specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances ({Desfluoroaniline analog, o-Fluorobenzene isomer, m-Fluoroaniline, Ezetimibe ketone, Unspecified Impurity, Total Impurities}, {Organic Impurities [Procedure-2 by HPLC*] S,S,S- Ezetimibe, R,R,R-Ezetimibe, R,R,S-Ezetimibe, S,S,R-Ezetimibe, R,S,R-Ezetimibe, Total chiral impurities, Total Impurities} specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Rosuvastatin Calcium: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Batches: RSV-201704101, RSV-201704102, RSV-201705101 Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: RSV-201704101, RSV-201704102, RSV-201705101 Ezetimibe: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Batches: EI0011117, EI0021217,

		EI0031217 Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: EI0011117, EI0021217, EI0031217
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader Zympass tablet 40/10mg is registered and being marketed by Sanofi Ireland., by performing quality tests (Description, Identification, Dissolution and Assay) CDP has been performed against the same brand that is Zympass tablet 40/10mg (Rosuvastatin Calcium 40mg + Ezetimibe 10mg) by Sanofi Ireland, in Acid media (pH 1.2), Acetate Buffer (pH 4.5 & pH 4.5 with 0.45% SLS {QC release media for Ezetimibe}) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Rosuvastatin Calcium Ruyan HEC PHARMA CO., LTD. Xiaba development zone, Ruyan Country, Shaoguan City, Guongdong Province, PR China Ezetimibe: Saptagir Laboratories Pvt. Ltd: Sy. No. Parts of 27, 46, 50 to 56 Ananthasagar (Vill), Chegunta (Mandal), Medak District, telagana , India Tel: 91-7815934034
API Lot No.	Rosuvastatin Calcium RSV-(RD)202104602 Ezetimibe: EZ0160621
Description of Pack (Container closure system)	Alu-Alu blister 10’s tablets packed in unit carton.

Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6(Months)		
Batch No.	488DS01	488DS02	488DS03
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	13-10-2021	13-10-2021	13-10-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Rosuvastatin Calcium : Copy of GMP certificate no DE_BE_01_GMP_2019_0042 issued by State Office for Health and Social Affairs, Germany valid till 29/11/2022. Ezetimibe: Copy of GMP certificate no. 82079/TS/2022 issued by Drugs Control Administration, Government of Telangana valid till 22/02/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Rosuvastatin Calcium Copy of invoice no WIS210069 dated 16-06-2021 duly attested by Assistant Director, DRAP, Karachi on 30-06-2021 was provide. Ezetimibe : Copy of Invoice No. 2122/SL/031 dated 20-07-2021 duly attested by Assistant Director, DRAP, Karachi on 17-08-2021 was provided.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S. no.	Sections	Observations/Deficiencies/ Short-comings	Reply of the Firm

<table>
<tr><td>1.</td><td>3.2. S.4.4</td><td>COA of Rosuvastatin calcium by drug substance manufacturer evident that the drug substance meet the requirements of A-SPC-RSV-A instead of USP specification, justify, how the drug product manufacturer use USP specifications for quality testing of drug substance as mentioned on their submitted raw material analysis report, when the drug substance did not conform to USP specification.</td><td>Firm submitted the reply that the COA of drug substance also complies USP specification and the analytical procedure by drug substance also complied USP monograph. However the chloride content is not included in the COA of drug substance by drug substance manufacturer.</td></tr>
<tr><td>2.</td><td colspan="3">According to the formulation development data, the applied product is bilayer film coated tablet, while the review report of innovator brand specifies that the roszet tablet is film coated pink color biconvex shaped tablet. Justify, how the applied product will be pharmaceutically equivalent to the innovator brand.
Firm submitted the patent document of innovator brand according to which the solid dosage form is bilayer tablet, document was extracted from the link https://ppubs.uspto.gov/pubwebapp/. However, the review report of innovator brand present on USFDA official website claim that the Roszet tablet is film coated tablet. Further, previously Registered all brands of Rosuvastatin and ezetimibe in Pakistan are film coated tablet.
<table>
<tr><th>FDA</th><th>TGA</th><th>MHRA</th></tr>
<tr><td>Orange book share patent of ROSZET which is US9763885 indicate product is bilayer film coated</td><td>Australian Public Assessment Report for Rosuzet, Ezalo
The Advisory Committee on Prescription Medicines (ACPM), having considered the evaluations and the Delegate’s overview, as well as the sponsor’s response to these documents, advised the following:
The ACPM resolved to recommend to the TGA delegate of the Minister and Secretary that:
The ACPM, taking into account the submitted evidence of efficacy, safety and quality, agreed with the Delegate and considered Rosuzet/Ezalo bilayer tablets, containing ezetimibe and rosuvastatin (as calcium) as a new combination of active ingredients in the doses of 10 mg/5 mg, 10 mg/10 mg, 10 mg/20 mg and 10 mg/40 mg.

All of these stregnths are uncoated bilayer tablet according to the product</td><td>Reference of product from “Public Assessment Report (NL/H/3647/001/DC)
Twicor 10 mg/10 mg, film-coated tablets (rosuvastatin calcium/ezetimibe)
As mention above, reference of Public Assessment report in section II Quality Aspects Introduction i.e.:
“Twicor is a pink colored round shaped bilayer film-coated tablet embossed with “AL” on one side.”
Moreover in manufacturing process it is stated that
The manufacturing process of the drug product can be divided in three steps: manufacture of rosuvastatin granules; manufacture of ezetimibe granules; compression into bi-layer tablets and film coating of tablets. The process is a standard manufacturing process.”
(Enclose for reference)</td></tr>
</table></td></tr>
</table>

			description available on the official website of TGA Australia.	Reference of product from MHRA (Summary Of Product Characteristics): NAME OF THE MEDICINAL PRODUCT: Twicor 20 mg/10 mg film-coated tablets QUALITATIVE AND QUANTITATIVE COMPOSITION: Each film-coated tablet contains 20 mg of rosuvastatin (as calcium) and 10 mg of ezetimibe. For the full list of excipients, see section 6.1.In section 6 of "Summary of Product Characteristics" it is clearly evident that product is bilayer tablet as separate core formulation for Rosuvastatin layer and separate core formulation for Ezetimibe layer is mention **Summary of product characteristic available on the official website of MHRA, describe the product as film coated tablet and the word bilayer is not mentioned in the document.Further,only the applied two stregnths i.e. 10/10 and 20/10 mg of Rosuvastatin/Ezetimibe is available in this brand.**
3.	3.2.P.5.2	Justify for using same dissolution medium for both active substances when the release behavior of both substance has varied across all three physiological mediums as evident from the submitted CDP report, similarly the innovator brand also recommended two different dissolution medium for both active substances.		Firm submitted the revised dissolution testing method in accordance with innovator brand Roszet tablet and performed 6th month stability studies as per revised finished product specification.
4.	3.2.P.8.2	Provide the valid GMP certificate of API manufacturer Rosuvastatin		Firm submitted the valid Drug manufacturing licence of M/s. Ruyuan HEC Pharm Co.

		calcium ,since the submitted certificate was of year 2019.	Ltd.,China,expiry date of license is 07th October,2026.

Decision: Regisration Board deliberated the above cited references from MHRA wherein composition for core of each drug substance has been mentioned separately making it evident that the reference product is approved as bi-layer tablet. Hence Regsitration Board approved the "Roviros Eze 40/10 mg Tablet".

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

259.	Name, address of Applicant / Marketing Authorization Holder	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial triangle, kahuta road, Islamabad-44000
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial triangle, kahuta road, Islamabad-44000
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32725 dated 01-12-2021
	Details of fee submitted	PKR 30,000/-: dated 23/11/2021
	The proposed proprietary name / brand name	Ivabradine 5mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ivabradine as Hydrochloride……5mg
	Pharmaceutical form of applied drug	Light Orange colored, round, biconvex shaped, film coated tablet
	Pharmacotherapeutic Group of (API)	hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers
	Reference to Finished product specifications	Innovator Specs
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Corlanor 5mg tablet by M/s AMGEN INC, USFDA Approved.
	For generic drugs (me-too status)	Ivadin 5mg Tablet by M/s PharmEvo Pvt. Ltd., Reg. No. 090910
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 11-02-2019, was

		valid till 09-05-2022 after extension for 3 months. Request for GMP inspection R&1 date: 22-12-2021 is provided.
	Name and address of API manufacturer.	M/s Lewens Labs Pvt., Ltd. Plant: D2/CH/376-377, G.I.D.C, Dahej, Dist. Bharuch, Gujarat, India-392130
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 2°C to 8°C for 60 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months Batches: (LIV0014001, LIV0014002, LIV0014003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Sivab 5mg tablet by Getz Pharmaceuticals Pvt. Ltd., by performing quality tests (Physical Appearance, identification, Average weight, Disintegration Time,

		Assay). CDP has been performed against the same brand that is Sivab 5mg tablet by Getz Pharmaceuticals Pvt. Ltd., in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Lewens Labs Pvt., Ltd. Plant: D2/CH/376-377, G.I.D.C, Dahej, Dist. Bharuch, Gujarat, India-392130		
API Lot No.	LFP003020009A1		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 3 months Accelerated: 3 months		
Frequency	Accelerated: 0, 2, 4, 6, 9, 12, 18, 24 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	NPD 228 T-01	NPD 228 T-02	NPD 228 T-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	12-06-2021	12-06-2021	12-06-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 286th meeting decided to approve registration of Sofovir-V 400mg/100mg Tablet. Inspection date: 5 & 15 October, 2018 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.

2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Submitted
4.	Stability study data of API from API manufacturer	Submitted
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML, License No. G/25/2241 issued by FDCA valid till 22/10/2022.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice to import Ivabradine HCl (0.350 Kg, invoice No: COM/20-21/PR002) and ADC (I&E) granted by DRAP dated on 10/02/2021
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted
9.	Drug-excipients compatibility studies (where applicable)	Not Applicable
10.	Complete batch manufacturing record of three stability batches.	Submitted
11.	Record of comparative dissolution data (where applicable)	Submitted
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S. no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Scientific justification is required for not performing the optical rotation test while analysis of drug substance, since the optical rotation test is the part of COA of drug substance manufacturer	Firm replied that Test for Optical rotation performed and included in the COA.

	and also included in the drug substance specification of innovator brand.	
2.	Justification is required for using different assay method by drug product manufacturer from that specified by the drug substance manufacturer.	Firm replied that we had mistakenly mentioned the outdated method from DMF in the dossier. Correct assay method has been submitted.
3.	Specify details including batch number and manufacturing date of the reference / comparator product against which pharmaceutical equivalence is performed. CDP performed against Getz pharma product Sivab 5mg and 7.5mg tablets. Sivab 5mg tablets Batch number 143F83 Mfg 12-2020 and expiry is 12-2022 Sivab 7.5mg tablets Batch number 019F84 Mfg 11-2019 and expiry is 11-2021.	
4.	Justification is required for not performing content uniformity test while establishing the pharmaceutical equivalence against the reference product.	Firm replied that Content uniformity test is performed on separate sheets. Not mentioned on COA.These will be provided.
5.	Review report of innovator brand revealed that the recommended acceptance criteria for disintegration test is ≤ 10 minutes, justify the disintegration limit adapted for the applied product i.e. NMT 30min in light of innovator's limit.	Firm replied that We had followed the limits of USP general monograph i.e NMT 30 minutes for coated tablets. However, during testing this can be seen that our tablets disintegrate in very less time almost 4 to 5 minutes. So, this can be reviewed.
6.	Specify the time point in the dissolution acceptance limit at which NLT 80% drug should be dissolved.	Firm replied that as per USP general chapter we selected the 30 minutes' time, while as per CDP profile the drug release in buffer medium is greater. Even in 20 minutes 92.8 % drug was released. However the innovator brand approved in USFDA revealed that the drug product dissolves (> % in 15 min) across the physiologically relevant range of pH.
7.	Submit complete stability data of 6 months performed at accelerated stability condition and stability data of minimum 6 moth or complete data till the claimed shelf performed at long term stability conditions.	Firm submitted the 6th month stability data of drug product.
8.	Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product.	Firm submitted DRAP attested documents of lot no. LFR003020009A1.

Decision: Approved.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the**

commitment submitted in the registration application. **• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** **• Registration Board further decided that registration letter will be issued after submission of revised dissolution and disintegration acceptance criteria in line with USFDA innovator brand and performance of both these test in accordance with revised specification on next time point of stability.** **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021**		
260.	Name, address of Applicant / Marketing Authorization Holder	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial triangle, kahuta road, Islamabad-44000
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial triangle, kahuta road, Islamabad-44000
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. dated 01-12-2021
	Details of fee submitted	PKR 30,000/-: dated 23/11/2021
	The proposed proprietary name / brand name	Ivabradine 7.5mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ivabradine as Hydrochloride……7.5mg
	Pharmaceutical form of applied drug	Light Orange colored, round shaped biconvex, film coated tablet
	Pharmacotherapeutic Group of (API)	hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers
	Reference to Finished product specifications	Innovator Specs
	Proposed Pack size	14’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Corlanor 7.5mg tablet by M/s AMGEN INC, USFDA Approved.
	For generic drugs (me-too status)	Ivadin 7.5mg Tablet by M/s PharmEvo Pvt. Ltd., Reg. No. 090911
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 11-02-2019, was valid till 09-05-2022 after extension for 3 months.

		Request for GMP inspection R&1 date: 22-12-2021 is provided.
	Name and address of API manufacturer.	M/s Lewens Labs Pvt., Ltd. Plant: D2/CH/376-377, G.I.D.C, Dahej, Dist. Bharuch, Gujarat, India-392130
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 2°C to 8°C for 60 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months Batches: (LIV0014001, LIV0014002, LIV0014003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Sivab 7.5mg tablet by Getz Pharmaceuticals Pvt. Ltd., by performing quality tests (Physical Appearance, identification, Average weight, Disintegration Time, Assay). CDP has been performed against the same

		brand that is Sivab 7.5mg tablet by Getz Pharmaceuticals Pvt. Ltd., in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Lewens Labs Pvt., Ltd. Plant: D2/CH/376-377, G.I.D.C, Dahej, Dist. Bharuch, Gujarat, India-392130		
API Lot No.	LFP003020009A1		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 3 months Accelerated: 3 months		
Frequency	Accelerated: 0, 2, 4, 6, 9, 12, 18, 24 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	NPD 231 T-01	NPD 231 T-02	NPD 231 T-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	12-06-2021	03-06-2021	03-06-2021
No. of Batches	03		

Administrative Portion		
13.	**Reference of previous approval of applications with stability study data of the firm**	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 286th meeting decided to approve registration of Sofovir-V 400mg/100mg Tablet. Inspection date: 5 & 15 October, 2018 The report shows that: The HPLC software is 21 CFR compliant. The firm has provided data loggers with stability chambers.
14.	**Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.**	Submitted
15.	**Method used for analysis of API from both API Manufacturer and Finished Product manufacturer**	Submitted

16.	**Stability study data of API from API manufacturer**	Submitted
17.	**Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.**	Copy of DML, License No. G/25/2241 issued by FDCA valid till 22/10/2022.
18.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice to import Ivabradine HCl (0.350 Kg, invoice No: COM/20-21/PR002) and ADC (I&E) granted by DRAP dated on 10/02/2021
19.	**Protocols followed for conduction of stability study**	Submitted
20.	**Method used for analysis of FPP**	Submitted
21.	**Drug-excipients compatibility studies (where applicable)**	Not Applicable
22.	**Complete batch manufacturing record of three stability batches.**	Submitted
23.	**Record of comparative dissolution data (where applicable)**	Submitted
24.	**Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.**	Submitted
25.	**Compliance Record of HPLC software 21CFR & audit trail reports on product testing.**	Submitted
26.	**Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)**	Submitted

Remarks OF Evaluator:

S. no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Scientific justification is required for not performing the optical rotation test while analysis of drug substance, since the optical rotation test is the part of COA of drug substance manufacturer and also included in the drug substance specification of innovator brand.	Firm replied that Test for Optical rotation performed and included in the COA.
2.	Justification is required for using different assay method by drug product manufacturer from that specified by the drug substance manufacturer.	Firm replied that we had mistakenly mentioned the outdated method from DMF in the dossier. Correct assay method has been submitted.
3.	Specify details including batch number and manufacturing date of the reference / comparator product against which pharmaceutical equivalence is performed. CDP performed against Getz pharma product Sivab 5mg and 7.5mg tablets.	

	Sivab 5mg tablets Batch number 143F83 Mfg 12-2020 and expiry is 12-2022 Sivab 7.5mg tablets Batch number 019F84 Mfg 11-2019 and expiry is 11-2021.	
4.	Justification is required for not performing content uniformity test while establishing the pharmaceutical equivalence against the reference product.	Firm replied that Content uniformity test is performed on separate sheets. Not mentioned on COA.These will be provided.
5.	Review report of innovator brand revealed that the recommended acceptance criteria for disintegration test is ≤ 10 minutes, justify the disintegration limit adapted for the applied product i.e. NMT 30min in light of innovator's limit.	Firm replied that We had followed the limits of USP general monograph i.e NMT 30 minutes for coated tablets. However, during testing this can be seen that our tablets disintegrate in very less time almost 4 to 5 minutes. So, this can be reviewed.
6.	Specify the time point in the dissolution acceptance limit at which NLT 80% drug should be dissolved.	Firm replied that as per USP general chapter we selected the 30 minutes' time, while as per CDP profile the drug release in buffer medium is greater. Even in 20 minutes 92.8 % drug was released. However the innovator brand approved in USFDA revealed that the drug product dissolves (> % in 15 min) across the physiologically relevant range of pH.
7.	Submit complete stability data of 6 months performed at accelerated stability condition and stability data of minimum 6 moth or complete data till the claimed shelf performed at long term stability conditions.	Firm submitted the 6th month stability data of drug product.
8.	Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product.	Firm submitted DRAP attested documents of lot no. LFR003020009A1.

Decision: Approved.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

• Registration Board further decided that registration letter will be issued after submission of revised dissolution and disintegration acceptance criteria in line with USFDA innovator brand and performance of both these test in accordance with revised specification on next time point of stability.

The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

261.	Name, address of Applicant / Marketing Authorization Holder	M/s PDH Laboratories (Pvt) Ltd. 9.5km Sheikhupura Road Lahore
	Name, address of Manufacturing site.	M/s PDH Laboratories (Pvt) Ltd. 9.5km

		Sheikhupura Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27452 dated 28/09/2022
	Details of fee submitted	PKR 30,000/-: dated 23/06/2022
	The proposed proprietary name / brand name	Pd-Lac Syrup 120ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	100ml Pd-Lac contains: 66.7g Lactulose USP
	Pharmaceutical form of applied drug	Clear viscous liquid , colorless or pale brownish yellow color Syrup
	Pharmacotherapeutic Group of (API)	Laxative
	Reference to Finished product specifications	Manufacturer Specs
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Duphalac Syrup 66.7g/100ml Abbott Laboratories.
	For generic drugs (me-too status)	Duphalac Syrup 66.7g/100ml Abbott Laboratories (Pakistan) Ltd. Reg #006655
	GMP status of the Finished product manufacturer	New GMP license was granted on 27/07/2022. New additional section for oral liquid syrup (General) was approved on June 7,2022.
	Name and address of API manufacturer.	Fresenius Kabi Austria Gmbh EstermannstraBe 17, A-4020 Linz.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug

		substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Lactulose solution is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity of related substances , specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5% RH for 6 months Batches: (17144742,17144852,17144861)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Duphalac syrup 66.7mg/100ml by M/s Abbott Laboratories (Pakistan) Ltd. by performing quality tests (Identification, Assay). Comparative dissolution profile is not applicable
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s Fresenius Kabi Austria Gmbh EstermannstraBe 17, A-4020 Linz.
API Lot No.	17203771
Description of Pack (Container closure system)	Clear viscous liquid , colorless or pale brownish yellow color Syrup filled in a ambered glass bottle sealed with aluminium cap packed in a unit carton along with leaflet.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	40 bottles	40 bottles	40 bottles
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	11-01-2022	12-01-2022	13-01-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. INS.480019-0065-001.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.5201/2020/DRAP-AD-CD(I&E) dated 16/04/2020 is submitted wherein the permission to import different APIs including Lactulose Solution for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings
1.	**Justify the finished product specifications as "Manufacturer's specifications" since the drug product monograph is available in USP. Revise your specifications along with submission of requisite fee.** Firm replied that they claimed innovator's specification as per the duphalac syrup brand of M/s. Abbott Lab., Karachi.
2.	**Clarification is required either you have import lactulose concentration or lactulose solution from the Fresenius Kabi, Austria, since the COA of drug substance reflect that that lactulose solution is the drug substance while the stability data and manufacturing data of drug substance reveal that the imported drug substance is lactulose concentrate.** Firm submitted the reply that they have imported Lactulose solution from M/s. Fresenius kabi, Austria and submit COA of drug substance (Lactulose solution as a reference.

3.	**Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required", since you have only submitted analytical procedure by drug substance manufacturer which is also not in accordance with USP.** Undertaking submitted, they will submit later.
4.	**Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted" Further specify how the testing of drug substance was carried out without performing verification studies.** Undertaking submitted, they will submit later.
5.	**Submit detailed analytical procedure used for testing of drug product in accordance with USP monograph of lactose solution.** Firm submit the analytical procedure which is not in accordance with USP in terms of assay procedure.
6.	**Justify for performing the verification of assay procedure using UV method since in USP monograph of lactose solution assay has been performed on HPLC.** Not submitted.
7.	***For quantitative tests, actual numerical results should be provided rather than vague statements such as "within limits" or "conforms"*, since the submitted batch analysis report of drug product only mentioned the statement complies and positive in result column.** Revised Batch analysis report submitted by the firm.
8.	• Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated). **Submitted** • Submit the valid GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin. **Submitted**
9.	**Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.** Submitted

Decision: Deferred for submission of following:

- **Revise specification in line with USP monograph of Lactose Solution along with requisite fee.**
- **Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required", since you have only submitted analytical procedure by drug substance manufacturer which is also not in accordance with USP.**
- **Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted" Further specify how the testing of drug substance was carried out without performing verification studies.**
- **Submit detailed analytical procedure used for testing of drug product in accordance with USP monograph of lactose solution along with the analytical method verification report.**

262.	Name, address of Applicant / Marketing	M/s Surge Laboratories Private Limited

	Authorization Holder	10th KM, Faisalabad Road, Bikhi District Sheikhupura, Pakistan.
	Name, address of Manufacturing site.	M/s Surge Laboratories Private Limited 10th KM, Faisalabad Road, Bikhi District Sheikhupura, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 20435 dated 27/07/2021
	Details of fee submitted	PKR 20,000/-: dated 05/05/2021
	The proposed proprietary name / brand name	Hemarest 250mg/5ml Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Tranexamic Acid BP … 250mg (BP Specifications)
	Pharmaceutical form of applied drug	Clear, Colorless liquid free from foreign particles.
	Pharmacotherapeutic Group of (API)	Antihaemorrhagics, Antifibrinolytics.
	Reference to Finished product specifications	BP Specifications
	Proposed Pack size	5ml x 5's 5ml x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Azeptil Injection 250mg/5mlt by M/s Medochemie Ltd., MHRA Approved.
	For generic drugs (me-too status)	Tranmax Injection by M/s Nabiqasim Industries (Pvt). Ltd., Reg. No. 057745
	GMP status of the Finished product manufacturer	New license granted on 19/12/2015 General Liquid Injectables (Including blow fill seal area) & Cephalosporin Dry Powder Injectables section approved.
	Name and address of API manufacturer.	Changzhou Yinsheng Pharmaceuticals Co. (Pvt). Ltd. Weitang, Chemical zone, Xinbei District, Changzhou, Jiangsu Province - 213033 China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form,

		manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Tranexamic Acid is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months. Batches: (100301, 100303, 100302)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Transamin Injection 250mg/5ml by Hilton Pharma by performing quality tests (Description, pH, Assay, Bacterial Endotoxins and Sterility).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity, Limit of Detection, Limit of Quantitation, Ruggedness & Robustness.

STABILITY STUDY DATA	
Manufacturer of API	Changzhou Yinsheng Pharmaceuticals Co. (Pvt). Ltd. Weitang, Chemical zone, Xinbei District, Changzhou, Jiangsu Province - 213033 China
API Lot No.	20141213

Description of Pack (Container closure system)	5ml Break Ring Clear Glass Ampoule (USP Type I) as 5ml x 5's 5ml x 10's		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TRI-001V	TRI-002W	TRI-003W
Batch Size	1500 Ampoules	1500 Ampoules	1500 Ampoules
Manufacturing Date	02-2015	08-2016	09-2016
Date of Initiation	02-2015	08-2016	09-2016
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. JS20170680 issued by China Food And Drug Administration valid till 20/06/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of Invoice No. 2014DW145-DRAP dated 08.01.2015 is submitted for Tranexamic Acid.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	**Sections**	**Observations/Deficiencies/ Short-comings**
1.	**3.2. S.4.3**	**Validation of analytical procedures** Provide analytical Method Verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.
2.	**3.2. P.2**	• Justification is required regarding the use of NaOH and HCl for pH adjustment as the innovator/reference product has not been used any excipient for pH adjustment. • Justify the performance of pharmaceutical equivalence with Transmin injection instead of using innovator / reference product.

		• Justify the process of terminal sterilization via autoclave at 121°C for 15minutes with reference to degradation occurred in the accelerated stability studies conducted at 40°C as claimed in pharmaceutical development section. If the degradation of product start at 40°C then how the product will bear the temperature of 121°C during terminal sterilization. • Justify the degradation of your product during accelerated stability studies because as per the innovator /reference product, the drug product remains stable during the accelerated stability studies conducted at 40 ° C, relative humidity 75%, 6 months and no overage has been used in their formulation.
3.	**3.2. P.5.1**	**Validation of analytical procedures:** You have submitted the validation studies of assay method of transic injection by spectrophotometer while according to the BP monograph of tranexamic acid injection assay has been performed via potentiometric titration, clarification is required in this regard.
4.	**3.2. P.8**	**Stability** • As per the submitted stability data, stability studies of all three batches has been initiated in the year 2015 and 2016 despite that firm has submitted only 6 months data of real time stability study for all three batches. Submit the remaining real time stability data of all three batches. • Submitted raw data sheets reflect that the assay of drug product has been performed via UV spectrophotometer while according to BP, assay of the drug product has been performed by potentiometric titration. Justify, how your product complies BP specification. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.
5.	**2.3. R.1.1**	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.
6.	**Amendment in QOS (Module 2) for above points.**	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

263.	Name, address of Applicant / Marketing Authorization Holder	M/s SAMI Pharmaceuticals (Pvt.) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.
	Name, address of Manufacturing site.	M/s SAMI Pharmaceuticals (Pvt.) Ltd. F-95, Off Hub River Road, S.I.T.E. Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11127 dated 09/05/2022
	Details of fee submitted	PKR 75,000/-: dated 26/02/2022

	The proposed proprietary name / brand name	AMPISOL 5mg/2ml Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2ml contains: Ampisulpride …….5mg Innovator's specs
	Pharmaceutical form of applied drug	IV Injection
	Pharmacotherapeutic Group of (API)	dopamine-2 (D2) antagonist
	Reference to Finished product specifications	Innovator Specs
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	BARHEMSYS (Amisulpride) Injection 5mg/2ml M/s ACACIA PHARMA Inc, 8440 Allison Pointe Blvd, Suite 100, Indianapolis, IN 46250 USA, USFDA Approved.
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 03-08-2022 Liquid Injectable (LVP/SVP) (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Sun Pharmaceutical Industries Limited, Sathammai Village, Karunkuzhi PostMadhuranthagam Taluk, Kancheepuram District Tamilnadu – 603 303, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 60 months, 9 months & 12 months respectively Batches: (PDAMSFL021, CCAMRNF002, AMRNF20052) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6

		months Batches: (PDNAMSFL017, PDNAMSFL019, PDNAMSFL018)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence	Pharmaceutical Equivalence have been established against the brand leader that is BARHEMSYS (Amisulpride) Injection 5mg/2ml M/s ACACIA PHARMA Inc, by performing quality tests (Appearance, Identification, Clarity, pH, Wt./ml, Osmolarity, Particulate matter, Assay, Organic impurities, Bacterial Endotoxin Test, Packaging material)
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, accuracy, precision including repeatability & intermediate precision, robustness, specificty.

STABILITY STUDY DATA			
Manufacturer of API	M/s Sun Pharmaceutical Industries Limited, Sathammai Village, Karunkuzhi PostMadhuranthagam Taluk, Kancheepuram District Tamilnadu – 603 303, India.		
API Lot No.	AMRNF20062		
Description of Pack (Container closure system)	Glass Vial USP Type-1 (Low Borosilicate)		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-07	Lab-08	Lab-09
Batch Size	1700ml	1700ml	1700ml
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	08-07-2021	08-07-2021	08-07-2021
No. of Batches	03		
Administrative Portion			

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Reference of our last onsite panel inspection for instant dosage form conducted during last two years i.e. IBRUO (Ibuprofen) 800mg/100 ml injection which was presented in 289th meeting of the registration board & hence approved & registered by registration board Date of inspection: 28th January 2019 The inspection report confirms following points The HPLC software is 21CFR Compliant • Audit trail on the testing reports is av • Adequate monitoring and control a stability chamber. Chambers are monitored through software having a alerts as well. • Related manufacturing area, equipr and utilities are GMP compliant.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Sun Pharmaceutical Industries Ltd., is valid until 31st December 2021and they have applied for further revalidation period from 01.01.2022to 31.12.2024 and their application is under process in this Directorate *(letter attached)*
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of Aramex Courier slip and declaration from API supplier regarding sending of Amisulpride (Quantity of 100gms) through Aramex Courier receipt No. 9155441378 dated 18-04-2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Raw data sheets alongwith chromatograph of Amisulpride COA & Summary data sheet are attached
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliance record of HPLC software 21CFR & Audit trail testing reports are attached
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Digital data logger for temperature and humidity monitoring of stability chambers are attached

Remarks OF Evaluator:

S. no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Justification is required for not using sterile drug substance for manufacturing of injection, as evident from the COA of drug substance by drug substance manufacturer.	Firm in their reply stated that The API *(Amisulpride)* used for development of our product Ampisol *(Amisulpride)* 5mg/2ml Injection is of injectable grade. API manufacturer has performed test for Bacterial Endotoxin test, Aerobic bacterial test, E. Coli, Salmonella, Pseudomonas & Staphylococcus

		aureus test to ensure the quality of injectable grade material. Certificate of Analysis of API manufacturer is enclosed for reference. Moreover it is not essential for the drug substance to be sterile for those drug products which are terminally sterilized/aseptically filled in their manufacturing process.
2.	As per the review literature of innovator brand, the drug product is subject to photo degradation within 12 hours, so there are no such precautionary measures included in the manufacturing procedure to protect the filled vials from light neither the step of packaging of filled vial in unit carton preferably within 12 hours after optical checking is included in the final stage. Clarification is required in this regard.	Firm replied that Precautionary measure for photo degradation during manufacturing process from Bulk manufacturing to secondary packaging have been taken and also mentioned in batch Manufacturing record *(BMR)* which is enclosed for reference *(Annex-C, Page no.7, 12, 17)* It is also included in CTD dossier 3.2.P.2.3 Manufacturing process development and in 3.2.P.3.4. Controls of Critical steps and intermediates as a critical parameter, Reference enclosed in *(Annex-D, Page no.4 & 9)* As far duration from optical checking to secondary packaging is concerned, your suggestion is highly valuable for us and we will include this control for commercial production i.e. secondary packaging will be done within 12 hours after optical checking
3.	Submit valid GMP certificate of drug substance manufacturer, since the submitted certificate was valid until 31-12-2021.	Firm submitted the copy of GMP certificate of API manufacturer.
4.	Submit documents for the procurement of API including copy of commercial invoice attested by AD (I&E) DRAP	Firm submit the consignment receipt of API only.
Decision: Deferred for justification of using non-injectable grade drug substance for preparation of parenteral solutions, along with submission of supporting reference from the ICH guidelines or other international stringent regulatory guidance documents.		

Cases of Export Facilitation priority:

264.	Name, address of Applicant / Marketing Authorization Holder	M/s ATCO LABORATORIES LTD, B-18, S.I.T.E, KARACHI.
	Name, address of Manufacturing site.	M/s ATCO LABORATORIES LTD, B-18, S.I.T.E, KARACHI.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1200 dated 13-01-2022
	Details of fee submitted	PKR 30,000/- dated 19/11/2021 PKR 45,000/- dated 17/10/2022
	The proposed proprietary name / brand name	APREMILAST TABLET 10MG.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Apremilast MS 10mg
	Pharmaceutical form of applied drug	Brick red colored, round, biconvex, film coated tablets having both sides plain.
	Pharmacotherapeutic Group of (API)	Apremilast belongs to a class of drugs known as phosphodiesterase 4 (PDE4) inhibitors.
	Reference to Finished product specifications	As per Innovator's Specifications.
	Proposed Pack size	Apremilast 10mg is available in Starter pack of 14's & 28's Starter pack of 14days Contains Pack of 4's 10mg (Pouch 1) Pack of 4's 20mg (Pouch 2) Pack of 5's &14's of 30mg (Pouch 3) And Starter pack of of 28days contains Pack of 4's 10mg (Pouch 1) Pack of 4's 20mg (Pouch 2) Pack of 5's & 3x 14's of 30mg (Pouch 3)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Otezla 10mg Amgen Ltd 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK
	For generic drugs (me-too status)	Not Applicable
	GMP status of the Finished product manufacturer	Renewal for DML dated 27-03-2021submitted along with previous copy DML.
	Name and address of API manufacturer.	M/s Enantiotech Corporation Limited 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development Zone, Guangdong Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.

	Module III (Drug Substance)	In-House specifications of Apremilast is provided. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C±2°C,65%±5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (AMTO3K150303, AMTO3K150401, AMTO3K151102)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Otezla 10mg Tablet by Amgen Ltd 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Otezla 10mg Tablet by Amgen Ltd 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Enantiotech Corporation Limited No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development Zone, Guangdong Province, China.
API Lot No.	AMT03R200603
Description of	ALU-PVC blister

Pack (Container closure system)	Aluminium foil pouch Printed carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months With three-month stability 13/01/2022 With six month stability 03/02/2022		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MY195C	MY196C	MY197C
Batch Size	2930 tablets	2930 tablets	2930Tablets
Manufacturing Date	05 – 2021	05 – 2021	05 – 2021
Date of Initiation	21-06-2021	21-06-2021	21-06-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Rofl 500mg tablet Approved in DRB 277 held on 27-29 December 2017.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of Enantiotech Corporation Limited issued by People's Republic of Chins valid till 01/04/2021 till 30/04/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide analytical Method verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Submitted

<table>
<tr><td>2.</td><td>Justification is required for not performing the assay test during stability studies of drug substance.</td><td>Revised stability studies including assay result are submitted by the firm.</td></tr>
<tr><td>3.</td><td colspan="2">Justify for setting the acceptance criteria of dissolution test other than adapted by innovator/reference product. The review report of innovator brand approved in USFDA revealed that the recommended dissolution criteria should be NLT (Q) in 30 minutes, while the dissolution criteria adapted for applied product was much wider i.e.NLT 80% (Q) in 60 minutes.
Firm submitted the reply that the recommended dissolution criteria as should be NLT (Q) in 30minutes in USFDA report is published in September 2013 with dissolution media having 0.3%SLS with 75RPM. In both above references we used the latest dissolution recommendation published in FDA Database Dated: 05/18/2017 and established the same on our applied product strengths in which the dissolution criteria are NLT 80% (Q) in 60 minutes. (Section 3.2.P.5.1)
Table 2: Comparison of US FDA Dissolution Parameters
<table>
<tr><th>Parameter</th><th>Updated 2013</th><th>Updated 2017</th><th>Changes</th></tr>
<tr><td>USP Apparatus</td><td>II (Paddle)</td><td>II (Paddle)</td><td>Same</td></tr>
<tr><td>Speed</td><td>75 RPM</td><td>60 RPM</td><td>Reduced</td></tr>
<tr><td>Medium</td><td>0.3% SLS in 25mM Sodium Phosphate Buffer, pH 6.8</td><td>0.15% SLS in 25mM Sodium Phosphate Buffer, pH 6.8</td><td>Reduced quan SLS</td></tr>
<tr><td>Volume</td><td>900 mL</td><td>900 mL</td><td>Same</td></tr>
</table>
In both above references we used the latest dissolution recommendation published in FDA Database Dated: 05/18/2017 and established the same on our applied product strengths in which the dissolution results achieved 85% on 60 minutes time point with less than 10% RSD, that's why we have taken T=60 Minutes and Q = 75% as per the procedure defined in SETTING DISSOLUTION RELEASE SPECIFICATIONS in 293rd Meeting minutes.
However, in the FDA dissolution database the recommended sampling time is till 45minutes and one-time point before has been adapted for the acceptance criteria of dissolution 30 minutes in this instant case.
Later, firm submitted the revised dissolution parameters in line with innovator brand approved in USFDA.</td></tr>
<tr><td>4.</td><td>How will the analyst determined the quantity of crushed powder equivalent to 30mg of Apremilast in the sample preparation of assay testing of 10mg and 20mg strength, further specify the concentration of final dilution of sample, as it is not mentioned in the assay procedure of all three strength</td><td>Firm submitted the reply that "The revised testing procedure with concentration in mg/mL of final dilutions of samples is being submitted to you for reference while the quantity of crushed powder as the portion of tablets considering the average weight of tablets is mentioned in all the strengths accordingly".</td></tr>
<tr><td>5.</td><td>Submit the revised pack size and display presentation of packaging container in accordance with the decision of registration of Apremilast tablet 321st meeting of Registration Board .</td><td>Firm replied that as advised in 321st meeting of DRB, we are hereby submitting the revised pack size and display presentation of packaging container for
1. 14 days Starter Pack
2. 28 days Starter Pack
3. Maintenance Pack of 56 Tablets for Apremilast 30mg.</td></tr>
<tr><td>6.</td><td>• Provide stability data of at least six months or till the claimed shelf life</td><td>submitted</td></tr>
</table>

	performed both at accelerated and long term stability condition. • Submit COA of relevant batch of drug substance used in product development and stability studies from both drug substance as well as drug product manufacturer in section 3.2.S.4.4.	
265.	Name, address of Applicant / Marketing Authorization Holder	M/s ATCO LABORATORIES LTD, B-18, S.I.T.E, KARACHI.
	Name, address of Manufacturing site.	M/s ATCO LABORATORIES LTD, B-18, S.I.T.E, KARACHI.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1201 dated 13-01-2022
	Details of fee submitted	PKR 30,000/- dated 19/11/2021 PKR 45,000/- dated 17/10/2022
	The proposed proprietary name / brand name	APREMILAST TABLET 20MG.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Apremilast MS 20mg
	Pharmaceutical form of applied drug	Buff colored, round, biconvex, film-coated tablets.
	Pharmacotherapeutic Group of (API)	Apremilast belongs to a class of drugs known as phosphodiesterase 4 (PDE4) inhibitors.
	Reference to Finished product specifications	As per Innovator's Specifications.
	Proposed Pack size	Apremilast 20mg is available in Starter pack of 14's & 28's Starter pack of 14days Contains Pack of 4's 10mg (Pouch 1) Pack of 4's 20mg (Pouch 2) Pack of 5's &14's of 30mg (Pouch 3) And Starter pack of of 28days contains Pack of 4's 10mg (Pouch 1) Pack of 4's 20mg (Pouch 2) Pack of 5's & 3x 14's of 30mg (Pouch 3)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Otezla 20mg

		Amgen Ltd 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK
	For generic drugs (me-too status)	Not Applicable
	GMP status of the Finished product manufacturer	Renewal for DML dated 27-03-2021submitted along with previous copy DML.
	Name and address of API manufacturer.	M/s Enantiotech Corporation Limited 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development Zone, Guangdong Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	In-House specifications of Apremilast is provided. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C±2°C,65%±5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (AMTO3K150303, AMTO3K150401, AMTO3K151102)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Otezla 20mg Tablet by Amgen Ltd 216

		Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Otezla 20mg Tablet by Amgen Ltd 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Enantiotech Corporation Limited No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development Zone, Guangdong Province, China.		
API Lot No.	AMT03-A06-200401		
Description of Pack (Container closure system)	ALU-PVC blister Aluminium foil pouch Printed carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months With three-month stability 13/01/2022 With six month stability 03/02/2022		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MY192C	MY193C	MY194C
Batch Size	4895 tablets	4895 tablets	4895 tablets
Manufacturing Date	05 – 2021	05 – 2021	05 – 2021
Date of Initiation	21-06-2021	21-06-2021	21-06-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Rofl 500mg tablet Approved in DRB 277 held on 27-29 December 2017.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of Enantiotech Corporation Limited issued by People's Republic of Chins valid till 01/04/2021 till 30/04/2024.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S. no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide analytical Method verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Submitted
2.	Justification is required for not performing the assay test during stability studies of drug substance.	Revised stability studies including assay result are submitted by the firm.
3.	Justify for setting the acceptance criteria of dissolution test other than adapted by innovator/reference product. The review report of innovator brand approved in USFDA revealed that the recommended dissolution criteria should be NLT (Q) in 30 minutes, while the dissolution criteria adapted for applied product was much wider i.e.NLT 80% (Q) in 60 minutes. Firm submitted the reply that the recommended dissolution criteria as should be NLT (Q) in 30minutes in USFDA report is published in September 2013 with dissolution media having 0.3%SLS with 75RPM. In both above references we used the latest dissolution recommendation published in FDA Database Dated: 05/18/2017 and established the same on our applied product strengths in which the dissolution criteria are NLT 80% (Q) in 60 minutes. (Section 3.2.P.5.1)	

Table 2: Comparison of US FDA Dissolution Parameters

Parameter	Updated 2013	Updated 2017	Changes
USP Apparatus	II (Paddle)	II (Paddle)	Same
Speed	75 RPM	60 RPM	Reduced
Medium	0.3% SLS in 25mM Sodium Phosphate Buffer, pH 6.8	0.15% SLS in 25mM Sodium Phosphate Buffer, pH 6.8	Reduced quant SLS
Volume	900 mL	900 mL	Same

In both above references we used the latest dissolution recommendation published in FDA Database Dated: 05/18/2017 and established the same on our applied product strengths in which the dissolution results achieved 85% on 60 minutes time point with less than 10% RSD, that's why we have taken T=60 Minutes and Q = 75% as per the procedure defined in SETTING DISSOLUTION RELEASE SPECIFICATIONS in 293rd Meeting minutes. (Section 3.2.P.5.1)

	However, in the FDA dissolution database the recommended sampling time is till 45minutes and one time point before has been adapted for the acceptance criteria of dissolution 30 minutes in this instant case. Later, firm submitted the revised dissolution parameters in line with innovator brand approved in USFDA.	
4.	How will the analyst determined the quantity of crushed powder equivalent to 30mg of Apremilast in the sample preparation of assay testing of 10mg and 20mg strength, further specify the concentration of final dilution of sample, as it is not mentioned in the assay procedure of all three strength	Firm submitted the reply that "The revised testing procedure with concentration in mg/mL of final dilutions of samples is being submitted to you for reference while the quantity of crushed powder as the portion of tablets considering the average weight of tablets is mentioned in all the strengths accordingly".
5.	Submit the revised pack size and display presentation of packaging container in accordance with the decision of registration of Apremilast tablet 321st meeting of Registration Board .	Firm replied that as advised in 321st meeting of DRB, we are hereby submitting the revised pack size and display presentation of packaging container for **4.** 14 days Starter Pack **5.** 28 days Starter Pack **6.** Maintenance Pack of 56 Tablets for Apremilast 30mg.
6.	• Provide stability data of at least six months or till the claimed shelf life performed both at accelerated and long term stability condition. • Submit COA of relevant batch of drug substance used in product development and stability studies from both drug substance as well as drug product manufacturer in section 3.2.S.4.4.	submitted

266.	Name, address of Applicant / Marketing Authorization Holder	M/s ATCO LABORATORIES LTD, B-18, S.I.T.E, KARACHI.
	Name, address of Manufacturing site.	M/s ATCO LABORATORIES LTD, B-18, S.I.T.E, KARACHI.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.1202 dated 13-01-2022
	Details of fee submitted	PKR 30,000/- dated 19/11/2021 PKR 45,000/- dated 17/10/2022
	The proposed proprietary name / brand	APREMILAST TABLET 30MG.

	name	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Apremilast MS 30mg
	Pharmaceutical form of applied drug	Blue colored, round, biconvex, film-coated tablets
	Pharmacotherapeutic Group of (API)	Apremilast belongs to a class of drugs known as phosphodiesterase 4 (PDE4) inhibitors.
	Reference to Finished product specifications	As per Innovator's Specifications.
	Proposed Pack size	Apremilast 30mg is available in Starter pack of 14's & 28's Starter pack of 14days Contains Pack of 4's 10mg (Pouch 1) Pack of 4's 20mg (Pouch 2) Pack of 5's &14's of 30mg (Pouch 3) And Starter pack of of 28days contains Pack of 4's 10mg (Pouch 1) Pack of 4's 20mg (Pouch 2) Pack of 5's & 3x 14's of 30mg (Pouch 3) Maintenance Pack of 56's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Otezla 30mg Amgen Ltd 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK
	For generic drugs (me-too status)	Apremist 30mg Crystolite Pharma, Islamabad
	GMP status of the Finished product manufacturer	Renewal for DML dated 27-03-2021submitted along with previous copy DML.
	Name and address of API manufacturer.	M/s Enantiotech Corporation Limited 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development Zone, Guangdong Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	In-House specifications of Apremilast is provided. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related

		substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C±2°C,65%±5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (AMTO3K150303, AMTO3K150401, AMTO3K151102)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Otezla 30mg Tablet by Amgen Ltd 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Otezla 30mg Tablet by Amgen Ltd 216 Cambridge Science Park, Milton Road, Cambridge, CB4 0WA, UK in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Enantiotech Corporation Limited No. 6, Zhongjing Rd, Zhongshan Torch Hi-Tech Industrial Development Zone, Guangdong Province, China.
API Lot No.	AMT03R200603
Description of Pack (Container closure system)	ALU-PVC blister Aluminium foil pouch Printed carton
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MY187C	MY188C	MY189C
Batch Size	7000 tablets	7000 tablets	7000 tablets
Manufacturing Date	05 – 2021	05 – 2021	05 – 2021
Date of Initiation	21-06-2021	21-06-2021	21-06-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Rofl 500mg tablet Approved in DRB 277 held on 27-29 December 2017.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate of Enantiotech Corporation Limited issued by People's Republic of Chins valid till 01/04/2021 till 30/04/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide analytical Method verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Submitted
2.	Justification is required for not performing the assay test during stability studies of drug substance.	Submitted

<table>
<tr><td>3.</td><td colspan="2">Justify for setting the acceptance criteria of dissolution test other than adapted by innovator/reference product. The review report of innovator brand approved in USFDA revealed that the recommended dissolution criteria should be NLT (Q) in 30 minutes, while the dissolution criteria adapted for applied product was much wider i.e.NLT 80% (Q) in 60 minutes.
Firm submitted the reply that the recommended dissolution criteria as should be NLT (Q) in 30minutes in USFDA report is published in September 2013 with dissolution media having 0.3%SLS with 75RPM. In both above references we used the latest dissolution recommendation published in FDA Database Dated: 05/18/2017 and established the same on our applied product strengths in which the dissolution criteria are NLT 80% (Q) in 60 minutes. (Section 3.2.P.5.1)
Table 2: Comparison of US FDA Dissolution Parameters
<table>
<tr><th>Parameter</th><th>Updated 2013</th><th>Updated 2017</th><th>Changes</th></tr>
<tr><td>USP Apparatus</td><td>II (Paddle)</td><td>II (Paddle)</td><td>Same</td></tr>
<tr><td>Speed</td><td>75 RPM</td><td>60 RPM</td><td>Reduced</td></tr>
<tr><td>Medium</td><td>0.3% SLS in 25mM Sodium Phosphate Buffer, pH 6.8</td><td>0.15% SLS in 25mM Sodium Phosphate Buffer, pH 6.8</td><td>Reduced quanti SLS</td></tr>
<tr><td>Volume</td><td>900 mL</td><td>900 mL</td><td>Same</td></tr>
</table>
In both above references we used the latest dissolution recommendation published in FDA Database Dated: 05/18/2017 and established the same on our applied product strengths in which the dissolution results achieved 85% on 60 minutes time point with less than 10% RSD, that's why we have taken T=60 Minutes and Q = 75% as per the procedure defined in SETTING DISSOLUTION RELEASE SPECIFICATIONS in 293rd Meeting minutes. (Section 3.2.P.5.1)
However in the FDA dissolution database the recommended sampling time is till 45minutes and one time point before has been adapted for the acceptance criteria of dissolution 30 minutes in this instant case.
Later, firm submitted the revised dissolution parameters in line with innovator brand approved in USFDA.</td></tr>
<tr><td>4.</td><td>How will the analyst determined the quantity of crushed powder equivalent to 30mg of Apremilast in the sample preparation of assay testing of 10mg and 20mg strength, further specify the concentration of final dilution of sample, as it is not mentioned in the assay procedure of all three strength</td><td>Firm submitted the reply that "The revised testing procedure with concentration in mg/mL of final dilutions of samples is being submitted to you for reference while the quantity of crushed powder as the portion of tablets considering the average weight of tablets is mentioned in all the strengths accordingly".</td></tr>
<tr><td>5.</td><td>Submit the revised pack size and display presentation of packaging container in accordance with the decision of registration of Apremilast tablet 321st meeting of Registration Board .</td><td>Firm replied that as advised in 321st meeting of DRB, we are hereby submitting the revised pack size and display presentation of packaging container for
1. 14 days Starter Pack
2. Maintenance Pack of 56 Tablets for Apremilast 30mg.</td></tr>
<tr><td>6.</td><td>• Provide stability data of at least six months or till the claimed shelf life performed both at</td><td>submitted</td></tr>
</table>

	accelerated and long term stability condition. • Submit COA of relevant batch of drug substance used in product development and stability studies from both drug substance as well as drug product manufacturer in section 3.2.S.4.4.	

Decision: Registration Board approved the aplications of Apremilast 10mg tablet. Apremilast 20mg tablet & Apremilast 30mg tablet with Innovator's specifications. Furthermore, in order to standardize the drug as per dosage regimen of the innovator's drug product as approved by reference regulatory authorities, the Board decided that the manufacturers shall adopt any of the presentation as decided by Registration Board in its 321st meeting for the "Apremilast "tablets" and registration letter will be issued accordingly.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of performance of dissolution testing in line with revised specification on next time point of stability.**

267.	Name, address of Applicant / Marketing Authorization Holder	M/s Wimits Pharmaceuticals (Pvt) Ltd. Lahore. Plot #129 Sundar Industrial Estate,Raiwind road,Lahore
	Name, address of Manufacturing site.	M/s Wimits Pharmaceuticals (Pvt) Ltd. Plot #129 Sundar Industrial Estate,Raiwind road,Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32416 dated 29/11/2021
	Details of fee submitted	PKR 30,000/-: dated 22/10/2021
	The proposed proprietary name / brand name	Zapnal 5mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Olanzapine …….5mg
	Pharmaceutical form of applied drug	Amost white coloured, film coated round plain tablets
	Pharmacotherapeutic Group of (API)	Atypical antipsychotic
	Reference to Finished product	USP

	specifications	
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Zyprexa 5mg tablet by M/s Eli lilly and company limited, USFDA Approved.
	For generic drugs (me-too status)	Olepra 5mg tablet by M/s Genetics Pharmaceuticlas Pvt. Ltd, Reg. No. 038671
	GMP status of the Finished product manufacturer	New license granted on 08/09/2021 Tablet (General) section approved.
	Name and address of API manufacturer.	M/s RAMPEX LABS PRIVATE LIMITED Plot No. 34-C Jawaharlal Nehru Pharma City PARAWADA.VISAKHAPATNAM – 531 019, ANDHRA PRADESH, INDIA.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of olanzapine is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity Malononitrile, 2-fluoro Nitrobenzone, Propanaldehyde, N-methyl piperazine, impurity A,B,C, Methanol, acetone, IPA, toluene, dimethyl Formamide, 1,4 dioxane & specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(LAN-4P/00613, LAN-4P/00713, LAN-4P/00813)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer

		medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Zapnal 5mg tablet by Wimits Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is olepra 5mg tablet by Genetics Pharmaceuticlas Pvt. Ltd in Acid media (pH-1.2), Acetate Buffer (pH-4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s RAMPEX LABS PRIVATE LIMITED Plot No. 34-C Jawaharlal Nehru Pharma City PARAWADA.VISAKHAPATNAM – 531 019, ANDHRA PRADESH, INDIA.		
API Lot No.	LAN/0040420		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TZP001	TZP002	TZP003
Batch Size	2500 tab	2500 tab	2500 tab
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	12-01-2021	15-01-2021	19-01-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 21/VP/AP/2011/B/CC/R issued by FDCA valid till 29/09/2024.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.8623/2020/DRAP-AD-CD(I&E) dated 03/07/2020 is submitted wherein the permission to import different APIs including olanzapine for the purpose of test/analysis and stability studies is granted. ZHI-CI/4506/0520, DATE: 14-05-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide raw data sheets and chromatograms of analytical method verification report as the submitted report did not specify the assay procedures.	Firm submitted the analytical procedure along verification report in accordance with USP monograph.
2.	Comparative dissolution profile report of drug product revealed that at 30 minutes not more than 80% drug release in all three physiological medium, justify the results with the acceptance limit of dissolution i.e. NLT 80% in 30min using pH 1.2 as the recommended dissolution medium as per USP monograph.	Firm submitted the revised CDP report in which more than 80% drug release within 30 minutes without justification/clarification.
3.	Adapt the acceptance limit of dissolution in term of Q, since the USP monograph specify the limit with Q value i.e. NLT 80% (Q) of the labelled amount of olanzapine dissolved.	Revised specification submitted by the firm.
4.	Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product. • Submit valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued	API lot no. LAN/0040420 has been used in manufacturing of each batch of drug product. GMP certificate of API manufacturer M/s. RAMPEX Labs Pvt. Ltd., India has been submitted by the firm which was vaild till 20-04-2021,however the manufacturing license of manufacturer is valid till 29-09-2024 as written on the said GMP certificate.

	by relevant regulatory authority of country of origin.	

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

268.	Name, address of Applicant / Marketing Authorization Holder	M/s Horizon Healthcare (Pvt.) Ltd. Plot no. 33 Sundar Industrial Estate Lahore.
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt.) Ltd. Plot no. 33 Sundar Industrial Estate Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐Domestic and Export sales
	Dy. No. and date of submission	Dy.No 33175 dated 21-12-2021
	Details of fee submitted	Rs.75,000/- dated 24-11-2021
	The proposed proprietary name / brand name	Bempp-Z Tablet 180/10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet contains: Bempedoic Acid…….180mg Ezetimibe……...10mg
	Pharmaceutical form of applied drug	Light blue color, oblong shaped, film coated tablets
	Pharmacotherapeutic Group of (API)	Bempedoic Acid: Lipid modifying agents, other lipid modifying agents. Adenosine triphosphate citrate lyase (ACL) inhibitor Ezetimibe: adenosine triphosphate-citrate lyase (ACL) inhibitor, Cholesterol absorption inhibitor.
	Reference to Finished product specifications	As per innovator
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nexlizet Tablets 180/10mg approved by US-FDA
	For generic drugs (me-too status)	Drug is not available in Pakistan
	GMP status of the Finished product manufacturer	Last inspection report dated 18.06.2020 concluded good level of cGMP compliance.

<table>
<tr><td></td><td>Name and address of API manufacturer.</td><td>Bempedoic Acid:
Metrochem API Private Limited, Unit-IV,
Plot No. 34B, 40B & 60B,
J.N. Pharma City, Thanam Village,
Parawada Mandal, Visakhapatnam District,
Andhra Pradesh, 531021,
India (IND).
Ezetimibe:
Zhejiang Tianyu Pharmaceutical Co., Ltd.
No.15, Donghai 5th Avenue, Zhejiang
Provincial Chemical and Medical Raw
Materials Base Linhai Zone, Taizhou City.</td></tr>
<tr><td></td><td>Module-II (Quality Overall Summary)</td><td>Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.</td></tr>
<tr><td></td><td>Module III (Drug Substance)</td><td>The firm as submitted detail of General information, General properties, Manufacturers, description of manufacturing process and process controls, Characterization, Impurities, Control of drug substance, Reference standard or materials container closure system and stability studies of drug substance.</td></tr>
<tr><td></td><td>Stability studies</td><td>Stability study conditions:
Bempedoic Acid:
Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months
Accelerated: 40°C ± 2°C/75% ± 5%RH for 6 months
<table>
<tr><th>Batch No</th><th>Accelerated</th><th>Long Term</th></tr>
<tr><td>BMPD-V/A070/44</td><td>6 Months</td><td>60 Months</td></tr>
<tr><td>BMPD-V/A070/45</td><td>6 Months</td><td>60 Months</td></tr>
<tr><td>BMPD-V/A070/46</td><td>6 Months</td><td>60 Months</td></tr>
</table>
Ezetimibe:
Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months
Accelerated: 40°C ± 2°C/75% ± 5%RH for 6 months</td></tr>
</table>

		<table><tr><td>Batch No</td><td>Accelerated</td><td>Long Term</td></tr><tr><td>10910-171101</td><td>6 Months</td><td>36 Months</td></tr><tr><td>10910-171102</td><td>6 Months</td><td>36 Months</td></tr><tr><td>10910-171103</td><td>6 Months</td><td>36 Months</td></tr></table>
	Module-III (Drug Product):	The firm has submitted detail of Drug Products including Description and composition of drug product, Pharmaceutical Development, Manufacturing process development, Microbiological attribution, Manufacturer, Master formulations, Description of Manufacturing Process and Process Controls, Control of Critical Steps and Intermediates, Process Validation and/ or Evaluation, Control of Excipients with specification and Analytical methods, Control of Drug Products including Finished product specifications and test methods, validation of Analytical methods, Batch analysis , Characterization of impurities, reference standard or impurities, Container closure and stabilities studies.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Nexlizet Tablets 180/10mg approved by US-FDA by performing quality tests (Identification, Assay, and Dissolution. CDP has been performed against the same brand that is Nexlizet Tablets 180/10mg approved by US-FDA approved by US-FDA in Acid media (pH 1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8)
	Analytical method validation/verification of product	Method verification studies have submitted including Introduction, Verification of assay method, Specificity, Accuracy, Precision, Linearity concentration and peak range.
STABILITY STUDY DATA		
Manufacturer of API		Bempedoic Acid: Metrochem API Private Limited, Unit-IV, Plot No. 34B, 40B & 60B, J.N. Pharma City, Thanam Village, Parawada Mandal, Visakhapatnam District, Andhra Pradesh, 531021, India (IND). Ezetimibe: Zhejiang Tianyu Pharmaceutical Co., Ltd. No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw

		Materials Base Linhai Zone, Taizhou City.	
API Lot No.		Bempedoic Acid: HANPC21002 Ezetimibe: 10910-170403	
Description of Pack (Container closure system)		Alu-Alu. Blisters with aluminum foil having leaflet and packed in unit carton	
Stability Storage Condition		Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH	
Time Period		Real time: 6 months Accelerated: 6 months	
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 8, 12, 16, 20, 24(Months)	
Batch No.		EZT-001	EZT-002
Batch Size		5000 tab	5000 tab
Manufacturing Date		08-2021	08-2021
Date of Initiation		08-2021	08-2021
No. of Batches		02	
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product: EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) Dayzol 30mg Capsules, Dayzol 60mg Capsules (Dexlansoprazole) which was conducted on 1st June, 2021 and was presented in 307th meeting of Registration Board held on 08-10th June, 2021. Registration Board decided to approve registration of EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) Dayzol 30mg Capsules, Dayzol 60mg Capsules (Dexlansoprazole) by M/s. Horizon Healthcare (Pvt) Ltd. Lahore. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report:	

<table>
<tr><td></td><td></td><td>i. The HPLC software is 21 CFR compliant.
ii. Audit trail on the testing reports of EMPAZON 10mg and 25mg Tablets, Dayzol 30mg and 60mg Capsules is available.
iii. Adequate monitoring and control are available for stability chamber. Chamber are controlled and monitored through software having alarm system for alerts as well.
iv. Verification of performance of dissolution test at buffer stage
pH 5.5 for Dayzol Capsules 30mg and 60mg.
Performance of dissolution test for EMPAZON 10mg and 25mg Tablets with revised specifications i.e not less than 80% (Q) in 15minutes at initial and 01-month time point.</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Bempedoic Acid:
Firm had provided valid GMP & DML Certificate of M/s Metrochem API Private Limited Issued by Drug Control Administration Telangana India
DML Valid upto: 29-09-2024
GMP Valid upto: 29-10-2022
Ezetimibe:
Firm had provided valid GMP & DML Certificate of M/s Zhejiang Tianyu Pharmaceutical Co., Ltd.
Issued by Zhejiang Province Food & Drug Administration Bureau
DML Valid upto: 16-06-2025
GMP Valid upto: 20-11-2024</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted.
Bempedoic Acid:
<table>
<tr><td>Batch No.</td><td>Invoice No.</td><td>Quantity Imported</td><td>Date of approval by DRAP</td></tr>
<tr><td>HANPC21002</td><td>AE/21/0576</td><td>2.0kgs</td><td>13-07-2021</td></tr>
<tr><td colspan="4">Ezetimibe:</td></tr>
<tr><td>Batch No.</td><td>Invoice No.</td><td>Quantity Imported</td><td>Date of approval by DRAP</td></tr>
<tr><td>10910-170403</td><td>TYI210608</td><td>0.150kgs</td><td>13-07-2021</td></tr>
</table></td></tr>
</table>

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail reports have been submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers.

Remarks of Evaluator:
Innovator brand Nexlizet Tablet (180/10) approved in USFDA with the following indications, warning and precautions:
Indications:
NEXLIZET, which contains an adenosine triphosphate-citrate lyase (ACL) inhibitor and a cholesterol absorption inhibitor, is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.
Limitations of Use: The effect of NEXLIZET on cardiovascular morbidity and mortality has not been determined.
Warning and Precautions:
Hyperuricemia: Elevations in serum uric acid have occurred. Assess uric acid levels periodically as clinically indicated. Monitor for signs and symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate.
Tendon Rupture: Tendon rupture has occurred. Discontinue NEXLIZET at the first sign of tendon rupture. Avoid NEXLIZET in patients who have a history of tendon disorders or tendon rupture.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

269.	Name, address of Applicant / Marketing Authorization Holder	M/s Horizon Healthcare (Pvt.) Ltd. Plot no. 33 Sundar Industrial Estate Lahore.
	Name, address of Manufacturing site.	M/s Horizon Healthcare (Pvt.) Ltd. Plot no. 33 Sundar Industrial Estate Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒Domestic sale ☐ Export sale ☐Domestic and Export sales
	Dy. No. and date of submission	Dy.No 16908 dated 24-12-2021
	Details of fee submitted	Rs.75,000/- dated 24-11-2021

	The proposed proprietary name / brand name	Bempex Tablet 180
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet contains: Bempedoic Acid…….180mg
	Pharmaceutical form of applied drug	white color, oval shaped, film coated tablets
	Pharmacotherapeutic Group of (API)	Bempedoic Acid: Lipid modifying agents, other lipid modifying agents. Adenosine triphosphate citrate lyase (ACL) inhibitor
	Reference to Finished product specifications	As per innovator
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nexlitol Tablets 180mg approved by US-FDA
	For generic drugs (me-too status)	Drug is not available in Pakistan
	GMP status of the Finished product manufacturer	Last inspection report dated 18.06.2020 concluded good level of cGMP compliance.
	Name and address of API manufacturer.	Bempedoic Acid: Metrochem API Private Limited, Unit-IV, Plot No. 34B, 40B & 60B, J.N. Pharma City, Thanam Village, Parawada Mandal, Visakhapatnam District, Andhra Pradesh, 531021, India (IND).
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to structure, general properties, Manufacturers, description of manufacturing process and controls, Characterization, Impurities, Specifications, Analytical procedures, Validation of analytical procedure, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of General information, General properties, Manufacturers, description of manufacturing process and process controls, Characterization, Impurities, Control of drug substance, Reference standard or materials container closure system and stability studies of drug substance.

<table>
<tr><td></td><td>Stability studies</td><td>Stability study conditions:
Bempedoic Acid:
Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months
Accelerated: 40°C ± 2°C/75% ± 5%RH for 6 months
<table><tr><th>Batch No</th><th>Accelerated</th><th>Long Term</th></tr><tr><td>BMPD-V/A070/44</td><td>6 Months</td><td>60 Months</td></tr><tr><td>BMPD-V/A070/45</td><td>6 Months</td><td>60 Months</td></tr><tr><td>BMPD-V/A070/46</td><td>6 Months</td><td>60 Months</td></tr></table></td></tr>
<tr><td></td><td>Module-III (Drug Product):</td><td>The firm has submitted detail of Drug Products including Description and composition of drug product, Pharmaceutical Development, Manufacturing process development, Microbiological attribution, Manufacturer, Master formulations, Description of Manufacturing Process and Process Controls, Control of Critical Steps and Intermediates, Process Validation and/ or Evaluation, Control of Excipients with specification and Analytical methods, Control of Drug Products including Finished product specifications and test methods, validation of Analytical methods, Batch analysis , Characterization of impurities, reference standard or impurities, Container closure and stabilities studies.</td></tr>
<tr><td></td><td>Pharmaceutical equivalence and comparative dissolution profile</td><td>Pharmaceutical Equivalence have been established against the brand leader that is Nexlitol Tablets 180mg approved by US-FDA by performing quality tests (Identification, Assay, and Dissolution. CDP has been performed against the same brand that is Nexlitol Tablets 180mg approved by US-FDA approved by US-FDA in Acid media (pH 1.2) , Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8)</td></tr>
<tr><td></td><td>Analytical method validation/verification of product</td><td>Method verification studies have submitted including Introduction, Verification of assay method, Specificity, Accuracy, Precision, Linearity concentration and peak range.</td></tr>
<tr><td colspan="3">STABILITY STUDY DATA</td></tr>
<tr><td colspan="2">Manufacturer of API</td><td>Bempedoic Acid:
Metrochem API Private Limited, Unit-IV,
Plot No. 34B, 40B & 60B,
J.N. Pharma City, Thanam Village,
Parawada Mandal, Visakhapatnam District,
Andhra Pradesh, 531021,
India (IND).</td></tr>
<tr><td colspan="2">API Lot No.</td><td>Bempedoic Acid:</td></tr>
</table>

		HANPC21002		
Description of Pack (Container closure system)		Alu-Alu. Blisters with aluminum foil having leaflet and packed in unit carton		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 8, 12, 16, 20, 24(Months)		
Batch No.		BD-001	BD-002	BD-003
Batch Size		4000 tab	4000 tab	4000 tab
Manufacturing Date		01-2021	01-2021	01-2021
Date of Initiation		01-2021	01-2021	01-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product: EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) Dayzol 30mg Capsules, Dayzol 60mg Capsules (Dexlansoprazole) which was conducted on 1st June, 2021 and was presented in 307th meeting of Registration Board held on 08-10th June, 2021. Registration Board decided to approve registration of EMPAZON 10mg Tablets, EMPAZON 25mg Tablets (Empagliflozin) Dayzol 30mg Capsules, Dayzol 60mg Capsules (Dexlansoprazole) by M/s. Horizon Healthcare (Pvt) Ltd. Lahore. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report: v. The HPLC software is 21 CFR compliant. vi. Audit trail on the testing reports of EMPAZON 10mg and 25mg Tablets, Dayzol 30mg and 60mg Capsules is available. vii. Adequate monitoring and control are available for stability chamber. Chamber are controlled		

<table>
<tr><td></td><td></td><td>and monitored through software having alarm system for alerts as well.
viii. Verification of performance of dissolution test at buffer stage
pH 5.5 for Dayzol Capsules 30mg and 60mg.
Performance of dissolution test for EMPAZON 10mg and 25mg Tablets with revised specifications i.e not less than 80% (Q) in 15minutes at initial and 01-month time point.</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Bempedoic Acid:
Firm had provided valid GMP & DML Certificate of M/s Metrochem API Private Limited Issued by Drug Control Administration Telangana India
DML Valid upto: 29-09-2024
GMP Valid upto: 29-10-2022</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Lahore, has been submitted.
Bempedoic Acid:<table><tr><td>Batch No.</td><td>Invoice No.</td><td>Quantity Imported</td><td>Date appr by D</td></tr><tr><td>HANPC21002</td><td>AE/21/0576</td><td>2.0kgs</td><td>13-07 2021</td></tr></table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms,
Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td>Audit trail reports have been submitted.</td></tr>
<tr><td>6.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers.</td></tr>
<tr><td colspan="3">Remarks of Evaluator:
INDICATIONS AND USAGE
NEXLETOL is an adenosine triphosphate-citrate lyase (ACL) inhibitor indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C.
Limitations of Use: The effect of NEXLETOL on cardiovascular morbidity and mortality has not been determined.
DOSAGE AND ADMINISTRATION
Administer 180 mg orally once daily with or without food.
DOSAGE FORMS AND STRENGTHS Tablets….. 180 mg
CONTRAINDICATIONS None.
WARNINGS AND PRECAUTIONS
• Hyperuricemia: Elevations in serum uric acid have occurred. Assess uric acid levels periodically as clinically indicated. Monitor for signs and symptoms of hyperuricemia, and initiate treatment with urate-lowering drugs as appropriate.</td></tr>
</table>

• Tendon Rupture: Tendon rupture has occurred. Discontinue NEXLETOL at the first sign of tendon rupture. Avoid NEXLETOL in patients who have a history of tendon disorders or tendon rupture.		
Decision: Approved. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
270.	Name, address of Applicant / Marketing Authorization Holder	Kaizen Pharmaceuticals (Pvt.) Ltd., E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.
	Name, address of Manufacturing site.	Kaizen Pharmaceuticals (Pvt.) Ltd., E-127-129, North Western Industrial Zone, Bin Qasim, Karachi-75020, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. dated 20/08/2021
	Details of fee submitted	PKR 20,000/-: dated 16/12/2020
	The proposed proprietary name / brand name	Teneglip 20mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: 20mg of teneligliptin
	Pharmaceutical form of applied drug	Red round biconcave film coated tablet
	Pharmacotherapeutic Group of (API)	Antidiabetic agent (dipeptidyl peptidase 4 inhibitors or gliptins)
	Reference to Finished product specifications	As per Innovator's specifications
	Proposed Pack size	10's, 20's, 30's (as per SRO)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Tenelia tablet 20mg tablet by Daiichi Sankyo Co. limited (Japan)
	For generic drugs (me-too status)	-------
	GMP status of the Finished product manufacturer	New license granted on 16/09/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Ami life sciences private limited, block no.82/B,ECP road, AT and post:karakhadi-391450,taluka:padre,district:Vadodara,gujarat,india

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(TNG/RD/20170816,TNG/RD/20180816, TNG/RD/20190816)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Tenelia 20mg tablet by Daiichi Sankyo Co limited performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Tenelia 20mg tablet by Daiichi Sankyo Co limited in Acid media (pH 0.1N HCl) & Phosphate Buffer (pH 6.8, 4.5). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, accuracy, precision, specificity,LOD,LOQ)

STABILITY STUDY DATA	
Manufacturer of API	Ami lifesciences private limited, block no.82/B,ECP road, AT and post:karakhadi-391450,taluka:padre,district:Vadodara,gujarat,india
API Lot No.	N/A
Description of Pack	PVC/ aluminum blister pack (10's, 20's, 30's)

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 18 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18(Months)		
Batch No.	TF-02	TF-03	TF-04
Batch Size	1000 tab	1000 tab	1000 tab
Manufacturing Date	24-04-2018	02-05-2018	04-05-2018
Date of Initiation	16-05-2018	16-25-2018	16-05-2018
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	S-GMP/1704043 issued by primal enterprises limited province FDA valid till 23-04-2019
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Form 6 license no. 0159 dated 12-01-2018
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.no.	Observations/Shortcoming	Reply of the Firm
1.	Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP on 20th Aug, 2021.	Firm submitted the fee of Rs.10,000/- vide slip no. 66093415 dated30-09-2022

2.	Submit copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by drug product manufacturer in section 3.2.S.4.1 as per the guidance document approved by Registration Board.	Firm submitted the analytical verification report of drug substance by drug product manufacturer.
3.	Submit stability data of drug substance till the claimed shelf life, since, according to the submitted data, study completion date is 16-09-2021.	Submitted
4.	Justify the dissolution acceptance criteria specified in section 3.2. P.5.1 i.e. "NLT 75% of labelled claim within 60 minutes" relative to the result of dissolution testing of three trial batches of drug product which revealed that more than 90% of drug release at each time point in all three batches. Further, justify, the setting of dissolution acceptance criteria in the light of general guidance of dissolution specification approved in 293rd meeting of Registration Board.	Firm replied that Dissolution of product specification is NLT 75% at 60min. This time point is verified in CDP in which 75%+Q dissolution is achieved at 60 min in all the 3 BCS dissolution medium while more than 90% of drug is released at only one time point i.e 60min and 75%+Q drug is also released in water AT 45 min that's why water was taken as dissolution medium which is in accordance with the 293rd meeting of the Registration Board.
5.	According to the procedure of dissolution test submitted in section 3.2. P.5.2 the dissolution medium is purified water, justify the choice of medium with the international reference/literature.	Firm replied that as Teneligliptin dissolution is not described in FDA guidelines then the dissolution parameters are selected using CDP criteria. CDP criteria were conducted in the 3 BCS dissolution medium (pH 1.2-6.8) and also in water. In the 3 BCS dissolution medium dissolution 75%+Q was attained in phosphate buffer 6.8 at 45 min time point but this was at border line. When we performed in water than dissolution was attained from 88.4% to 100.72% for test product at 45 min and 92.18% to 99.73% for innovator product. That's why CDP shows dissolution of both 27% at 15 min, 50% at 30 min, 75% at 45 min and more than 90% at 60 min.
6.	According the given procedure of assay in section 3.2.P.5.2, injection volume should be 10µl and the flow rate should be set at 1.4ml/min, while the chromatogram of analytical method validation studies reveals that the injection volume was 20µl and the flow rate maintained at 1.0ml/min. Justification is required for changing the chromatographic conditions while performing the analytical method validation studies of drug product from that specified in section 3.2. P.5.2.	Firm replied that It was a typographic error which is now corrected

7.	Clarify, either the assay results mentioned in stability data sheets are the content of teneligliptin or the content of hydrobromide hydrate salt form of active. Similarly, dissolution results were mentioned without the time point at which the results are obtained and the acceptance limit were also mentioned without the acceptable time frame.	Firm replied that Results are of teneligliptin on as is basis.
Decision: Deferred for justification of dissolution parameter considering USP general chapter 1092 and innovator product literature.		

Form 5-D Cases Received with Stability Data

271.	Name and address of manufacturer / Applicant	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."
	Brand Name +Dosage Form + Strength	Maxit Sachets 50mg Powder for Oral Solution
	Composition	Each sachet contains: Diclofenac potassium …… 50mg (Pack size: 10's, 20's & 30's)
	Diary No. Date of R& I & fee	Dy.No. 12649 dated 21-08-2017 Rs.50,000/-
	Pharmacological Group	Non-Steroidal Anti-inflammatory Drug
	Type of Form	Form 5 D
	Finished product Specifications	USP specification
	Pack size & Demanded Price	As per SRO
	Approval status of product in Reference Regulator Authorities	Voltfast Sachet 50mg Powder for Oral Solution by M/s Mipharm S.p.A, Millan Italy for Novartis Pharma AG, Basle, Switzerland, FDA Approved.
	Me-too status	Not Available
	GMP status	Section for Sachet (General) was granted after renewal of Drug Manufacturing Licence inspection vide letter No. F. 2-14/85-Lic (Vol-V) Dated: 30/06/2020

STABILITY STUDY DATA	
Drug	Maxit Sachets 50mg (Diclofenac Potassium)
Name of Manufacturer	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."
Manufacturer of API	M/s. Aarti Drug Limited, Plot No. G-60, M.I.D.C., Tarapur, Boisar, Tal, Palghar. Dist. Thane, India. Tel.: 9970052099
API Lot No.	As per invoice attested by DRAP batch no. DFK/10060080 has been imported
Description of Pack (Container closure system)	Alu-Alu Paper foil

Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: MAX-148-05/21 (6 months), MAX-157-06/21 (6 months), MAX-158-07/21 (6 months), Accelerated: 6 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 Accelerated: 0, 3, 6		
Batch No.	MAX-148-05/21	MAX-157-06/21	MAX-158-07/21
Batch Size	2.0 Kg (2,222 Sachets)	2.0 Kg (2,222 Sachets)	2.0 Kg (2,222 Sachets)
Manufacturing Date	07.2021	07.2021	07.2021
Date of Initiation	30.07.2021	30.07.2021	30.07.2021
No. of Batches	03		
Date of Submission	21-08-2017		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status
15.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product "HILVEL 400mg + 100mg (Sofosbuvir +Velpatasvir)", which was conducted on 14th December, 2017 and was presented in 277th meeting of Registration Board held on 27-29th December, 2017. Registration Board decided to approve registration of "HILVEL 400mg / 100mg (Sofosbuvir + Velpatasvir" by M/s. Hilton Pharma (Pvt.) Ltd., Karachi. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report: i. The HPLC software is 21 CFR compliant. ii. Audit trail on the testing reports of Hilvel Tablets 400mg+100mg is available. Adequate monitoring and control are available for stability chamber. Chamber are controlled and monitored through software having alarm system for alerts as well.
16.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Submitted
17.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Submitted
18.	Stability study data of API from API manufacturer	Stability study conditions:

<table>
<tr><td></td><td></td><td>Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months
Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months
Diclofenac Potassium:
Batches #: (DFK/10070024, DFK/10070025, DFK/10070026)</td></tr>
<tr><td>19.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Copy of GMP certificate No.
Diclofenac Potassium: No: 6102298 issued by Food and Drugs Administration, KONKAN Division.</td></tr>
<tr><td>20.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>The firm has provided the copy of procurement invoices of API; details are as follow.
<table><tr><td>API Name</td><td>Invoice No. & Date</td></tr><tr><td>Diclofenac Potassium</td><td>EXP/845/20-21 01/07/2020</td></tr></table></td></tr>
<tr><td>21.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>22.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>23.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA</td></tr>
<tr><td>24.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has been submitted copy of Trial batch manufacturing record.
Details are as under:
<table><tr><td colspan="3">Maxit Sachet 50mg</td></tr><tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr><tr><td>MAX-148-05/21</td><td>2.0 Kg (2,222 Sachets)</td><td>20.07.2021</td></tr><tr><td>MAX-157-06/21</td><td>2.0 Kg (2,222 Sachets)</td><td>20.07.2021</td></tr><tr><td>MAX-158-07/21</td><td>2.0 Kg (2,222 Sachets)</td><td>20.07.2021</td></tr></table></td></tr>
<tr><td>25.</td><td>Record of comparative dissolution data (where applicable)</td><td>Submitted</td></tr>
<tr><td>26.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Yes</td></tr>
<tr><td>27.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
<tr><td>28.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Submitted</td></tr>
<tr><td colspan="3">Remarks of the Evaluator:
<table><tr><td>Sr.no.</td><td>Shortcoming/Deficiencies</td><td>Reply of the Firm</td></tr></table></td></tr>
</table>

1.	Justify the finished product specifications as "In-house specifications" since the drug product monograph is available in USP Pharmacopoeia. Revise your specifications along with submission of requisite fee.	Firm has submitted the revised finished product specification as per USP monograph of Diclofenac potassium for oral solution along with fee of RS. 7,500/- paid vide challan no.297845546. dated 24-10-2022
2.	Submit pharmaceutical equivalence report performed against the innovator/reference product.	Firm submit pharmaceutical equivalence report performed against Volfast Sachet 50mg of M/s. Novartis Pharma Batch no. AMPA2T2.

Decision: Approved. Firm shall submit perfromance of stability studies at athe next time point of long term stability study as per USP monograph of "Diclofenac potassium for oral solution" before issuance of registration letter.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

272.	Name and address of manufacturer / Applicant	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."
	Brand Name +Dosage Form + Strength	Ertisit Tablets 5mg + 100mg
	Composition	Each film-coated tablet contains: Ertugliflozin L-Pyroglutamic acid equivalent to Ertugliflozin … 5 mg, Sitagliptin Phosphate monohydrate eq. to Sitagliptin … 100 mg
	Diary No. Date of R& I & fee	Dy. No.16316 dated 03-05-2018 Rs.50,000/-
	Pharmacological Group	Antidiabetic
	Type of Form	Form 5-D
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	As per SRO(Pack size: 7's, 10's, 14's, 28's & 30's)
	Approval status of product in Reference Regulator Authorities	Steglujan Tablets 5mg/100mg by M/s Merck Sharp & Dohme B.V., FDA Approved.
	Me-too status	Not Available
	GMP status	Section for Sachet (General) was granted after renewal of Drug Manufacturing Licence inspection vide letter No. F. 2-14/85-Lic (Vol-V) Dated: 30/06/2020

STABILITY STUDY DATA

Drug	Ertisit Tablets 5mg + 100mg Ertugliflozin L-Pyroglutamic acid & Sitagliptin Phosphate Monohydrate)
Name of Manufacturer	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."
Manufacturer of API	Ertugliflozin L-Pyroglutamic acid M/s. Chifeng Arker Pharmaceutical Technology Co., Ltd. No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng, Inner Mongolia, China

	Sitagliptin Phosphate M/s. Ruyuan HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R.China Postal code: 512721		
API Lot No.	As per invoice attested by DRAP for Ertugliflozin L-Pyroglutamic acid for batch no. D84-201101, Sitagliptin Phosphate for batch no. 1827-0001-20091 have been imported.		
Description of Pack (Container closure system)	Alu-Alu foil		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: ERS-041-02/21 (6 months) ERS-042-03/21 (6 months) ERS-043-04/21 (6 months) Accelerated: 6 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 Accelerated: 0, 3, 6		
Batch No.	ERS-041-02/21	ERS-042-03/21	ERS-043-04/21
Batch Size	1000 G (2,500 Tablets)	1000 G (2,500 Tablets)	1000 G (2,500 Tablets)
Manufacturing Date	02.2021	02.2021	02.2021
Date of Initiation	20.02.2021	20.02.2021	20.02.2021
No. of Batches	03		
Date of Submission	06.05.2022		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product "HILVEL 400mg + 100mg (Sofosbuvir +Velpatasvir)", which was conducted on 14th December, 2017 and was presented in 277th meeting of Registration Board held on 27-29th December, 2017. Registration Board decided to approve registration of "HILVEL 400mg / 100mg (Sofosbuvir + Velpatasvir" by M/s. Hilton Pharma (Pvt.) Ltd., Karachi. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report: iii. The HPLC software is 21 CFR compliant. iv. Audit trail on the testing reports of Hilvel Tablets 400mg+100mg is available. Adequate monitoring and control are available for stability chamber. Chamber are controlled and

<table>
<tr><td></td><td></td><td>monitored through software having alarm system for alerts as well.</td></tr>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Submitted</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer</td><td>Submitted</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Stability study storage conditions:
Long term: 30°C ± 2°C / 65% ± 5%RH for 06 months
Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months
<u>Ertugliflozin L-Pyroglutamic acid</u>:
Batches #: (D84-161201, D84-161202, D84-170101)
<u>Sitagliptin Phosphate</u>:
Batches #: (STP-201312001, STP-201312002, STP-201401001)</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Submitted</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>The firm has provided the copy of procurement invoices of API; details are as follow.
<table><tr><td>API Name</td><td>Invoice No. & Date</td></tr><tr><td>Ertugliflozin LPGA</td><td>PSPW-201113 13.11.2020</td></tr><tr><td>Sitagliptin Phosphate</td><td>C05S05ZEP200933 26.10.2020</td></tr></table></td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Not Applicable</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has been submitted copy of Trial batch manufacturing record.
Details are as under:
<table><tr><td colspan="3">Ertisit Tablets 5mg/100mg</td></tr><tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr><tr><td>ERS-041-02/21</td><td>1000 G (2,500 Tab.)</td><td>04.02.2021</td></tr><tr><td>ERS-042-03/21</td><td>1000 G (2,500 Tab.)</td><td>04.02.2021</td></tr><tr><td>ERS-043-04/21</td><td>1000 G (2,500 Tab.)</td><td>04.02.2021</td></tr></table></td></tr>
</table>

11.	Record of comparative dissolution data (where applicable)	Submitted
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of the Evaluator:

Sr.no.	Shortcoming/Deficiencies	Reply of the Firm
1.	Submit the translated version and instant API related GMP certificate of drug substance ertugliflozin L-Pyroglutamic acid.	Firm submitted the Drug Manufacturing license of API manufacturer Ertugliflozin L-PGA which is valid till 28-12-2025
2.	Submit stability study data of both API from API manufacturer	Firm has submitted stability data of both drug substance.
3.	Submit pharmaceutical equivalence report performed against the innovator/reference product.	Firm has submitted pharmaceutical equivalence report performed against Steglujan Tablet 5mg/100mg Batch no. U001351.
4.	Sample solution preparation of assay testing of finished product did not specify the concentration of ertugliflozin and sitagliptin in the final dilution of sample solution.	Revised analytical procedure of finished product has submitted by the firm.
5.	Justify the acceptance criteria of disintegration test adapted by you for both strength i.e. NMT 15 minutes in the light of review literature of innovator brand approved in USFDA. Since the review report of innovator brand reveal that disintegration is the discriminating test for the applied product, so more stringent disintegration acceptance limit has been recommended for both strengths.	Firm has revised the acceptance limit of Disintegration test from 15 minutes to 5minutes for core tablet and 10 minutes for film coated tablet.

Decision: Approved with innovator's specifications.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

273.	Name and address of manufacturer / Applicant	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."

	Brand Name +Dosage Form + Strength	Ertisit Tablets 15mg + 100mg
	Composition	Each film-coated tablet contains: Ertugliflozin L-Pyroglutamic acid equivalent to Ertugliflozin … 15 mg, Sitagliptin Phosphate monohydrate eq. to Sitagliptin … 100 mg
	Diary No. Date of R& I & fee	Dy. No.16316 dated 03-05-2018 Rs.50,000/-
	Pharmacological Group	Antidiabetic
	Type of Form	Form 5-F
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	As per SRO(Pack size: 7's, 10's, 14's, 28's & 30's)
	Approval status of product in Reference Regulator Authorities	Steglujan Tablets 15mg/100mg by M/s Merck Sharp & Dohme B.V., FDA Approved.
	Me-too status	Not Available
	GMP status	Section for Sachet (General) was granted after renewal of Drug Manufacturing Licence inspection vide letter No. F. 2-14/85-Lic (Vol-V) Dated: 30/06/2020

STABILITY STUDY DATA	
Drug	Ertisit Tablets 15mg + 100mg Ertugliflozin L-Pyroglutamic acid & Sitagliptin Phosphate Monohydrate)
Name of Manufacturer	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."
Manufacturer of API	Ertugliflozin L-Pyroglutamic acid M/s. Chifeng Arker Pharmaceutical Technology Co., Ltd. No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng, Inner Mongolia, China Sitagliptin Phosphate M/s. Ruyuan HEC Pharm Co., Ltd. Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R.China Postal code: 512721
API Lot No.	As per invoice attested by DRAP for Ertugliflozin L-Pyroglutamic acid for batch no. D84-201101, Sitagliptin Phosphate for batch no. 1827-0001-20091 have been imported.
Description of Pack (Container closure system)	Alu-Alu foil
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH
Time Period	Real time: ERS-044-03/21 (6 months) ERS-045-04/21 (6 months) ERS-046-05/21 (6 months) Accelerated: 6 months

Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 Accelerated: 0, 3, 6		
Batch No.	ERS-044-03/21	ERS-045-04/21	ERS-046-05/21
Batch Size	1000 G (2,500 Tablets)	1000 G (2,500 Tablets)	1000 G (2,500 Tablets)
Manufacturing Date	02.2021	02.2021	02.2021
Date of Initiation	26.02.2021	26.02.2021	26.02.2021
No. of Batches	03		
Date of Submission	06.05.2022		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product "HILVEL 400mg + 100mg (Sofosbuvir +Velpatasvir)", which was conducted on 14th December, 2017 and was presented in 277th meeting of Registration Board held on 27-29th December, 2017. Registration Board decided to approve registration of "HILVEL 400mg / 100mg (Sofosbuvir + Velpatasvir" by M/s. Hilton Pharma (Pvt.) Ltd., Karachi. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report: v. The HPLC software is 21 CFR compliant. vi. Audit trail on the testing reports of Hilvel Tablets 400mg+100mg is available. Adequate monitoring and control are available for stability chamber. Chamber are controlled and monitored through software having alarm system for alerts as well.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Submitted
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Submitted
4.	Stability study data of API from API manufacturer	Stability study storage conditions: Long term: 30°C ± 2°C / 65% ± 5%RH for 06 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Ertugliflozin L-Pyroglutamic acid: Batches #: (D84-161201, D84-161202, D84-170101) Sitagliptin Phosphate:

<table>
<tr><td></td><td></td><td>Batches #: (STP-201312001, STP-201312002, STP-201401001)</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Submitted</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>The firm has provided the copy of procurement invoices of API; details are as follow.
<table><tr><td>API Name</td><td>Invoice No. & Date</td></tr><tr><td>Ertugliflozin LPGA</td><td>PSPW-201113 13.11.2020</td></tr><tr><td>Sitagliptin Phosphate</td><td>C05S05ZEP200933 26.10.2020</td></tr></table></td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Not Applicable</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has been submitted copy of Trial batch manufacturing record.
Details are as under:<table><tr><td colspan="3">Ertisit Tablets 15mg/100mg</td></tr><tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr><tr><td>ERS-044-03/21</td><td>1000 G (2,500 Tab.)</td><td>09.02.2021</td></tr><tr><td>ERS-045-04/21</td><td>1000 G (2,500 Tab.)</td><td>09.02.2021</td></tr><tr><td>ERS-046-05/21</td><td>1000 G (2,500 Tab.)</td><td>09.02.2021</td></tr></table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Submitted</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Yes</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
<tr><td>14.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Submitted</td></tr>
<tr><td colspan="3">Remarks of the Evaluator:<table><tr><td>Sr.no.</td><td>Shortcoming/Deficiencies</td><td>Reply of the Firm</td></tr><tr><td>1.</td><td>Submit the translated version and instant API related GMP certificate of drug substance ertugliflozin L-Pyroglutamic acid.</td><td>Firm submitted the Drug Manufacturing license of API manufacturer Ertugliflozin L-PGA which is valid till 28-12-2025</td></tr></table></td></tr>
</table>

2.	Submit stability study data of both API from API manufacturer	Firm has submitted stability data of both drug substance.
3.	Submit pharmaceutical equivalence report performed against the innovator/reference product.	Firm has submitted pharmaceutical equivalence report performed against Steglujan Tablet 5mg/100mg Batch no. U001351.
4.	Sample solution preparation of assay testing of finished product did not specify the concentration of ertugliflozin and sitagliptin in the final dilution of sample solution.	Revised analytical procedure of finished product has submitted by the firm.
5.	Justify the acceptance criteria of disintegration test adapted by you for both strength i.e. NMT 15 minutes in the light of review literature of innovator brand approved in USFDA. Since the review report of innovator brand reveal that disintegration is the discriminating test for the applied product, so more stringent disintegration acceptance limit has been recommended for both strengths.	Firm has revised the acceptance limit of Disintegration test from 15 minutes to 5minutes for core tablet and 10 minutes for film coated tablet.

Decision: Approved with innovator's specifications.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

274.	Name and address of manufacturer / Applicant	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."
	Brand Name +Dosage Form + Strength	Golix Tablets 200mg
	Composition	Each film-coated tablet contains: Elagolix Sodium equivalent to Elagolix …… 200m
	Diary No. Date of R& I & fee	Dy.No.43243 dated 19-12-2018 Rs.50,000/-
	Pharmacological Group	Gonadotropin-releasing hormone (GnRH) receptor antagonist
	Type of Form	Form 5 D
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	As per SRO(Pack size: 7's, 14's & 28's)
	Approval status of product in Reference Regulator Authorities	Orilissa Tablets 200mg by M/s AbbVie Inc. North Chicago, IL 60064, FDA Approved.
	Me-too status	Not Available
	GMP status	Section for Sachet (General) was granted after renewal of Drug Manufacturing Licence inspection vide letter No. F. 2-14/85-Lic (Vol-V) Dated: 30/06/2020

STABILITY STUDY DATA

Drug	Golix Tablets 200mg (Elagolix Sodium)		
Name of Manufacturer	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."		
Manufacturer of API	M/s. Aurisco Pharmaceutical Co., Ltd., Badu Industrial Park Zone, Tiantai Country, Zhejiang Province 317200, P.R. China		
API Lot No.	As per invoice attested by DRAP batch no. ELS-201101P has been imported		
Description of Pack (Container closure system)	Alu-Alu foil		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: GOL-087-02/21 (6 months), GOL-088-03/21 (6 months), GOL-089-04/21 (6 months) Accelerated: 6 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 Accelerated: 0, 3, 6		
Batch No.	GOL-087-02/21	GOL-088-03/21	GOL-089-04/21
Batch Size	900 G (1500 Tablets)	900 G (1500 Tablets)	900 G (2,000 Tablets)
Manufacturing Date	03.2021	03.2021	03.2021
Date of Initiation	12.04.2021	12.04.2021	12.04.2021
No. of Batches	03		
Date of Submission	13.12.2018		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product "HILVEL 400mg + 100mg (Sofosbuvir +Velpatasvir)", which was conducted on 14th December, 2017 and was presented in 277th meeting of Registration Board held on 27-29th December, 2017. Registration Board decided to approve registration of "HILVEL 400mg / 100mg (Sofosbuvir + Velpatasvir" by M/s. Hilton Pharma (Pvt.) Ltd., Karachi. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report: vii. The HPLC software is 21 CFR compliant. viii. Audit trail on the testing reports of Hilvel Tablets 400mg+100mg is available. Adequate monitoring and control are available for stability chamber. Chamber are controlled and

<table>
<tr><td></td><td></td><td>monitored through software having alarm system for alerts as well.</td></tr>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Submitted</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer</td><td>Submitted</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Stability study conditions:
Long term: 2-8°C for 09 months
Accelerated: 25°C ± 2°C / 65% ± 5%RH for 06 months
Elagolix Sodium:
Batches #: (200301P, 200302P, 200303P)</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Copy of GMP certificate No.
Elagolix Sodium: No: ZJ20170053 issued by China food and drug administration.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>The firm has provided the copy of procurement invoices of API; details are as follow.
<table><tr><td>API Name</td><td>Invoice No. & Date</td></tr><tr><td>Elagolix Sodium</td><td>20T-442
17.12.2020</td></tr></table></td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Not Applicable</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has been submitted copy of Trial batch manufacturing record.
Details are as under:<table><tr><td colspan="3">Golix Tablets 200mg</td></tr><tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr><tr><td>GOL-087-02/21</td><td>900 G (1500 Tablets)</td><td>17.03.2021</td></tr><tr><td>GOL-088-03/21</td><td>900 G (1500 Tablets)</td><td>17.03.2021</td></tr><tr><td>GOL-089-04/21</td><td>900 G (1500 Tablets)</td><td>18.03.2021</td></tr></table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Submitted</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Yes</td></tr>
</table>

13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of the Evaluator

Sr.no.	Shortcoming/Deficiencies	Reply of Firm
1.	According to the assay method by drug substance manufacturer the retention time of major peak is about 13.5 minutes, than justify the retention time of about 17.6 minutes of major peak as evident from the submitted chromatogram of assay of drug substance by drug product manufacturer, despite of using same chromatographic condition, gradient program and mobile phase as of drug substance manufacturer.	Firm replied that " assay was carried out with in used column C8 ,water symmetry and retention time was achieved 17.6 minutes as compared to 13.5 minutes due to changes in column.

Decision: Approved with innovator's specifications.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

275.	Name and address of manufacturer / Applicant	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."
	Brand Name +Dosage Form + Strength	Golix Tablets 150mg
	Composition	Each film-coated tablet contains: Elagolix Sodium equivalent to Elagolix …… 150m
	Diary No. Date of R& I & fee	Dy.No.43242 dated 19-12-2018 Rs. 50,000/-
	Pharmacological Group	Gonadotropin-releasing hormone (GnRH) receptor antagonist
	Type of Form	Form 5 D
	Finished product Specifications	Innovator's Specification
	Pack size & Demanded Price	As per SRO(Pack size: 7's, 14's & 28's)
	Approval status of product in Reference Regulator Authorities	Orilissa Tablets 150mg by M/s AbbVie Inc. North Chicago, IL 60064, FDA Approved.
	Me-too status	Not Available
	GMP status	Section for Sachet (General) was granted after renewal of Drug Manufacturing Licence inspection vide letter No. F. 2-14/85-Lic (Vol-V) Dated: 30/06/2020

STABILITY STUDY DATA	
Drug	Golix Tablets 150mg (Elagolix Sodium)

Name of Manufacturer	"M/s. Hilton Pharma (Pvt.) Ltd. Plot No. 13-14 & 15, Sector-15, Korangi, Industrial Area, Karachi."		
Manufacturer of API	M/s. Aurisco Pharmaceutical Co., Ltd., Badu Industrial Park Zone, Tiantai Country, Zhejiang Province 317200, P.R. China		
API Lot No.	As per invoice attested by DRAP batch no. ELS-201101P has been imported		
Description of Pack (Container closure system)	Alu-Alu foil		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: GOL-084-02/21 (6 months), GOL-085-03/21 (6 months), GOL-086-04/21 (6 months) Accelerated: 6 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 Accelerated: 0, 3, 6		
Batch No.	GOL-084-02/21	GOL-085-03/21	GOL-086-04/21
Batch Size	900 G (2,000 Tablets)	900 G (2,000 Tablets)	900 G (2,000 Tablets)
Manufacturing Date	03.2021	03.2021	03.2021
Date of Initiation	06.04.2021	06.04.2021	06.04.2021
No. of Batches	03		
Date of Submission	13.12.2018		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product "HILVEL 400mg + 100mg (Sofosbuvir +Velpatasvir)", which was conducted on 14th December, 2017 and was presented in 277th meeting of Registration Board held on 27-29th December, 2017. Registration Board decided to approve registration of "HILVEL 400mg / 100mg (Sofosbuvir + Velpatasvir" by M/s. Hilton Pharma (Pvt.) Ltd., Karachi. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months. Following two observations were reported in the report: ix. The HPLC software is 21 CFR compliant. x. Audit trail on the testing reports of Hilvel Tablets 400mg+100mg is available. Adequate monitoring and control are available for stability chamber. Chamber are controlled and monitored through software having alarm system for alerts as well.

<table>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>Submitted</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer</td><td>Submitted</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Stability study conditions:
Long term: 2-8°C for 09 months
Accelerated: 25°C ± 2°C / 65% ± 5%RH for 06 months
Elagolix Sodium:
Batches #: (200301P, 200302P, 200303P)</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Copy of GMP certificate No.
Elagolix Sodium: No: ZJ20170053 issued by China food and drug administration.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>The firm has provided the copy of procurement invoices of API; details are as follow.
<table><tr><td>API Name</td><td>Invoice No. & Date</td></tr><tr><td>Elagolix Sodium</td><td>20T-442
17.12.2020</td></tr></table></td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Not Applicable</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has been submitted copy of Trial batch manufacturing record.
Details are as under:
<table><tr><td colspan="3">Golix Tablets 150mg</td></tr><tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr><tr><td>GOL-084-02/21</td><td>900 G (2,000 Tablets)</td><td>08.03.2021</td></tr><tr><td>GOL-085-03/21</td><td>900 G (2,000 Tablets)</td><td>08.03.2021</td></tr><tr><td>GOL-086-04/21</td><td>900 G (2,000 Tablets)</td><td>09.03.2021</td></tr></table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Submitted (performed against Orillisa Tablet 150mg Batch no.2155200)</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Yes</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
</table>

14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of the Evaluator

Sr.no.	Shortcoming/Deficiencies	Reply of Firm
2.	According to the assay method by drug substance manufacturer the retention time of major peak is about 13.5 minutes, than justify the retention time of about 17.6 minutes of major peak as evident from the submitted chromatogram of assay of drug substance by drug product manufacturer, despite of using same chromatographic condition, gradient program and mobile phase as of drug substance manufacturer.	Firm replied that " assay was carried out with in used column C8 ,water symmetry and retention time was achieved 17.6 minutes as compared to 13.5 minutes due to changes in column.

Decision: Approved with innovator's specifications.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

276	Name and address of manufacturer / Applicant	M/s. Otsuka Pakistan Ltd. F/4-9, Hub Industrial Trading Estate, Distt. Lasbella, Balochistan.
	Brand Name +Dosage Form + Strength	Ibufen 400mg I.V Infusion
	Composition	Each 100ml contains: Ibuprofen…..400mg
	Diary No. Date of R& I & fee	Dy.No. 24085 Dated 11-07-2018 Rs. 20,000/- Dated 11-07-2018 (DSN: 0741916)
	Pharmacological Group	NSAID
	Type of Form	Form 5
	Finished product Specifications	Manufacturer's specification
	Pack size & Demanded Price	100ml: Rs. 312/-
	Approval status of product in Reference Regulatory Authorities	Approved in Germany. (Ibuprofen B. Braun 400 mg/100ml solution for infusion)
	Me-too status	…..
	GMP status	GMP compliance level is rated as Satisfactory. Inspection conducted on 15th March 2022.

Remarks of Evaluator:

Remarks	Response
Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.	Firm has submitted evidence of IX IV Infusion of M/s. Searl IV solutions (M-278).

Evidence of reference product packed in LDPE bottle.	Applicant has submitted leaflet of of Ibuprofen 400mg solution of B.Barun, Germany with highlighted the availability in LDPE bottle.
Approval of section/manufacturing facility by the Central Licensing Board. However, you may submit panel inspection report for renewal of DML verifying the section/manufacturing facility.	Applicant has submitted a letter of CLB bearing a No. F. 2-1/879-Lic (Vol-II) dated 1st July, 2015 showing following sections: • Plabottle infusion section 500ml (Large Volume Parenteral). • Plabottle (Small Volume Parenteral). • Aseptically filled injection Plabottle (Plastic bottles).

Decision of 293rd meeting of Registration Board:
Registration Board defer the case for submission of stability studies of applied formulation as per guidelines provided in 251st & later amended in 278th meeting of Registration Board.

STABILITY STUDY DATA

Drug	Ibufen		
Name of Manufacturer	M/s. Otsuka Pakistan Ltd. F/4-9, Hub Industrial Trading Estate, Distt. Lasbella, Balochistan.		
Manufacturer of API	Hubei Granules- Biocause Pharmaceutical Company Ltd., 122 Yangwan Road, China - 448000		
API Lot No.	As per invoice attested by DRAP batch no. C100-1901237M, C100-1901449M, C100-1901453M has been imported		
Description of Pack (Container closure system)	Plastic bottles of 100ml		
Stability Storage Condition	Real time: 30°C ± 2° C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH		
Time Period	Real time: 36 months Accelerated: 6 months		
Frequency	IBH01D19: Accelerated:0,1,2,3,4,6 (month) Real Time: 0,3,6,9,12,18,24,36 (month) IB001B20: Accelerated:0,1,2,3,4,6 (month) Real Time: 0,3,6,9,12,18,24,36 (month) IB002B20: Accelerated:0,1,2,3,4,6 (month) Real Time: 0,3,6,9,12,18,24,36 (month)		
Batch No.	IBH01D19	IB001B20	IB002B20
Batch Size	100 Bottles	24,000 Bottles	24,000 Bottles
Manufacturing Date	2019.04.08	2020.02.14	2020.02.14
Date of Initiation	2019.04.23	2020.03.02	2020.03.02
No. of Batches	03		
Date of Submission	10-07-2018		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents To Be Provided	Status

<table>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm</td><td>None</td></tr>
<tr><td>2.</td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>COA of API from API Manufacturer and Finished Product manufacturer has been submitted.</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product manufacturer</td><td>Method used for analysis of API from API Manufacturer and Finished Product manufacturer has been submitted.</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 72 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches.</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Firm has submitted copy of GMP certificate of Drug Substance manufacturer.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of Commercial Invoice no. GIB19017074 Dated: JAN.29, 2019 from Hubei Granules-Biocause Pharmaceutical Company Ltd.,
122 Yangwan Road, Jingmen City, Hubei Province, China attested by AD DRAP (Quetta) dated 17-03-2019 has been submitted.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Yes</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>N/A</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted copy of Trial batch manufacturing record.
Details are as under:
<table>
<tr><td colspan="3">Ibufen 400mg Injection</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Started</td></tr>
<tr><td>IBH01D19</td><td>100 Bottles</td><td>2019.04.08</td></tr>
<tr><td>IB001B20</td><td>24,000 Bottles</td><td>2020.02.14</td></tr>
<tr><td>IB002B20</td><td>24,000 Bottles</td><td>2020.02.14</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>N/A</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Yes</td></tr>
</table>

13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Certificate of compliance submitted.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Yes

Remarks of the Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Submit real time stability data of drug substance as per zone-IV-A condition or submit long term stability studies data of the drug product for 6 months along with degradation studies as per decision of registration Board in its 297th meeting.	Firm submitted the stability data of drug substance performed at zone iv-a condition.

Decision: Approved with innovator's specifications.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

Cases of New Licenses received on FORM 5-F

277.	Name, address of Applicant / Marketing Authorization Holder	M/s Pinnacle Biotech (Pvt.) Ltd.
	Name, address of Manufacturing site.	M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25822 dated 13/08/2022
	Details of fee submitted	PKR 30,000/-: dated 02/09/2022
	The proposed proprietary name / brand name	Empaxo 10mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin……..….10mg
	Pharmaceutical form of applied drug	White, round, film coated tablet plain on both sides.

	Pharmacotherapeutic Group of (API)	Sodium-glucose co-transporter 2 (SGLT2) inhibitors
	Reference to Finished product specifications	Innovator's Specs
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	JARDIANCE 10mg Tablet by BOEHRINGER INGELHEIM PHARMACEUTICALS INC, USFDA Approved.
	For generic drugs (me-too status)	Diampa 10mg Tablet by Getz Pharma Pakistan (Pvt.) Ltd.
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021 Tablet (general), Capsule (general), Sachet (general) and Research and Development Laboratory section is approved.
	Name and address of API manufacturer.	API: Empagliflozin M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted drug substance data for sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	API: Empagliflozin. Firm has submitted signed and stamped stability data sheets as per zone IV-A in which real time stability data Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical

		procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence studies with reference product i.e., Jardiance 10mg Tablet
	Analytical method validation/verification of product	Method validation studies have submitted including System Suitability, Linearity, Accuracy, precision, Specificity, Limit of Quantification, Limit of Detection, Robustness.

STABILITY STUDY DATA			
Manufacturer of API	API: Empagliflozin M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China.		
API Lot No.	API: Empagliflozin. H-E-20210605-D01-E06-02		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22TTEMP002	22TTEMP003	22TTEMP004
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	06-04-2022	06-04-2022	06-04-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	License Number: LIAO 20150233 Issue Date: May 18, 2020
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: • Permission to import different APIs including Empagliflozin for the purpose of test/analysis and stability studies is granted. • License No.3942/21/DRAP-AD-CD(I&E) dated 10/12/2021

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted" Further specify how the testing of drug substance was carried out without performing verification studies.	Firm submit the requisite document.
2.	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.	Firm submitted the BMR of all three trail batches.

Decision: Approved with innovator's specifications.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

278.	Name, address of Applicant / Marketing Authorization Holder	M/s Pinnacle Biotech (Pvt.) Ltd.
	Name, address of Manufacturing site.	M/s Pinnacle Biotech (Pvt.) Ltd. Plot No. FD-49-A8, FD-50-A8, FD-51-A8, Korangi Creek Industrial Park, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale

		☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 26383 dated 19/09/2022
	Details of fee submitted	PKR 30,000/-: dated 02/09/2022
	The proposed proprietary name / brand name	Empaxo 25mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin……..….25mg
	Pharmaceutical form of applied drug	Yellow color, round shape, film coated tablet plain on both sides.
	Pharmacotherapeutic Group of (API)	Sodium-glucose co-transporter 2 (SGLT2) inhibitors
	Reference to Finished product specifications	Innovator's Specs
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	JARDIANCE 25mg Tablet by BOEHRINGER INGELHEIM PHARMACEUTICALS INC, USFDA Approved.
	For generic drugs (me-too status)	Diampa 25mg Tablet by Getz Pharma Pakistan (Pvt.) Ltd.
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021 Tablet (general), Capsule (general), Sachet (general) and Research and Development Laboratory section is approved.
	Name and address of API manufacturer.	API: Empagliflozin M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted drug substance data for sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch

		analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	API: Empagliflozin. Firm has submitted signed and stamped stability data sheets as per zone IV-A in which real time stability data Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence studies with reference product i.e., Xenglu-Met 12.5mg-1000mg Tablet.
	Analytical method validation/verification of product	Method validation studies have submitted including System Suitability, Linearity, Accuracy, precision, Specificity, Limit of Quantification, Limit of Detection, Robustness.

STABILITY STUDY DATA			
Manufacturer of API	API: Empagliflozin M/s. Fuxin Long Rui Pharmaceutical Co. Ltd. Address: Fluoride Industrial Park, Fumeng County (Yi Ma Tu), Fuxin City, Liaoning Province -123000, China		
API Lot No.	API: Empagliflozin. H-E-20210605-D01-E06-02		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	22TTEMP001	22TTEMP002	22TTEMP003
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	05-04-2022	05-04-2022	05-04-2022
No. of Batches	03		
Administrative Portion			

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	License Number: LIAO 20150233 Issue Date: May 18, 2020
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Empagliflozin: • Permission to import different APIs including Empagliflozin for the purpose of test/analysis and stability studies is granted. • License No.3942/21/DRAP-AD-CD(I&E) dated 10/12/2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted" Further specify how the testing of drug substance was carried out without performing verification studies.	Firm submit the requisite document.
2.	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.	Firm submitted the BMR of all three trail batches.

Decision: Approved with innovator's specifications.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

279.	Name, address of Applicant / Marketing Authorization Holder	M/S Qadir Pharmaceuticals 6-Km G.T Road Wazirabad Sialkot Veerum, Fateh Garh Sahuwala Road Sailkot

		Pakistan.
	Name, address of Manufacturing site.	M/S Qadir Pharmaceuticals 6-Km G.T Road Wazirabad Sialkot Veerum, Fateh Garh Sahuwala Road Sailkot Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23368 dated 18-08-2022
	Details of fee submitted	PKR 30,000/-: dated 05-07-2022
	The proposed proprietary name / brand name	Cain-Q 1% Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule 2ml contains: Lidocaine HCl……20mg
	Pharmaceutical form of applied drug	2ml Ampoule for IM
	Pharmacotherapeutic Group of (API)	Local or regional anesthesia
	Reference to Finished product specifications	BP Spec
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lidocaine HCl(1%) injection(IM) by M/s Mercury Pharma B. Braun Melsungen AG, Mistelweg 2, 12357 Berlin, Germany.
	For generic drugs (me-too status)	Global Pharmaceuticals
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021 Tablet (General) ,Capsule (General), Capsule (cephalosporin) Oral Dry Suspension (cephalosporin) Oral liquid, liquid injectable vial& Ampoule(Gerenal) Dry powder Injectable(Gerenal) section approved.
	Name and address of API manufacturer.	Gufic Biosciences Limited Subhash Road-A, Vile Parle (E), Mumbai-400 057,India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis

		and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Lidocain Hydrochloride is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (1884, 1885, 1886)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Lidocain 2ml Injection manufacture by Global Pharma by performing quality tests
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA	
Manufacturer of API	GUFIC BIOSCIENCES LIMITED SUBHASH ROAD-A, VILE PARLE (E), MUMBAI-400 057, INDIA. TEL :+91- 22-56919191 FAX : +91-22-26169008 Email :dhapalapur@guficbio.com
API Lot No.	2725
Description of Pack (Container closure system)	Liquid for injection filled in glass ampoule Type 1 (1×1's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	1000 Amp	1000 Amp	1000 Amp
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	17-10-2021	17-10-2021	17-10-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Remarks OF Evaluator:

S.no.	Sections	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	3.2. S.4.2	Provide detailed analytical procedures used for the testing of drug substance by drug product manufacturer.	Submitted
2.	3.2. S.4.3	Provide analytical Method validation studies of drug substance performed by the drug product manufacturer.	Submitted
3.	3.2. P.1	Scientific justification is required for using 3 preservatives in sterile single dose injection, since the reference product approved in MHRA do not use any preservative in their formulation.	Firm submitted the revised formulation in which they use only one preservative.
4.	3.2.P.8	Justify for not performing the sterility test at the last time point of accelerated stability condition.	Firm replied that According to international guidelines (FDA) the sterility testing of a product is performed on initial stage (first

			time point) and terminal stage (last time point) i.e at time point zero and at 24th month stability studies. We adopted the same guide line and developed the SOP accordingly. Due to the previously mentioned reason the sterility test was not performed at the final time point i.e 6th month.
5.	2.3.R.1.1	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product under section 2.3.R.1.1, for which stability studies data is provided in Module 3 section 3.2. P.8.	Submitted

Decision: Approved. Firm shall submit revised formulation excluding preservatives as per innovator product along with applicable fee for revision /correction of master formulation no. as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

280.	Name, address of Applicant / Marketing Authorization Holder	M/S Qadir Pharmaceuticals 6-Km G.T Road Wazirabad Sialkot Veerum, Fateh Garh Sahuwala Road Sailkot Pakistan.
	Name, address of Manufacturing site.	M/S Qadir Pharmaceuticals 6-Km G.T Road Wazirabad Sialkot Veerum, Fateh Garh Sahuwala Road Sailkot Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23663 dated 22-08-2022
	Details of fee submitted	PKR 30,000/-: dated 05-07-2022
	The proposed proprietary name / brand name	Aqua-Q 5ml Injection(WFI)
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each filled ampule contains: Water for Injection……5mL
	Pharmaceutical form of applied drug	Solvent for Injection

	Pharmacotherapeutic Group of (API)	Solvent
	Reference to Finished product specifications	BP Spec
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Manufacturer: Mercury pharmaceuticals Address:Capital House,85King Walliam StreetLondon EC4N7BL UK
	For generic drugs (me-too status)	Surge Labortories Pvt Ltd
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021 Tablet (General) ,Capsule (General), Capsule (cephalosporin) Oral Dry Suspension (cephalosporin) Oral liquid, liquid injectable vial& Ampoule(Gerenal) Dry powder Injectable(Gerenal) section approved.
	Name and address of API manufacturer.	M/S QADIR PHARMACEUTICALS 6-KM G.T Road Wazirabad Sialkot Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of WFI is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T001, T002, T003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical

		procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is WFI 5 ml Injection manufacture by Global Pharma by performing quality tests
	Analytical method validation/verification of product	NA

STABILITY STUDY DATA			
Manufacturer of API	M/S QADIR PHARMACEUTICALS 6-KM G.T Road Wazirabad Sialkot Pakistan		
API Lot No.	NA		
Description of Pack (Container closure system)	Solvent for injection filled in glass ampoule Type 1 (1×1's)		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	1000 Amp	1000 Amp	1000 Amp
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	16-10-2021	16-10-2021	16-10-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms,	Submitted

	Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	NA
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Provide detailed analytical procedures used for the testing of drug substance (bulk water for injection) since the submitted procedure only reflect the acceptance limit.	Submitted
2.	Provide quantitative results in batch analysis report of drug substance as per the decision of 293rd meeting of Registration Board, which states that "*For quantitative tests, actual numerical results should be provided rather than vague statements such as "within limits" or "conforms*".	Submitted
3.	Provide detailed analytical procedure for testing of pH value,conductivity,endotoxin,sterility test, liquid particulate matter ,sulfate, Aluminum and ammonium.	Submitted
4.	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product under section 2.3.R.1.1, for which stability studies data is provided in Module 3 section 3.2. P.8.	Submitted

Decision: Approved.

• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.

• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.

281.	Name, address of Applicant / Marketing Authorization Holder	M/s Pasteur & Fleming Pharmaceuticals Pvt. Ltd. Industrial Estate Hattar.
	Name, address of Manufacturing site.	M/s Pasteur & Fleming Pharmaceuticals (Pvt). Ltd. Plot No. 70-A, Road No. 04, Phase 3, Industrial Estate. Hattar, Khyber Pakhtunkhwa Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.27898 dated 03/10/2022
	Details of fee submitted	PKR 30,000/-: dated. 04/08/2022. Slip No. 7108803872
	The proposed proprietary name / brand name	PF-Zole 40mg Capsules
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Hard Gelatin Capsule contains: Esomeprazole Magnesium Trihydrate enteric coated pellets eq. to Esomeprazole…..... 40mg (USP Specs)
	Pharmaceutical form of applied drug	White to off-white color EC Pellets filled in Hard Gelatin Capsule Shell
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	USP
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nexium 20mg Capsules by Astra Zeneca UK Limited 2 Pancras Square, 8th Floor, London, N1C 4AG, UK USFDA Approved.
	For generic drugs (me-too status)	Esim 20mg Capsule by M/s Genome Pharmaceuticals Reg. No. 053581
	GMP status of the Finished product manufacturer	New license granted on 10/11/2021 Capsules (General) section approved.
	Name and address of API manufacturer.	Vision Pharmaceuticals (Pvt.) Limited Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Esomeprazole Magnesium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , specifications, analytical

		procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 75 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches # EMZ045859, EMZ045908, EMZ045898
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Esim 20mg Capsules by M/S Genome Pharma by performing quality tests (Identification, Assay, Dissolution, and Uniformity of dosage form). CDP has been performed against the same brand that is 20mg Capsules by Genome Pharma in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA

Manufacturer of API	Vision Pharmaceuticals (Pvt.) Limited Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan.		
API Lot No.	EMZ 046492		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-04	T-05	T-06
Batch Size	1000 Caps	1000 Caps	1000 Caps
Manufacturing Date	03-2022	03-2022	03-2022

Date of Initiation	24-03-2022	25-03-2022	26-03-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. F.3-26/2019-Addl.Dir. (QA & LT-1) by DRAP valid till 10/02/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Locally Purchased from Vision Pharma Islamabad • D.C # 802250 , dated 18/03/2022
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Submit label claim in module 1 as per the reference product along with submission of requisite fee.	Firm submit the correct label claim of the applied product without fee.
2.	Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted" Further specify how the testing of drug substance was carried out without performing verification studies.	Firm submitted only the summary tablet of analytical verification report.
3.	Justify the label claim without mentioning the salt form of esomeprazole while the pellets contain esomeprazole magnesium trihydrate. Furthermore, also submit master formulation keeping in view the salt	Firm submitted the revised formulation table in which the magnesium has not been adjusted in the filled weight of capsule and the magnesium factor is 1.035.

	factor and percentage of pellets used in the development of stability batches.	
4.	Justify why the pharmaceutical equivalence and comparative dissolution profile studies were conducted against the comparator product instead of using innovator / reference product.	Firm replied that Now we are doing Pharmaceuticals Equivalence & Comparative dissolution with Nexium 40mg Capsules & Report summary will be provided soon because revised CDP Testing is being perform at HPLC with Nexum Capsules 20mg Reg# 033891 & remaining ongoing real time stability study Dissolution tests will be shifted on HPLC as per U.S.P while our Assay tests already performed on HPLC Chromatograms & Reports are Attached in dossier.
5.	Justify for performance of dissolution test on UV when the USP monograph recommend HPLC method for dissolution testing.	Firm replied that remaining ongoing real time stability study Dissolution tests will be shifted on HPLC.
6.	Submit verification report of analytical method of the drug product in section 3.2.P.5.3.	Firm submitted only the summary tablet of analytical verification report.
7.	Justify, how the average weight of capsule with shell become 302mg, when the average filled weight was 234.2 mg and the empty capsule shell weight was 1.03mg as per the submitted BMR.	Correct BMR has been submitted by the firm in which the weight of empty capsule is 105mg.
8.	• Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. • Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm replied that, "We purchased 3.0 Kg Esomeprazole Pellets from Vision Pharmaceuticals whole lot Batch # EMZ046452 was utilized for the 3 trial batches of PF-Zole 20mg & the three trial batches of PF-Zole 40mg. Invoice & COA of raw material is attached."
9.	Provide compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm replied that "We have used Shemadzu HPLC there was a problem in the software of the attached computer system due to this problem the audit trail couldn't be turned on the whole process of stability study. Now we purchased another Water Alliance CFR-21 Compliance HPLC with software backup."

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Manufacturer shall adopt the calculations for potency adjustment for commercial manufacturing on basis of potency determined during drug substance anlaysis.**
- **Registration letter will be issued upon submission of analytical method verification studies of drug product, performance of stability study at next time point of long term stability studies as per USP monograph and CDP report in accordance with revised analytical method based upon HPLC.**

• **Full fee of Rs. 30,000/-, for revision of data as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**		
282.	Name, address of Applicant / Marketing Authorization Holder	M/s Pasteur & Fleming Pharmaceuticals Pvt. Ltd. Industrial Estate Hattar.
	Name, address of Manufacturing site.	M/s Pasteur & Fleming Pharmaceuticals (Pvt). Ltd. Plot No. 70-A, Road No. 04, Phase 3, Industrial Estate. Hattar, Khyber Pakhtunkhwa Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.26564 dated 20/09/2022
	Details of fee submitted	PKR 30,000/-: dated. 04/08/2022. Slip No. 67351827467
	The proposed proprietary name / brand name	PF-Zole 20mg Capsules
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Hard Gelatin Capsule contains: Esomeprazole Magnesium Trihydrate enteric coated pellets eq. to Esomeprazole…..... 20mg (USP Specs)
	Pharmaceutical form of applied drug	White to off-white color EC Pellets filled in Hard Gelatin Capsule Shell
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	USP
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nexium 20mg Capsules by Astra Zeneca UK Limited 2 Pancras Square, 8th Floor, London, N1C 4AG, UK USFDA Approved.
	For generic drugs (me-too status)	Esim 20mg Capsule by M/s Genome Pharmaceuticals Reg. No. 046196
	GMP status of the Finished product manufacturer	New license granted on 10/11/2021 Capsules (General) section approved.
	Name and address of API manufacturer.	Vision Pharmaceuticals (Pvt.) Limited Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Esomeprazole Magnesium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 75 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches # EMZ045058, EMZ0446320, EMZ044858
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Esim 20mg Capsules by M/S Genome Pharma by performing quality tests (Identification, Assay, Dissolution, and Uniformity of dosage form). CDP has been performed against the same brand that is 20mg Capsules by Genome Pharma in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Vision Pharmaceuticals (Pvt.) Limited Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan.
API Lot No.	EMZ 046492

Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	1000 Caps	1000 Caps	1000 Caps
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	24-03-2022	25-03-2022	26-03-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. F.3-26/2019-Addl.Dir. (QA & LT-1) by DRAP valid till 10/02/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Locally Purchased from Vision Pharma Islamabad • D.C # 802250 , dated 18/03/2022
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Submit label claim in module 1 as per the reference product along with submission of requisite fee.	Firm submit the correct label claim of the applied product without fee.
2.	Submit data in section 3.2.S.4.3 as per the guidance document approved by Registration Board which specifies that "Analytical Method Verification studies including specificity, accuracy	Submitted only the summary table of Module-2.

	and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted" Further specify how the testing of drug substance was carried out without performing verification studies.	
3.	Justify the label claim without mentioning the salt form of esomeprazole while the pellets contain esomeprazole magnesium trihydrate. Furthermore, also submit master formulation keeping in view the salt factor and percentage of pellets used in the development of stability batches.	Firm submitted the revised formulation table in which the magnesium has not been adjusted in the filled weight of capsule and the magnesium factor is 1.035.
4.	Justify why the pharmaceutical equivalence and comparative dissolution profile studies were conducted against the comparator product instead of using innovator / reference product.	Firm replied that Now we are doing Pharmaceuticals Equivalence & Comparative dissolution with Nexium 40mg Capsules & Report summary will be provided soon because revised CDP Testing is being perform at HPLC with Nexum Capsules 20mg Reg# 033891 & remaining ongoing real time stability study Dissolution tests will be shifted on HPLC as per U.S.P while our Assay tests already performed on HPLC Chromatograms & Reports are Attached in dossier.
5.	Justify for performance of dissolution test on UV when the USP monograph recommend HPLC method for dissolution testing.	Firm replied that remaining ongoing real time stability study Dissolution tests will be shifted on HPLC.
6.	Submit verification report of analytical method of the drug product in section 3.2.P.5.3.	Submitted only the summary table of Module-2.
7.	Justify, how the average weight of capsule with shell become 302mg, when the average filled weight was 234.2 mg and the empty capsule shell weight was 1.03mg as per the submitted BMR.	Correct BMR has been submitted by the firm in which the weight of empty capsule is 105mg.
8.	• Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. • Provide Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm replied that, "We purchased 3.0 Kg Esomeprazole Pellets from Vision Pharmaceuticals whole lot Batch # EMZ046452 was utilized for the 3 trial batches of PF-Zole 20mg & the three trial batches of PF-Zole 40mg. Invoice & COA of raw material is attached."
9.	Provide compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm replied that "We have used Shemadzu HPLC there was a problem in the software of the attached computer

		system due to this problem the audit trail couldn't be turned on the whole process of stability study. Now we purchased another Water Alliance CFR-21 Compliance HPLC with software backup."

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Manufacturer shall adopt the calculations for potency adjustment for commercial manufacturing on basis of the content of "Esomeprazole" determined during drug substance analysis.**
- **Registration Board further decided that registration letter will be issued upon submission of following:**
  - **Analytical verification studies of drug product in accordance with USP monograph.**
  - **CDP studies performed by revised analytical method based upon HPLC.**
  - **Performance of stability study at next time point of long term stability studies wherein analysis shall be conducted as per USP monograph.**
  - **Full fee of Rs. 30,000/-, for revision of data as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

283.	Name, address of Applicant / Marketing Authorization Holder	VARIANT PHARMACEUTICALS (PVT.) LTD
	Name, address of Manufacturing site.	PLOT # 5, M-2, PHARMAZONE, 26 KM MAIN SHARAQPUR ROAD DISTRICT SHEIKHUPURA.PAKISTAN
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10572 dated 27/04/2022
	Details of fee submitted	PKR 30,000/-: dated 09/03/2022
	The proposed proprietary name / brand name	V-MONT 05mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Chewable tablet contains Montelukast Sodium eq. to Montelukast …..5mg
	Pharmaceutical form of applied drug	Film coated tablet.
	Pharmacotherapeutic Group of (API)	Leukotriene antagonist
	Reference to Finished product specifications	USP specifications

	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	SINGULAIR 5mg tablet by MERCK & CO., INC, USFDA Approved.
	For generic drugs (me-too status)	BRONSECUR 5 mg tab by M/s Pfizer Pharma (Pvt.) Ltd., Reg. No. 061335
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020 General Tablet, General Capsule, General Sachet and General dry powder injectable (pre-lyophilized)
	Name and address of API manufacturer.	Zhejiang Tianyu Pharmaceutical Co., Ltd. Address: No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China. P.C.:317016
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Montelukast Sodium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(201310301, 201310302,201310303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and

		stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product that is Floaid 5mg Tablet by M/s. Highnoon Labs Ltd, Reg.no. 032075 Batchno.212149, expiry date 07-2023. by performing quality tests (Identification, Assay, Dissolution,). CDP has been performed against the same brand that is Floaid 5mg Tablet by M/s. Highnoon Labs Ltd, Reg.no. 032075 Batchno.212149, expiry date 07-2023, in Acid media (pH 1.2), Acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA			
Manufacturer of API	Zhejiang Tianyu Pharmaceutical Co., Ltd. Address: No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China. P.C.:317016		
API Lot No.	11001-200509		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	11-08-2021	24-08-2021	25-08-2021
Date of Initiation	23-08-2021	28-08-2021	28-08-2021
No. of Batches	03		

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. ZJ20180033 issued by China FDA valid till 14-03-2023.

9.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.4111/2020/DRAP-AD-CD(I&E) dated 02/03/2020 is submitted wherein the permission to import different APIs including Montelukast Sodium for the purpose of test/analysis and stability studies is granted. • Invoice # TYI2020704211 AD date 04-07-2020
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	3.2.S.4.2: Analytical procedures Provide detailed analytical procedures for the testing of drug substance by drug product manufacturer. 3.2.S.4.3: Validation of analytical procedures Provide analytical Method validation studies performed by the Drug Product manufacturer.	Firm submitted the analytical procedure and analytical verification report of drug substance by drug product manufacturer.
2.	Justify the use of a different analytical method for assay testing of drug product in terms of concentration of sample solution and standard solution from that specified in USP monograph.	Firm submitted the analysis sheet in which the sample preparation method is in accordance with USP monograph of montelukast chewable tablet

Decision: Deferred for justification of using Montelukast sodium as reference standard in analytical procedures instead of Montelukast dicyclohexylamine as specified by USP monograph.

284.	Name, address of Applicant / Marketing Authorization Holder	VARIANT PHARMACEUTICALS (PVT.) LTD
	Name, address of Manufacturing site.	PLOT # 5, M-2, PHARMAZONE, 26 KM MAIN SHARAQPUR ROAD DISTRICT SHEIKHUPURA.PAKISTAN
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11698 dated 14/05/2022
	Details of fee submitted	PKR 30,000/-: dated 29/04/2022
	The proposed proprietary name / brand name	V-MONT 04mg Sachet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Sachet contains Montelukast Sodium eq. to Montelukast …..4mg
	Pharmaceutical form of applied drug	Sachet.
	Pharmacotherapeutic Group of (API)	Leukotriene antagonist
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Montelukast 4 mg Granules by TORRENT PHARMA (UK) Ltd, MHRA approved.
	For generic drugs (me-too status)	FLOAID 4mg Sachet by M/s Highnoon Labs Ltd, Reg. No. 044768
	GMP status of the Finished product manufacturer	New license granted on 13/02/2020 General Tablet, General Capsule, General Sachet and General dry powder injectable (pre-lyophilized)
	Name and address of API manufacturer.	Zhejiang Tianyu Pharmaceutical Co., Ltd. Address: No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China. P.C.:317016
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Montelukast Sodium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances,

		specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(201310301, 201310302,201310303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is FLOAID 4mg Sachet by M/s Highnoon Labs Ltd, Reg. No. 044768 by performing quality tests (Identification, Assay, Dissolution,). CDP has been performed against the same brand that is FLOAID 4mg Sachet by M/s Highnoon Labs Ltd, in Acid media (pH 1.2), Acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Zhejiang Tianyu Pharmaceutical Co., Ltd. Address: No.15, Donghai 5th Avenue, Zhejiang Provincial Chemical and Medical Raw Materials Base Linhai Zone, Taizhou City, Zhejiang Province, China. P.C.:317016		
API Lot No.	11001-200509		
Description of Pack (Container closure system)	Alu-Alu Sachet packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003

Batch Size	1000 Sachet	1000 Sachet	1000 Sachet
Manufacturing Date	03-09-2021	07-09-2021	07-09-2021
Date of Initiation	08-09-2021	11-09-2021	11-09-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. ZJ20180033 issued by China FDA valid till 14-03-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.4111/2020/DRAP-AD-CD(I&E) dated 02/03/2020 is submitted wherein the permission to import different APIs including Montelukast Sodium for the purpose of test/analysis and stability studies is granted. • Invoice # TYI2020704211 AD date 04-07-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	3.2.S.4.2: Analytical procedures Provide detailed analytical procedures for the testing of drug substance by drug product manufacturer. 3.2.S.4.3: Validation of analytical procedures Provide analytical Method validation studies performed by the Drug Product manufacturer.	Firm submitted the analytical procedure and verification report of drug substance by drug product manufacturer.

Decision: Deferred for justification of using Montelukast sodium as reference standard in analytical procedures instead of Montelukast dicyclohexylamine as specified by USP monograph.

285.	Name, address of Applicant / Marketing Authorization Holder	M/s Fortune Pharmaceuticals Private Limited Karachi
	Name, address of Manufacturing site.	M/s Fortune Pharmaceutical Private Limited

		Plot K/201 S.I.T.E. (SHW) Phase II, Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12392 dated 21/05/2022
	Details of fee submitted	PKR 30,000/-: dated 27/04/2022
	The proposed proprietary name / brand name	F -OMEZOL 20mg Gastro-resistance Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Omeprazole 22.5% Enteric coated pellets E.q to to Omeprazole 20mg
	Pharmaceutical form of applied drug	A Green cap with grey body size "3" hard Gelatin filled capsule having white pallets.
	Pharmacotherapeutic Group of (API)	Drugs for acid-related disorders, Proton pump inhibitors
	Reference to Finished product specifications	USP
	Proposed Pack size	1×14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved Omeprazole 20mg Gastro – resistant capsule MHRA
	For generic drugs (me-too status)	LOSEC CAPSUL 20 mg BARRETT HODGSON PAKISTAN (PVT) LTD
	GMP status of the Finished product manufacturer	New license granted on 21/02/2021 Tablet, Capsule (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	SAAKH PHARMA. Address: Plot # C -7/1, North West Industrial Zone, Karachi
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Omeprazole is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (OME-EC – 22.5-001-19, OME-EC – 22.5-008-19, OME -EC – 22.5-009-19)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is LOSECCAPSULE 20 mg Capsule by BARRETT HODGSON PAKISTAN (PVT) LTD. performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is LOSEC CAPSULE 20 mg by BARRETT HODGSON PAKISTAN (PVT) LTD. in Acid media (pH 1.2), pH 4.5& Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.
STABILITY STUDY DATA		
Manufacturer of API	SAAKH PHARMA.	

	Address: Plot # C -7/1, North West Industrial Zone,		
API Lot No.	22GT2 2002		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	FE-001	FE-002	FE-003
Batch Size	1400 capsule	1400 capsule	1400 capsule
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	02-04-2021	02-04-2021	02-04-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document. Because of new DML
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP Certificate No. 83/2020-DRAP(K) dated 23-06-2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Local purchase from M/s. Saakh Pharma,Karachi
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	HPLC software 21CFR not Installed
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.no.	Observations/Shortcomings	Reply of the Form
1.	Justify how you claim USP specification for drug substance, when the submitted analytical method is not in accordance with USP neither similar to the assay method of drug substance manufacturer. Further, the assay method given in section	Firm submitted the specification of drug substance by drug substance manufacturer which is also not incompliance of USP monograph.

	3.2. S. 4.2 is different from the method which is validated in section 3.2.S.4.3, clarification is required in this regard.	
2.	Clarification is required regarding the assay results of stability data of drug substance, either the quantity is of dried basis of omeprazole magnesium or the labelled amount of omeprazole, since the COA of drug substance claim the content of active on dried basis.	Firm submitted the stability data sheet of drug substance in which assay results are specified on dried basis, while in USP monograph the content of active should be quantify on the basis of labelled amount of omeprazole. Further the dissolution result of acidic stage has not been included in the stability data sheet of the drug substance.
3.	Provide complete method of dissolution testing along with details of HPLC parameters used during the dissolution testing of drug product in line with USP.	Firm has not submitted the reply in response of this query.
4.	Provide complete analytical method verification studies of drug product including the specificity and repeatability parameter along with raw data sheets and chromatogram.	Firm has not submitted the analytical verification report of drug product.
5.	Performance of comparative dissolution profile is not in accordance with guidelines approved in 293rd meeting of Registration Board with reference to following points: ✓ For f2 calculations a minimum of three time points (excluding point zero) must be used; mentioned the time point which were considered for the calculation of f2 value. ✓ A maximum of one time-point should be considered after 85% dissolution of the innovator / reference product has been reached; but as per the submitted documents you have used all time point until 30minutes, which are all below 85%. Clarify how you have calculated the f2 without considering the time point after 85% drug release.	Firm submitted the revised Comparative dissolution profile data in which all 12 units of both test product and reference shows below 65% release in pH 6.8 medium till 45 minutes while the dissolution results of stability data reveals that more than 90% drug release at pH 6.8 medium within 30 minutes.
6.	Clarify, why you have not mentioned the results of dissolution test in acidic medium in the stability data of drug product. Further, the specification of dissolution test did not mention the time limit in which NLT 75% (Q) should be achieved.	Firm has submitted the revised stability data in which results of assay of esomeprazole has been mentioned instead of omeprazole.

Decision: Deferred for submission of following:

- **Justify how you claim USP specification for drug substance, when the submitted analytical method is not in accordance with USP neither similar to the assay method of drug substance manufacturer. Further, the assay method given in section 3.2. S. 4.2 is different**

	from the method which is validated in section 3.2.S.4.3, clarification is required in this regard. • **Stability data sheet of drug substance including the results of dissolution test of acidic stage.** • **Provide complete method of dissolution testing along with details of HPLC parameters used during the dissolution testing of drug product in line with USP.** • **Provide complete analytical method verification studies of drug product including the specificity and repeatability parameter along with raw data sheets and chromatogram.** • **Justify the dissolution results of stability data in which more than 90% drug release at pH 6.8 medium within 30 minutes, while the revised Comparative dissolution profile data evident that both test product and reference product release below 65% in pH 6.8 medium till 45 minutes.** • **Revised stability data of drug product specify the results of assay of esomeprazole, clarification is required in this regard.**	
286.	Name, address of Applicant / Marketing Authorization Holder	M/s Fortune Pharmaceuticals Private Limited Karachi
	Name, address of Manufacturing site.	M/s Fortune Pharmaceutical Private Limited Plot K/201 S.I.T.E. (SHW) Phase II, Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12393 dated 21/05/2022
	Details of fee submitted	PKR 30,000/-: dated 27/04/2022
	The proposed proprietary name / brand name	F -OMEZOL 40mg Gastro-resistance Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Omeprazole 22.5% Enteric coated pellets E.q to to Omeprazole 40mg
	Pharmaceutical form of applied drug	A Green cap with grey body size “3” hard Gelatin filled capsule having white pallets.
	Pharmacotherapeutic Group of (API)	Drugs for acid-related disorders, Proton pump inhibitors
	Reference to Finished product specifications	USP
	Proposed Pack size	1×14’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Approved Omeprazole 40mg Gastro – resistant capsule MHRA

	For generic drugs (me-too status)	LOSEC CAPSUL 40 mg BARRETT HODGSON PAKISTAN (PVT) LTD
	GMP status of the Finished product manufacturer	New license granted on 21/02/2021 Tablet, Capsule (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	SAAKH PHARMA. Address: Plot # C -7/1, North West Industrial Zone,
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Omeprazole is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (OME-EC – 22.5-001-19, OME-EC – 22.5-008-19, OME -EC – 22.5-009-19)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is LOSEC CAPSULE 40 mg Capsule by BARRETT HODGSON PAKISTAN (PVT) LTD. performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is LOSEC CAPSULE 40 mg by BARRETT HODGSON PAKISTAN (PVT) LTD in all three physiological mediums. The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA			
Manufacturer of API	SAAKH PHARMA. Address: Plot # C -7/1, North West Industrial Zone,		
API Lot No.	22GT2 2002		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	FE-001	FE-002	FE-003
Batch Size	1400 capsule	1400 capsule	1400 capsule
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	02-04-2021	02-04-2021	02-04-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document. Because of new DML
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP Certificate No. 83/2020-DRAP(K) dated 23-06-2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Local purchase from M/s. Saakh Pharma, Karachi
4.	Data of stability batches will be supported by attested respective documents like chromatograms,	Submitted

	Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	HPLC software 21CFR not Installed
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.no.	Observations/Shortcomings	Reply of the Form
1.	Justify how you claim USP specification for drug substance, when the submitted analytical method is not in accordance with USP neither similar to the assay method of drug substance manufacturer. Further, the assay method given in section 3.2. S. 4.2 is different from the method which is validated in section 3.2.S.4.3, clarification is required in this regard.	Firm submitted the specification of drug substance by drug substance manufacturer which is also not incompliance of USP monograph.
2.	Clarification is required regarding the assay results of stability data of drug substance, either the quantity is of dried basis of omeprazole magnesium or the labelled amount of omeprazole, since the COA of drug substance claim the content of active on dried basis.	Firm submitted the stability data sheet of drug substance in which assay results are specified on dried basis, while in USP monograph the content of active should be quantify on the basis of labelled amount of omeprazole. Further the dissolution result of acidic stage has not been included in the stability data sheet of the drug substance.
3.	Provide complete method of dissolution testing along with details of HPLC parameters used during the dissolution testing of drug product in line with USP.	Firm has not submitted the reply in response of this query.
4.	Provide complete analytical method verification studies of drug product including the specificity and repeatability parameter along with raw data sheets and chromatogram.	Firm has not submitted the analytical verification report of drug product.
5.	Performance of comparative dissolution profile is not in accordance with guidelines approved in 293rd meeting of Registration Board with reference to following points: ✓ For f2 calculations a minimum of three time points (excluding point zero) must be used; mentioned the time point which were considered for the calculation of f2 value. ✓ A maximum of one time-point should be considered after 85%	Firm submitted the revised Comparative dissolution profile data in which all 12 units of both test product and reference shows below 65% release in pH 6.8 medium till 45 minutes while the dissolution results of stability data reveals that more than 90% drug release at pH 6.8 medium within 30 minutes.

	dissolution of the innovator / reference product has been reached; but as per the submitted documents you have used all time point until 30minutes, which are all below 85%. Clarify how you have calculated the f2 without considering the time point after 85% drug release.	
6.	Clarify, why you have not mentioned the results of dissolution test in acidic medium in the stability data of drug product. Further, the specification of dissolution test did not mention the time limit in which NLT 75% (Q) should be achieved.	Firm has submitted the revised stability data in which results of assay of esomeprazole has been mentioned instead of omeprazole.

Decision: Deferred for submission of following:

- **Justify how you claim USP specification for drug substance, when the submitted analytical method is not in accordance with USP neither similar to the assay method of drug substance manufacturer. Further, the assay method given in section 3.2. S. 4.2 is different from the method which is validated in section 3.2.S.4.3, clarification is required in this regard.**
- **Stability data sheet of drug substance including the results of dissolution test of acidic stage.**
- **Provide complete method of dissolution testing along with details of HPLC parameters used during the dissolution testing of drug product in line with USP.**
- **Provide complete analytical method verification studies of drug product including the specificity and repeatability parameter along with raw data sheets and chromatogram.**
- **Justify the dissolution results of stability data in which more than 90% drug release at pH 6.8 medium within 30 minutes, while the revised Comparative dissolution profile data evident that both test product and reference product release below 65% in pH 6.8 medium till 45 minutes.**
- **Revised stability data of drug product specify the results of assay of esomeprazole, clarification is required in this regard.**

287.	Name, address of Applicant / Marketing Authorization Holder	M/s Fortune Pharmaceuticals Private Limited Karachi
	Name, address of Manufacturing site.	M/s Fortune Pharmaceutical Private Limited Plot K/201 S.I.T.E. (SHW) Phase II, Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 12391 dated 21/05/2022

	Details of fee submitted	PKR 30,000/-: dated 27/04/2022
	The proposed proprietary name / brand name	F -EZOLE 40mg Gastro resistant Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Esomeperazole Magnisium Trihydrate E.q to to Esomeperazole 40mg
	Pharmaceutical form of applied drug	A dark blue cap with blue body size "3" hard Gelatin filled capsule having white pallets.
	Pharmacotherapeutic Group of (API)	Drugs for acid-related disorders, Proton pump inhibitors
	Reference to Finished product specifications	USP
	Proposed Pack size	1×14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	NEXIUM 40mg Capsule USFDA. Esomeprazole 40mg Gastro – resistant capsule MHRA
	For generic drugs (me-too status)	ACIREG CAPSUL 40 mg BARRETT HODGSON PAKISTAN (PVT) LTD
	GMP status of the Finished product manufacturer	New license granted on 21/02/2021 Tablet, Capsule (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	SAAKH PHARMA. Address: Plot # C -7/1, North West Industrial Zone,Karachi
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Esomeprazole Mg is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance

	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (ESO-EC – 22.5-001-19, ESO-EC – 22.5-002-19, ESO-EC – 22.5-003-19)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is ACIREG CAPSULE 40 mg Capsule by BARRETT HODGSON PAKISTAN (PVT) LTD. performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is ACIREG CAPSULE 40 mg by BARRETT HODGSON PAKISTAN (PVT) LTD.in Acid media (pH 1.2), pH 4.5 & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA

Manufacturer of API	SAAKH PHARMA. Address: Plot # C -7/1, North West Industrial Zone,		
API Lot No.	21GT1 2003		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	FE-001	FE-002	FE-003
Batch Size	1400 capsule	1400 capsule	1400 capsule
Manufacturing Date	03-2021	03-2021	03-2021

Date of Initiation	02-03-2021	02-03-2021	02-03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document. Because of new DML
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP Certificate No. 83/2020-DRAP(K) dated 23-06-2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Local purchase from M/s. Saakh Pharma, Karachi
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	HPLC software 21CFR not Installed
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.no.	Observations/Shortcomings	Reply of the Form
1.	Justify how you claim USP specification for drug substance, when the submitted analytical method is not in accordance with USP neither similar to the assay method of drug substance manufacturer. Further, the assay method given in section 3.2. S. 4.2 is different from the method which is validated in section 3.2.S.4.3, clarification is required in this regard.	Firm submitted the specification of drug substance by drug substance manufacturer which is also not incompliance of USP monograph with reference to the assay results.
2.	Provide COA of primary / secondary reference standard including source and lot number used for testing of drug substance.	Firm submitted the COA of working standard of Esomeprazole, while the USP recommends Omeprazole RS for the assay testing of Esomeprazole delayed release capsule.
3.	Clarification is required regarding the assay results of stability data of drug substance, either the quantity is of dried basis of omeprazole magnesium or the labelled amount of omeprazole, since the COA of drug substance claim the content of active on dried basis.	Firm submitted the stability data sheet of drug substance in which assay results are specified on anhydrous basis, while in USP monograph the content of active should be quantify on the basis of labelled amount of Esomeprazole. Further the dissolution result of acidic stage has not been included in the stability data sheet of the drug substance.

4.	Provide complete method of dissolution testing along with details of HPLC parameters used during the dissolution testing of drug product in line with USP.	Firm has submitted the reply in response of this query.
5.	Provide complete analytical method verification studies of drug product including the specificity and repeatability parameter along with raw data sheets and chromatogram.	Firm has not submitted the analytical verification report of drug product neither the drug substance.
6.	Performance of comparative dissolution profile is not in accordance with guidelines approved in 293rd meeting of Registration Board with reference to following points: ✓ For f2 calculations a minimum of three time points (excluding point zero) must be used; mentioned the time point which were considered for the calculation of f2 value. ✓ A maximum of one time-point should be considered after 85% dissolution of the innovator / reference product has been reached; but as per the submitted documents you have used all time point until 30minutes, which are all below 85%. Clarify how you have calculated the f2 without considering the time point after 85% drug release.	Firm submitted the revised Comparative dissolution profile data in which all 12 units of both test product and reference shows below 65% release in pH 6.8 medium till 45 minutes while the dissolution results of stability data reveals that more than 90% drug release at pH 6.8 medium within 30 minutes.
7.	Clarify, why you have not mentioned the results of dissolution test in acidic medium in the stability data of drug product. Further, the specification of dissolution test did not mention the time limit in which NLT 75% (Q) should be achieved.	Firm has submitted the revised stability data in which more than 90% drug release at buffer stage within 30 minutes.
8.	Raw data sheets of dissolution testing and assay testing have not been attached in section 3.2. P.8., provide raw data sheet to analyse the result of dissolution and assay. Firm has submitted the raw data sheets and chromatograms of dissolution and assay testing, which evident that the assay was not performed in comply with USP specification in term of sample and standard solution conc and the total run time which is consist of 25 minutes' gradient elution program. Further, the chromatogram of standard evident that the esomeprazole has been used as a standard, while USP monograph recommends omeprazole RS for the Esomeprazole capsule.	
9.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not submitted

Decision: Deferred for submission of following:

- **Justify how you claim USP specification for drug substance, when the submitted analytical method is not in accordance with USP neither similar to the assay method of drug substance manufacturer. Further, the assay method given in section 3.2. S. 4.2 is different from the method which is validated in section 3.2.S.4.3, clarification is required in this regard.**

- **Scientific justification for use of Esomeprazole as reference standard in analytical procedures instead of Omeprazole RS as specified by USP monograph.**
- **Stability data sheet of drug substance including the results of dissolution test of acidic stage.**
- **Provide complete analytical method verification studies of drug product including the specificity and repeatability parameter along with raw data sheets and chromatogram.**
- **Justify the dissolution results of stability data in which more than 90% drug release at pH 6.8 medium within 30 minutes, while the revised Comparative dissolution profile data evident that both test product and reference product release below 65% in pH 6.8 medium till 45 minutes.**
- **Scientific justification for using assay method different from that specified in USP monograph in term of gradient program, total run time and reference standard.**
- **Compliance Record of HPLC software 21CFR & audit trail reports on product testing.**

288.	Name, address of Applicant / Marketing Authorization Holder	M/s Fortune Pharmaceuticals Private Limited Karachi
	Name, address of Manufacturing site.	M/s Fortune Pharmaceutical Private Limited Plot K/201 S.I.T.E. (SHW) Phase II, Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.12972 dated 27/05/2022
	Details of fee submitted	PKR 30,000/-: dated 27/04/2022
	The proposed proprietary name / brand name	Fungazole 150mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Fluconazole...150mg
	Pharmaceutical form of applied drug	A dark blue cap with blue body size "3" hard Gelatin filled capsule having white pallets.
	Pharmacotherapeutic Group of (API)	Antifungal
	Reference to Finished product specifications	BP
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved
	For generic drugs (me-too status)	Zolanix 150mg capsule of M/s. Glaxo smithkline,Karachi
	GMP status of the Finished product	New license granted on 21/02/2021

	manufacturer	Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Hema Pharmaceuticals Plot no.6201/A&B Opp. Ewac Alloys Ltd. GIDC Ankleshwar,Gujrat,India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Fluconazole is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (12PDFC001,12PDFC002,12PDFC003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the comparator product that is Flozex capsule of M/S. Martin Dow Pharmaceuticals Pvt. Ltd,Karachi Batch no. 225 expiry date 03-2023. performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).

		CDP has been performed against the same brand that is Flozex capsule of M/S. Martin Dow Pharmaceuticals Pvt. Ltd,Karachi Batch no. 225 expiry date 03-2023.in Acid media (pH 1.2), pH 4.5 & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA			
Manufacturer of API	Hema Pharmaceuticals Plot no.6201/A&B Opp. Ewac Alloys Ltd. GIDC Ankleshwar,Gujrat,India		
API Lot No.	Not mentioned		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	FL-001	FL-002	FL-003
Batch Size	1500 capsule	1500 capsule	1500 capsule
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	25-10-2021	25-10-2021	25-10-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document. Because of new DML
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP Certificate No. S-GMP/2062028 dated 12-06-2020 valid till 11/06/2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Consignment slip and DHL courier slip has been attached only
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	HPLC software 21CFR not Installed
6.	Record of Digital data logger for temperature and humidity monitoring of	Submitted

	stability chambers (real time and accelerated)	

Remarks OF Evaluator:

Sr.no.	Observations/Shortcomings	Reply of the Form
1.	Clarify the specification of drug product since the JP monograph of fluconazole capsule is not applicable for 150mg strength. Revise your specification along with the requisite fee.	Firm submitted the revised specification of drug product which is neither in comply of BP monograph nor in compliance of JP.
2.	The validation of analytical procedure has been performed using assay method (HPLC) with flow rate 1.0ml/min, column temperature 35°C, UV detector set at 261nm and mobile phase sodium acetate: methanol: acetonitrile while USP recommended flow rate 0.5ml/min, column temperature 40°C, UV detector 260nm and mobile phase Acetonitrile and water (20:80). Justify, how have comply USP specification by keeping the chromatographic condition different from USP monograph of fluconazole.	Not submitted
3.	Clarify, how you have performed accuracy parameter in the verification studies of drug substance that, despite spiking the sample 25%,50%,75%,100%,125% and 150%, the amount of fluconazole has not been changed in all these spiked sample.	Not submitted any reply of this query
4.	Identification test specified on the COA of working standard of fluconazole attached in section 3.2.S.5 stated that IR absorption spectrum of test solution should be concordant with that of clotrimazole working standard, clarification is required in this regard. Further, the COA reflect that batch qualified against Indian pharmacopeia reference standard, justify how you can standardize the drug substance that comply with USP specification to the working standard that qualified against Indian pharmacopeia.	.Not submitted any reply of this query
5.	Scientific justification is required for using 3mg overage of active substance as evident from the composition given in section 3.2. P.1.	Firm has not submitted any reply.

6.	Clarify, that the dissolution method given in section 3.2.P.5.2 is different from the method via which dissolution has been performed in section 3.2.P.2.2.1 for comparative dissolution profile of drug product.	Firm submitted the revised Comparative dissolution profile in which the dissolution were not in accordance with BP monograph.
7.	• Justify selection of dissolution parameters i.e. USP apparatus-II paddle with 50rpm, water as dissolution medium and acceptance criteria NLT 75% of the labeled amount of the claim content, since JP monograph of fluconazole capsule is recommending the dissolution testing for 50mg and 100mg fluconazole capsule strength. • Justify the variation in dissolution parameters in different section of dossier, acceptance limit specified in section 3.2.P.5.2 is NLT 75% in 45 minutes while the dissolution specifications mentioned on batch analysis report is NLT 80%.	Firm has not submitted any justification regarding these queries.
8.	Provide complete analytical method verification studies of drug product including the specificity and repeatability parameter along with raw data sheets and chromatogram.	Not submitted.
9.	Justify the weight of sample between 33-34mg, while as per the analytical method given in section 3.2.P.5.2 the weight of content equivalent to 50mg of fluconazole should be taken initially for preparation of final dilution of sample solution.	Not submitted
10.	Provide COA of primary / secondary reference standard including source and lot number used for testing of drug product.	Not submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not submitted

Decision: Deferred for submission of following:

- **Clarify the specification of drug product since the JP monograph of fluconazole capsule is not applicable for 150mg strength. Revise your specification along with the requisite fee.**
- **The validation of analytical procedure has been performed using assay method (HPLC) with flow rate 1.0ml/min, column temperature 35°C, UV detector set at 261nm and mobile phase sodium acetate: methanol: acetonitrile while USP recommended flow rate 0.5ml/min, column temperature 40°C, UV detector 260nm and mobile phase Acetonitrile and water (20:80). Justify, how have comply USP specification by keeping the chromatographic condition different from USP monograph of fluconazole.**

- **Clarify, how you have performed accuracy parameter in the verification studies of drug substance that, despite spiking the sample 25%,50%,75%,100%,125% and 150%, the amount of fluconazole has not been changed in all these spiked sample.**
- **Identification test specified on the COA of working standard of fluconazole attached in section 3.2.S.5 stated that IR absorption spectrum of test solution should be concordant with that of clotrimazole working standard, clarification is required in this regard. Further, the COA reflect that batch qualified against Indian pharmacopeia reference standard, justify how you can standardize the drug substance that comply with USP specification to the working standard that qualified against Indian pharmacopeia.**
- **Justify, for adopting the dissolution parameter specified in JP monograph, since the JP monograph recommends the acceptance limits for 50mg and 100g fluconazole strength.**
- **Provide complete analytical method verification studies of drug product including the specificity and repeatability parameter along with raw data sheets and chromatogram.**
- **Provide COA of primary / secondary reference standard including source and lot number used for testing of drug product.**
- **Compliance Record of HPLC software 21CFR & audit trail reports on product testing.**

Previously Deferred Cases of Form 5-F:

289.	Name, address of Applicant / Importer	M/s Himmel Pharmaceuticals (Pvt.) Ltd. 793-D, Block ''C'', Faisal Town Lahore.
	Details of Drug Sale License of importer	License No: 05-352-0065-016174-D Address: 793-D, Block-C, Faisal Town Lahore Address of Godown: NA Validity: 06. Feb.2022 Status: License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s BEACON Pharmaceuticals Limited Plant address: Kathali, Bhaluka, Mymensingh Bangladesh Office address: 9/B/2, Toynbee Circular Road, Motijheel Dhaka, Bangladesh
	Name, address of manufacturer(s)	M/s BEACON Pharmaceuticals Limited Plant address: Kathali, Bhaluka, Mymensingh Bangladesh Office address: 9/B/2, Toynbee Circular Road, Motijheel Dhaka, Bangladesh
	Name of exporting country	Bangladesh
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	CoPP: Original legalized COPP (Certificate# DA/6-110/2016/3300 issued on 01-06-2020 by Government of the people's republic of Bangladesh, Ministry of Health & Family welfare, Directorate General of Drug Administration, Oushad Bhaban, Mohkhali Dhaka-1212, Bangladesh. GMP: Firm has submitted Legalized GMP certificate (Certificate No. DA/6-110/06/10002) issued by M/s Beacon Pharmaceuticals limited. Also, Renewal certificate is submitted (Certificate No. DA/6-110/06/4950).
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of letter of distribution certificate from Beacon Pharmaceuticals limited. The letter specifies that the manufacturer appoints M/s Himmel Pharmaceuticals Pvt. Ltd. to register

		their products in Pakistan. The authorization letter is valid till June, 2025.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No.16561 Date:15.06.2021
	Details of fee submitted	PKR: 100,030/- Date: Dec-2020
	The proposed proprietary name / brand name	Pazonix 200mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains Pazopanib Hydrochloride INN….200mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-cancer
	Reference to Finished product specifications	In house
	Proposed Pack size	30’s (HDPE Bottle)
	Proposed unit price	As per current pricing policy of DRAP
	The status in reference regulatory authorities	Votrient 200mg Tablet
	For generic drugs (me-too status)	Votrient (Novartis)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Ace bright (India) Pharma Private Limited Address: No. 77D &116/117, KIADB Industrial Area Jigani, Bangalore - 560 105 Karnataka, India.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure,

		general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted long term stability study data of 3 batches of drug substance at 25°C ± 2°C / 60 ± 5% RH for 12 months. The accelerated stability data is conducted at 40°C ± 2°C / 75 ± 5% RH for 6 months
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Comparative analysis Studies against the reference product Votrient 200mg (Novartis) has been submitted
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	HDPE Bottle
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. Accelerated stability studies have been conducted at 40°C±2°C and 75%±5% RH for 6 months. Real time stability studies conducted at 30°C±2°C and 65% ± 5% for 24 months

Evaluation by PEC:

Sr. no.	Shortcomings/Deficiencies	Response of the Firm
1.	Submit data of analytical Method verification studies including specificity, accuracy and repeatability (method precision).	Firm has submitted analytical method validation studies of drug substance performed by drug product manufacturer.
2.	Justify acceptance criteria set for dissolution test i.e. NLT 70% (Q) in 60 minutes, which is not as per the international guidelines as well as the decision of Registration Board i.e. "*For all type of drug products, the value of "Q" should not be less than 75% in any case as per the recommendations of United States Pharmacopoeia (USP) General Chapter <711> Dissolution, Dissolution testing in BP finished*	Firm has submitted the reply, in which it is stated that "The dissolution time for pazonix 200mg tablet has been selected 60 minutes as per the FDA dissolution database. In the database, USP apparatus Type-II and 10,20,30,45 and 50 min has been mentioned for profiling. For the immediate release tablet, we have selected 60 mins as a single time point. Firm has not given any scientific justification for selecting the extreme time point i.e. 60 minutes for dissolution of drug product, while the FDA review document of innovator product reveals that the

	products monographs for solid oral dosage forms and The International Pharmacopoeia Ninth Edition, 2019 -Dissolution testing of tablets and capsules". As per the submitted data percentage of drug release at 30 minutes was 55.09% in the USFDA recommended release media. Justify, how your formulation can be considered equivalent to the innovator product which shows release more than Q+5% in 30 minutes.	dissolution criteria should be Q= at 30 minutes using the following conditions. Apparatus: USP Apparatus 2 Volume: 900 mL Medium: 50 mM sodium acetate buffer, pH 4.5, containing 0.75% SDS Agitation: Paddle speed of 75 rpm. Analysis: UV at 270 nm with a background correction at 400 nm. Temperature: 37°C.
3.	• Justify how the results of all quality tests for every batch in stability studies are same at all time points. • Justification is required regarding the out of specification assay results i.e. 46.5mg content of pazopanib per tablet at 6-month time interval during the accelerated stability studies of batch no. 3860003 and 3860004.	Firm has not provided any justification regarding these queries, instead submit the stability data of commercial batches. (batch no. 3860005,3860006,3860007)
4.	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product under section 2.3.R.1.1, for which stability studies data is provided in Module 3 section 3.2. P.8.	Firm has submitted the Batch Manufacturing Record of batch no. 3860002, 3860003 and 3860004.
5.	Firm has submitted the differential fee of Rs. 50,000 vide Challan no.78134245317 dated 22-08-2022 for finished import drug product, as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.	

Decision of M-321:
Deferred for Scientific justification regarding difference in dissolution limits in terms of %age released and time point from that recommended by the US FDA for innovator product.

Firm revised the Dissolution parameters as per the recommendation of USFDA approved innovator product, however the submitted document did not clarify the percentage release which should be achieved at 30 minutes.

Decision: Deferred for submission of dissolution test in compliance to revised dissolution parameters as per innovator drug product.

290.	Name, address of Applicant / Marketing Authorization Holder	M/s Hiranis Pharmaceuticals (Pvt.) Ltd
	Name, address of Manufacturing site.	M/s Hirais Pharmaceuticals (Pvt.) Ltd Plot E-145-149, North western industrial zone, Port Qasim, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1099 dated 12/01/2022
	Details of fee submitted	PKR 75,000/-: dated 06/12/2021
	The proposed proprietary name / brand name	Parofen 150/500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ibuprofen 150mg + Paracetamol 500mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Analgesics and antipyretics
	Reference to Finished product specifications	Manufacturer's Spec.
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA, TGA Australia Tachifene Tablet M/s Angelini Pharma Italian Medicine Agency approved.
	For generic drugs (me-too status)	Provas Duo Tablet 500/150 of M/s. Sami Pharmaceuticals, Karachi Reg.no.108837
	GMP status of the Finished product manufacturer	DML by way of formulation No. 000785 dated 03-02-2019
	Name and address of API manufacturer.	Ibuprofen M/s Hubei BiocauseHeilen Pharmaceutical Co., Ltd Address:122 Yangwan Road, Jingmen City, Hubei Province 448000, People's Republic of China Paracetamol M/s Zafa Chemie Address: Raiwind Manga Bypass, Near Sundar Industrial Estate, Mouza Bhaikot, Tehsil & District Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Ibuprofen:

		Official monograph is present in United States pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Paracetamol: Official monograph is present in British pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Ibuprofen: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: C100-1507197M, C100-1507198M & C100-1507199M Paracetamol: Real time: 30°C ± 2°C / 65% ± 5%RH for 54 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: 1331, 1332 & 1333
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Tachifene Tablet by M/s Angelini Francesco S.p.A (Lot no.021) by performing quality tests (Identification, Assay, Dissolution, and Uniformity of dosage form). CDP has been performed against the same brand that is Tachifene Tablet by M/s Angelini Pharma in Acid media (0.1 N HCL) & Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8).

		For Ibuprofen: •It was found that both reference & test product shows low solubility in 0.1N HCl but resemblance in dissolution profile, the similarity factor, f2 is 93 which is greater than 50 & the difference factor f1 is 6 which is less than 15. •It was found that both reference & test product show low solubility in acetate Buffer pH 4.5 but resemblance in dissolution profile, the profile similarity factor, f2 is 93 which is greater than 50 & the difference factor f1 is 4 which is less than 15. •It was found that both reference & test product show greater than 85% dissolution within 15 minutes in Phosphate Buffer pH 6.8, therefore they are considered as similar & f2 value calculation is not applicable. For Paracetamol: • It was found that both reference & test product shows 85% dissolution within 15 minutes in 0.1N HCl shows resemblance in dissolution profile, the profile similarity factor, f_2 value calculation is not applicable. • It was found that both reference & test product shows greater than 85% dissolution within 15 minutes in acetate Buffer pH 4.5, therefore they are considered as similar & f_2 value calculation is not applicable. • It was found that both reference & test product show 85% dissolution within 15 minutes in Phosphate Buffer pH 6.8 shows resemblance in dissolution profile, therefore they are considered as similar & f_2 value calculation is not applicable.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Ibuprofen M/s Hubei Biocause Heilen Pharmaceutical Co., Ltd Address:122 Yangwan Road, Jingmen City, Hubei Province 448000, People's Republic of China Paracetamol M/s Zafa Chemie Address: Raiwind Manga Bypass, Near Sundar Industrial Estate, Mouza Bhaikot, Tehsil & District Lahore.
API Lot No.	Ibuprofen C100-1711278M Paracetamol 6019
Description of Pack (Container closure	Alu-PVC blister packed in unit carton (3×10's)

system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TF-020520	TF-030520	TF-040520
Batch Size	1800 tablets	1800 tablets	1800 tablets
Manufacturing Date	05-2020	05-2020	05-2020
Date of Initiation	02-05-2020	04-05-2020	05-05-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Etoxib 90mg Tablet Etoxib 120mg Tablet Approved in 294th minutes of meeting of DRB
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Ibuprofen: Copy of GMP certificate No. HB20170363 issued by China Food and Drug Administration valid till 28/08/2022. Paracetamol: Copy of DML certificate No. 000589 issued by Drug Regulatory Authority of Pakistan valid till 02/10/2019*. (*Request for DML audit has already been submitted by M/s Zafa Chemie, DRAP against this letter has also instructed the concerned authority for conduct of timely audit of M/s Zafa Chemie via letter no. F.1-1/2006-Lic (Vol-II) dtd. 29-09-2021, copy of the same attached for reference in dossier).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Attested invoice from ADC attached for Ibuprofen Invoice No. W180316-035 Attested invoice from ADC attached for Paracetamol
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks of Evaluator:		

S. no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Justify the dissolution parameter of applied drug product with reference to dissolution medium, acceptance criteria and other dissolution conditions, considering the USP general chapter <1092> and review report of innovator product.	Firm replied that they adopted following dissolution condition and acceptance criteria Proposed Dissolution conditions: 1. Dissolution Test parameter (Paracetamol): i. Apparatus: Paddle ii. Dissolution medium: Phosphate buffer pH 5.8 iii. Medium volume: 900ml iv. RPM: 50 v. Time: 30 minutes vi. Temperature: 37°C vii. Acceptance Criteria: NLT 80% (Q) 2. Dissolution Test parameter 2. (Ibuprofen): i. Apparatus: Paddle ii. Dissolution medium: Phosphate buffer pH 7.2 iii. Medium volume: 900ml iv. RPM: 50 v. Time: 30 minutes vi. Temperature: 37°C vii. Acceptance Criteria: NLT 80% (Q) considering the guidance document: 1. USP chapter 1092 2. FDA guidance document for Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances (August 2018) 3. DRB Minutes of 293rd Meeting of Registration Board (6 – 8th January, 2020) 4. Pharmaceutical equivalence study with reference product. 5. CDP study with reference product. 6. Innovator review report (Nuromol tablet 200/500mg Reckitt Benckisar Healthcare, MHRA) 7. USP monograph of acetaminophen tablet.
2.	Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product.	Submitted

Decision: Approvedwith innovator's specifications. Registration letter will be issued upon submission of performance of dissolution test as per dissolution parameters by USFDA in the literature review of innovator alongwith fee of RS. 7,500/- for revision/correction of drug product specifcations as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

291.	Name, address of Applicant / Marketing Authorization Holder	M/s Hiranis Pharmaceuticals (Pvt.) Ltd
	Name, address of Manufacturing site.	M/s Hiranis Pharmaceuticals (Pvt.) Ltd Plot E-145-149, North western industrial zone, Port Qasim, Karachi.

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10870 dated 29/04/2022
	Details of fee submitted	PKR 75,000/- dated 21/04/2022
	The proposed proprietary name / brand name	Parofen Rapid Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Ibuprofen 200mg + Paracetamol 500mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	Analgesics and antipyretics
	Reference to Finished product specifications	Manufacturer's Spec.
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Nuromol Tablet M/s Reckitt Benckiser Pharma MHRA approved.
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	DML by way of formulation No. 000785 dated 03-02-2019
	Name and address of API manufacturer.	Ibuprofen M/s Hubei Biocause Heilen Pharmaceutical Co., Ltd Address:122 Yangwan Road, Jingmen City, Hubei Province 448000, People's Republic of China Paracetamol M/s Zafa Chemie Address: Raiwind Manga Bypass, Near Sundar Industrial Estate, Mouza Bhaikot, Tehsil & District Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Ibuprofen: Official monograph is present in United States pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Paracetamol: Official monograph is present in British pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Ibuprofen: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: C100-1507197M, C100-1507198M & C100-1507199M Paracetamol: Real time: 30°C ± 2°C / 65% ± 5%RH for 54 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: 1331, 1332 & 1333
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of

		drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Neuromol Tablet of M/s. Reckitt & Benckiser Sydney NSW, Australia by performing quality tests (Identification, Assay, Dissolution, and Uniformity of dosage form). CDP has been performed against the same brand that is Neuromol Tablet of M/s. Reckitt & Benckiser Sydney NSW, Australia in Acid media (0.1 N HCL) & Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). For Ibuprofen: •It was found that both reference & test product shows low solubility in 0.1N HCl but resemblance in dissolution profile, the similarity factor, f2 is 93 which is greater than 50 & the difference factor f1 is 6 which is less than 15. •It was found that both reference & test product shows low solubility in acetate Buffer pH 4.5 but resemblance in dissolution profile, the profile similarity factor, f2 is 93 which is greater than 50 & the difference factor f1 is 4 which is less than 15. •It was found that both reference & test product shows greater than 85% dissolution within 15 minutes in Phosphate Buffer pH 6.8, therefore they are considered as similar & f2 value calculation is not applicable. For Paracetamol: • It was found that both reference & test product show 85% dissolution within 15 minutes in 0.1N HCl shows resemblance in dissolution profile, the profile similarity factor, f_2 value calculation is not applicable. • It was found that both reference & test product show greater than 85% dissolution within 15 minutes in acetate Buffer pH 4.5, therefore they are considered as similar & f_2 value calculation is not applicable. • It was found that both reference & test product show 85% dissolution within 15 minutes in Phosphate Buffer pH 6.8 shows resemblance in dissolution profile, therefore they are considered as similar & f_2 value calculation is not applicable.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	Ibuprofen M/s Hubei Biocause Heilen Pharmaceutical Co., Ltd Address:122 Yangwan Road, Jingmen City, Hubei Province 448000, People's Republic of China	

	Paracetamol M/s Zafa Chemie Address: Raiwind Manga Bypass, Near Sundar Industrial Estate, Mouza Bhaikot, Tehsil & District Lahore.		
API Lot No.	Ibuprofen C100-1711278M Paracetamol 6019		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (3×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TF-050520	TF-060520	TF-080520
Batch Size	1800 tablets	1800 tablets	1800 tablets
Manufacturing Date	05-2020	05-2020	05-2020
Date of Initiation	05-05-2020	06-05-2020	08-05-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Etoxib 90mg Tablet Etoxib 120mg Tablet Approved in 294th minutes of meeting of DRB
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Ibuprofen: Copy of GMP certificate No. HB20170363 issued by China Food and Drug Administration valid till 28/08/2022. Paracetamol: Copy of DML certificate No. 000589 issued by Drug Regulatory Authority of Pakistan valid till 02/10/2019*. (*Request for DML audit has already been submitted by M/s Zafa Chemie, DRAP against this letter has also instructed the concerned authority for conduct of timely audit of M/s Zafa Chemie via letter no. F.1-1/2006-Lic (Vol-II) dtd. 29-09-2021, copy of the same attached for reference in dossier).
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Attested invoice from ADC attached for Ibuprofen Invoice No. W180316-035
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Justify the dissolution parameter of applied drug product with reference to dissolution medium, acceptance criteria and other dissolution conditions, considering the USP general chapter <1092> and review report of innovator product.	Firm replied that they adopted following dissolution condition and acceptance criteria Proposed Dissolution conditions: 1. Dissolution Test parameter (Paracetamol): i. Apparatus: Paddle ii. Dissolution medium: Phosphate buffer pH 5.8 iii. Medium volume: 900ml iv. RPM: 50 v. Time: 30 minutes vi. Temperature: 37°C vii. Acceptance Criteria: NLT 80% (Q) 2. Dissolution Test parameter 2. (Ibuprofen): i. Apparatus: Paddle ii. Dissolution medium: Phosphate buffer pH 7.2 iii. Medium volume: 900ml iv. RPM: 50 v. Time: 30 minutes vi. Temperature: 37°C vii. Acceptance Criteria: NLT 80% (Q) considering the guidance document: 1. USP chapter 1092 2. FDA guidance document for Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances (August 2018) 3. DRB Minutes of 293rd Meeting of Registration Board (6 – 8th January, 2020) 4. Pharmaceutical equivalence study with reference product. 5. CDP study with reference product. 6. Innovator review report (Nuromol tablet 200/500mg Reckitt Benckisar Healthcare, MHRA) 7. USP monograph of acetaminophen tablet.
2.	Provide details that which lot number of drug substance has been used in manufacturing of each batch of drug product. Also provide documents confirming evidence of import of each lot of drug substance used in manufacturing of these batches of drug product.	Submitted

Decision: Decision: Approvedwith innovator's specifications. Registration letter will be issued upon submission of performance of dissolution test as per dissolution parameters by USFDA in the literature review of innovator alongwith fee of RS. 7,500/- for revision/correction of drug product specifcations as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
292.	Name, address of Applicant / Marketing Authorization Holder	M/s Sami Pharmaceuticals, F-95, SITE, Karachi.
	Name, address of Manufacturing site.	Name: M/s Sami Pharmaceuticals, F-95, SITE, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11278 dated 13-04-2021
	Details of fee submitted	PKR 50,000/-: dated 09/03/2021 slip no. 2050054
	The proposed proprietary name / brand name	LISTIM 150mg Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Sterile Colistimethate sodium equivalent to Colistin base ….150mg USP Specs
	Pharmaceutical form of applied drug	Lyophilized Injection
	Pharmacotherapeutic Group of (API)	Polymixins ATC code: J01XB
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Coly-Mycin M 150mg/2ml Injection
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020
	Name and address of API manufacturer.	Mac-Chem Products (India) Pvt. Ltd. N-211/2/10.MIDC, Boisar, Thane-401506, Maharashtra State, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls,

		impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Colistimethate Sodium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(CMT0219001, CMT0219002, CMT0219003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Coly-Mycin M 150mg/2ml Injection by ERFA Canada by performing quality tests (Identification, Assay, Sterility, bacterial endotoxin, pH, loss on drying, Free colistin, appearance of reconstituted solution) CDP is not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Mac-Chem Products (India) Pvt. Ltd.
API Lot No.	CMS0217012
Description of Pack (Container closure system)	10ml clear glass vial, USP Type-I
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 1,2,3,4, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	625 vials	625 vials	625 vials
Manufacturing Date	Nov 2019	Nov 2019	Nov 2019
Date of Initiation	Dec 2019	Dec 2019	Dec 2019
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted the relevant document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. New-WHO-GMP/CERT/KD/74238/2018/11/24897 issued by FDA valid till 10/09/2021
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No. MCEX180129 /DRAP-AD-CD (I&E) dated 13/2/2018 is submitted wherein the permission to import different APIs including Colistimethate sodium for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable as not run on HPLC
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

The median concentration i.e. U3 of colistimethate sodium should be 1mcg/ml as per USP, while the submitted assay method indicate that the median concentration U3 was 5mcg/ml. Clarification is required in this regard. For assay of drug substance, sample has been prepared using reference standard of colistimethate sodium, so justification/clarification is required for using standard material for preparation of sample stock solution.	Firm Stated that USP allows to adjust the Median conc. To optimize the zone sizes if the data remain in the linear range (linearity has been verified), USP <81> chapter has been attached for reference. However, the method of analysis is not as per USP, For the cylinder-plate assay, each plate includes only two treatments, the reference treatment (median level standard, i.e., S3) and one of the other four concentrations of the standard (S1, S2, S4 and S5) or the sample (U3). Firm revised the method in accordance with USP. Firm has submitted the reply that "it is a typo error, for sample preparation we use the test sample, accordingly worksheet has been revised and attached.
Validation of analytical procedures	Firm has submitted the reply that "Specificity was done compartively with blank, standard and sample , results are compared, method found selective that

Verification of analytical procedure has not been performed in accordance with recommended USP. How the specificity of method has been verified without comparing the results of sample with standard and placebo, as in the submitted data sample solution has not been prepared.	was missed in the method verification report, method verification report has been revised and attached for ready reference"
Reference Standards or Materials COA of primary/secondary reference standard including source and lot no. is required.	Firm submitted the COA of working standard supplied by API Manufacturer i.e. M/s. Mac-Chem Products (India) Pvt. Limited batch no. CMS0217012.
Component of drug product: Formulation Development According to the product description, it is white to slightly yellow lyophilized cake of colistimethate sodium while the label claim of product mentioned in the pharmaceutical equivalence data is "sterile lyophilized powder of colistimethate sodium. Correction of label claim is required accordingly.	Firm clarified that it is lyophilized cake as per the innovator coly-Mycin but the label claim of product will be written as Sterile colistimethate sodium equivalent to colistin base ….150mg as per the innovator.
Provide detail of type and quantity of diluent used for reconstitution of applied product. Inform about quantity of diluent used for reconstitution when the product is used for inhalation as nebulizer solution. Compatibility Provide compatibility studies data with its diluent Provide compatibility study data of drug product with its suitable diluent, after reconstitution as per the instructions provided in individual label of the drug product	Firm submitted following reply: We have developed LISTIM 150mg/2ml Injection against the reference listed drug (RLD) i.e. Coly-Mycin M 150mg /2ml injection. Quantity and type of diluents used are as under; INTRAVENOUS OR INTRAMUSCULAR: 2ml of water for injection. Reference: Coly-Mycin M ® Parenteral (Colistimethate for Injection, USP) (Distributed by M/s. Par Pharmaceutical) - INHALATION AS NEBULIZER SOLUTION: LISTIM 150mg/2ml is Lyophilized powder for injection only and product is not used for inhalation as nebulizer solution. Compatibility Study data conducted with water for injection, 0.9% NaCl, 5% Dextrose in water, 10% inverted sugar solution, 5% Dextrose in 0.9% NaCl, 5% Dextrose in 0.45% NaCl, 5% Dextrose in 0.225% NaCl, Lactated Ringers Solution as per the instruction on individual label of drug product has been submitted by the firm.
Analytical procedure: Sample stock solution has been prepared in distilled water while as per the reference product, water for injection or 0.9% sodium chloride should be used as diluent for "colistimethate for injection". Justification is required for using distilled water for preparation of sample solution.	Firm has stated that "This is typo error and sample stock solution prepared using Water for Injection. Revised testing method has been submitted for ready reference"
The median concentration i.e. U3 colistimethate sodium should be	Firm Stated that USP allows to adjust the Median conc. To optimize the zone sizes if the data remain

1mcg/ml as per USP, while the submitted assay method indicate that the median concentration U3 was 5mcg/ml. Clarification is required in this regard.	in the linear range (linearity has been verified), USP <81> chapter has been attached for reference. However, the method of analysis is not as per USP, For the cylinder-plate assay, each plate includes only two treatments, the reference treatment (median level standard, i.e., S3) and one of the other four concentrations of the standard (S1, S2, S4 and S5) or the sample (U3). While, according to the submitted assay procedure each plate contains three treatments (S3, STANDARD and U3) which is not in accordance to USP. Firm submitted the revised analytical method in accordance with USP.
Provide assay method for the infusion and inhalation route of administration, as the amount of diluent will be varying accordingly for the preparation of sample stock solution.	Firm has submitted that Colistimethate sodium 150mg injection will only be use for injection and same testing method will be used for the sample preparation. LISTIM 150mg/2ml is Lyophilized powder for injection only and product is not used for inhalation as nebulizer solution.
Justification is required for using ±5% acceptance criteria for weight variation, provide the calculation of acceptance value as per USP.	Firm has submitted that "Basis for the limit of weight Variation is BP General Monograph (Consistency of formulated Preparation, sub heading of Uniformity of Weight (Mass), which allows the 10% weight variation for powder for parenteral administration for more than 40mg dosage form. We set the stringent of 5% instead of 10%. For the calculation of weight variation as per USP, calculation sheet has been attached "
Analytical verification report reflects that weight of sample used for sample solution is 240mg instead of 360mg (content per vial) justification/clarification required in this regard. How the specificity of method has been verified without comparing the results of sample with standard and placebo, as in the submitted data sample solution has not been prepared.	Firm has replied that "It was typo error. For sample preparation we use the whole content of product. The revised analytical verification report has been attached for ready reference". Firm has submitted the reply that "Specificity was done compartively with blank, standard and sample , results are compared, method found selective that was missed in the method verification report, method verification report has been revised and attached for ready reference"
Batch Analyses Appearance of lyophilized cake should be mentioned on batch analysis report rather the appearance of powder of colistimethate sodium for injection.	Firm has submitted that "appearance of lyophilized cake has been revised/amended in the batch analysis report. In the batch analysis report this is missed although available on raw data sheet. Batch analysis report amended and attached for ready reference".
Acceptance criteria of assay is not as per labelled claimed of USP monograph of "Colistimethate for Injection". It is not clear that the given percentage is of colistin or Colistimethate sodium.	Firm has stated that results obtained by our calculation is labelled amount of Colistin according to USP
Stability Appearance of lyophilized cake should be mentioned on stability data sheets	Firm submitted the reply that Appearance of lyophilized cake has been revised/amended in the batch analysis report. The amended stability data sheets have been attached for ready reference.

rather the appearance of powder of Colistimethate sodium for injection. Provide in use stability data of reconstituted solution along with give the detail of proposed in-use storage statement and in-use shelf-life.	Firm has submitted the in-use stability studies data at storage condition 2-8°c and 20-25°C for 7 days.

Decision of 316th meeting of Registration Board:
Deferred for further deliberation regarding the label claim of Colistimethate sodium in line with the product approved in reference regulatory agencies and pharmacopeia.

Decision: Deferred for following clarification:

- **Manufacturing facility (lyophilized or dry powder filling) wherein the trial batches have been manufactured along with evidence of approval of required manufacturing facility from CLB.**
- **Applied label claim against the recommendations of USP monograph of Colistimethate for injection.**

293.	Name, address of Applicant / Marketing Authorization Holder	M/s Sami Pharmaceuticals, F-95, SITE, Karachi.
	Name, address of Manufacturing site.	Name: M/s Sami Pharmaceuticals, F-95, SITE, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10737 dated 07/04/2021
	Details of fee submitted	PKR 20,000/-: dated 28/02/2021 slip no. 2050087
	The proposed proprietary name / brand name	LISTIM 1 MIU Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Sterile powder of Colistimethate Sodium USP….1 MIU (1 Million International Unit) USP Specs
	Pharmaceutical form of applied drug	Dry powder Injection
	Pharmacotherapeutic Group of (API)	Polymixins ATC code: J01XB
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Colomycin 1 MIU Injection UK MHRA
	For generic drugs (me-too status)	Colimate by MTI Medical Limited (Reg. 097779)

	GMP status of the Finished product manufacturer	GMP Certificate issued date 11-08-2020
	Name and address of API manufacturer.	Livzon Group Fuzhou Fuxing Pharmaceutical Co. Ltd. No. 8 Nangang Road, Jiangyin Industrial Concentration Zone, Fuqing, Fuzhou City, Fujian Province, P.R China,350309
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Colistimethate Sodium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (CMS1707001, CMS1707002, CMS1707003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Colomycin Injection 1 MIU Injection by Penn Pharmaceutical services Tredegar Gwent NP223AA, UK by performing quality tests (Identification, Assay, Sterility, bacterial endotoxin, pH, loss on drying, Free colistin, appearance of reconstituted solution) CDP is not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, accuracy, precision, specificity.
STABILITY STUDY DATA		

Manufacturer of API	Livzon Group Fuzhou Fuxing		
API Lot No.	CMS1811001		
Description of Pack (Container closure system)	10ml clear glass vial, USP Type-I		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	Oct 2019	Oct 2019	Oct 2019
Date of Initiation	Oct 2019	Oct 2019	Oct 2019
No. of Batches	03		

Administrative Portion		
	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted the relevant document.
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. FJ200006 issued by Fujian FDA valid till 21/09/2022
	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice specifying import of 1 kg of Colistimethate Sodium (Batch # CMS181101). (invoice # FXIN1812252) attested by AD (I&E), Karachi dated 11/1/2019
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable as not run on HPLC
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Control of Drug Substance Analytical procedures The median concentration i.e. U3 of colistimethate sodium should be 1mcg/ml as per USP, while the submitted assay method indicate that the median concentration U3 was 5mcg/ml. Clarification is required in this regard.	Firm Stated that USP allows to adjust the Median conc. to optimize the zone sizes if the data remain in the linear range (linearity has been verified), USP <81> chapter has been attached for reference. However, the method of analysis is not as per USP, For the cylinder-plate assay, each plate includes only two treatments, the reference

	treatment (median level standard, i.e., S3) and one of the other four concentrations of the standard (S1, S2, S4 and S5) or the sample (U3). While, according to the submitted assay procedure each plate contains three treatments (S3, STANDARD and U3) which is not in accordance to USP. Firm submitted the revised analytical method in accordance with USP.
For assay of drug substance, sample has been prepared using reference standard of colistimethate sodium, so justification/clarification is required for using standard material for preparation of sample stock solution.	Firm has submitted the reply that "it is a typo error, for sample preparation we use the test sample, accordingly worksheet has been revised and attached.
Validation of analytical procedures How the specificity of method has been verified without comparing the results of sample with standard and placebo, as in the submitted data sample solution has not been prepared.	Firm has submitted the reply that "Specificity was done compartively with blank, standard and sample , results are compared, method found selective that was missed in the method verification report, method verification report has been revised and attached for ready reference". Method verification protocol submitted along with the reply reflects that the API manufacturer is M/s. Mac-Chem Products (India) Pvt. Ltd. while the CTD dossier submitted previously shows that the API manufacturer is M/s. Livzon Group Fuzhou Fuxing Pharmaceuticals, China.
Component of drug product: Formulation Development Provide detail of type and quantity of diluents used for reconstitution of applied product. Inform about quantity of diluent used for reconstitution when the product is used for inhalation as nebulizer solution. Compatibility Provide compatibility studies data with its diluent Provide compatibility study data of drug product with its suitable diluent, after reconstitution as per the instructions provided in individual label of the drug product	We have developed LISTIM 1 MIU Injection against the reference listed drug (RLD) i.e. Colomycin 1 Million International Units (IU) Powder for solution for injection, infusion or inhalation. The package leaflet of RLD Colomycin 1 Million International Units (IU) Powder for solution for injection, infusion or inhalation, (Marketing authorization holder M/s. Forest Laboratories UK Limited whiddon valley, Barnstaple, North Devon EX32 8NS United Kingdom) has been attached for reference. Quantity and type of diluents used are as under; BOLUS INJECTION: 2ml of water for injection or 0.9% sodium chloride INFUSION: Reconstituted vial will be further diluted in 50 ml 0.9% sodium chloride solution INTRATHECAL AND INTRAVENTRICULAR: Not more than 1 ml of water for injection or 0.9% sodium chloride will be used for reconstitution. INHALATION AS NEBULIZER SOLUTION: 2ml of water for injection or saline (0.9% sodium chloride solution) for reconstitution

	when the product is used for inhalation as nebulizer solution. Firm has submitted compatibility and in-use stability studies with water for injection and Sterile sodium chloride sol (0.9%), on 3 batches at the start of study and at 18th Month, interval. summary report and raw data has attached. Before opening: 3 years. Reconstituted solutions: Hydrolysis of colistimethate is significantly increased when reconstituted and diluted below its critical micelle concentration of about 80,000 IU per ml. Solutions below this concentration should be used immediately For solutions for bolus injection or nebulization, the chemical and physical in-use stability of reconstituted solution in the original vial, with a concentration ≥ 80,000 IU/mL, has been demonstrated for 24 hours at 2 to 8°C. From a microbiological point of view, unless the method of opening/ reconstitution/ dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of user. Solutions for infusion, which have been diluted beyond the original vial volume and / or with a concentration < 80,000 IU/mL should be used immediately. For solutions for intrathecal and intraventricular administration, the reconstituted product should be used immediately.
Analytical procedure: Sample stock solution has been prepared in distilled water while as per the reference product, water for injection or 0.9% sodium chloride should be used as diluent for "colistimethate for injection". Justification is required for using distilled water for preparation of sample solution.	Firm stated that "it was the typo error we actually use water for injection for reconstitution of sample. The method has been revised and attached".
The median concentration i.e. U3 of colistimethate sodium should be 1mcg/ml as per USP, while the submitted assay method indicate that the median concentration U3 was 5mcg/ml. Clarification is required in this regard.	Firm Stated that USP allows to adjust the Median conc. to optimize the zone sizes if the data remain in the linear range (linearity has been verified), USP <81> chapter has been attached for reference. However, the method of analysis is not as per USP, For the cylinder-plate assay, each plate includes only two treatments, the reference treatment (median level standard, i.e., S3) and one of the other four concentrations of the standard (S1, S2, S4 and S5) or the sample (U3).

	While, according to the submitted assay procedure each plate contains three treatment (S3, STANDARD and U3) which is not in accordance to USP. Firm submitted the revised analytical method in accordance with USP.
Provide assay method for the infusion and inhalation route of administration, as the amount of diluent will be varying accordingly for the preparation of sample stock solution.	Firm stated that the constitution volume for both infusion and inhalation route of administration is same i.e. 2ml of water for injection or 0.9 % saline, therefore same method will be applied Volume of diluent used for reconstitution is different for intrathecal/intraventricular route of administration and for infusion and according to USP monograph for sample preparation "Constitute Colistimethate for Injection in a volume of water, accurately measured, corresponding to the volume of diluent specified in the labeling."
Analytical verification report of drug product reflects that weight of sample used for sample solution is 240mg instead of 80mg (content per vial) justification/clarification required in this regard. How the specificity of method has been verified without comparing the results of sample with standard and placebo, as in the submitted data sample solution has not been prepared.	Firm stated that It was typo graphical error, the amount of standard used was 240 mg and the vial of sample directly reconstituted with diluent. Revised method and report have been attached. Firm has submitted the reply that "Specificity was done compartively with blank, standard and sample , results are compared, method found selective that was missed in the method verification report, method verification report has been revised and attached for ready reference".
Batch Analyses Acceptance criteria of assay is not as per labelled claimed of USP monograph of "colistimethate for Injection". It is not clear that the given percentage is of colistin or colistimethate sodium.	Firm has stated that results obtained by our calculation is labelled amount of Colistin according to USP.
Reference Standards or Materials Working standard supplied by MAC-chem Products (India) has been used while the drug substance manufacturer used USP reference standard. Justification is required for not using the primary standard or the working standard supplied by the drug substance manufacturer.	The material supplied by MAC-chem Products (India) was tested against reference standard and same lot is standardized against USP reference standard and use accordingly. However, the API manufacturer is M/s. Livzon Group Fuzhou Fuxing Pharmaceuticals, China as per the CTD dossier.
Stability Provide in use stability data of reconstituted solution along with give the detail of proposed in-use storage statement and in-use shelf-life.	Firm has submitted the in-use stability data and the proposed in-use storage statement and in-use shelf life is as under: Store at 2-8°C for 24hours After 24hours of reconstitution the product found stable with respect to quality, strength and compatibility
Decision of 316th meeting of Registration Board:	

Deferred for further deliberation regarding the label claim of Colistimethate sodium in line with the product approved in reference regulatory agencies and pharmacopeia.		
Decision: Deferred for following clarification: • **Manufacturing facility (lyophilized or dry powder filling) wherein the trial batches have been manufactured along with evidence of approval of required manufacturing facility from CLB.** • **Applied label claim against the recommendations of USP monograph of Colistimethate for injection.**		
294.	Name, address of Applicant / Marketing Authorization Holder	M/s Sami Pharmaceuticals, F-95, SITE, Karachi.
	Name, address of Manufacturing site.	Name: M/s Sami Pharmaceuticals, F-95, SITE, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10089 dated 31/3/2021
	Details of fee submitted	PKR 20,000/-: dated 28/02/2021 SLIP NO. 2050089
	The proposed proprietary name / brand name	LISTIM 2 MIU Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Sterile powder of Colistimethate sodium USP….2 MIU (2 Million International Unit) USP Specs
	Pharmaceutical form of applied drug	Dry powder Injection
	Pharmacotherapeutic Group of (API)	Polymixins ATC code: J01XB
	Reference to Finished product specifications	USP
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Colomycin 2 MIU Injection MHRA
	For generic drugs (me-too status)	Colistimethate Sodium powder for Injection 2MIU of M/s. Mukhtar Enterprises (Reg.no.094757)
	GMP status of the Finished product manufacturer	GMP certificate issued dated: 11-08-2020
	Name and address of API manufacturer.	Livzon Group Fuzhou Fuxing Pharmaceutical Co. Ltd.

		No. 8 Nangang Road, Jiangyin Industrial Concentration Zone, Fuqing, Fuzhou City, Fujian Province, P.R China,350309
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Colistimethate Sodium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (CMS1707001, CMS1707002, CMS1707003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Colomycin Injection 1 MIU Injection by Penn Pharmaceutical services Tredegar Gwent NP223AA, UK by performing quality tests (Identification, Assay, Sterility, bacterial endotoxin, pH, loss on drying, Free colistin, appearance of reconstituted solution) CDP is not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Livzon Group Fuzhou Fuxing
API Lot No.	CMS1811001
Description of Pack	10ml clear glass vial, USP Type-I

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-01	Lab-02	Lab-03
Batch Size	500 vials	500 vials	500 vials
Manufacturing Date	Oct 2019	Oct 2019	Oct 2019
Date of Initiation	Nov 2019	Nov 2019	Nov 2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted the relevant document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. FJ200006 issued by Fujian FDA valid till 21/09/2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice specifying import of 1 kg of Colistimethate Sodium (Batch # CMS181101). (invoice # FXIN1812252) attested by AD (I&E), Karachi dated 11/1/2019
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable as not run on HPLC
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Control of Drug Substance Analytical procedures The median concentration i.e. U3 of colistimethate sodium should be 1mcg/ml as per USP, while the submitted assay method indicate that the median concentration U3 was 5mcg/ml. Clarification is required in this regard. For assay of drug substance, sample has been prepared using reference standard of colistimethate sodium, so	Firm Stated that USP allows to adjust the Median conc. to optimize the zone sizes if the data remain in the linear range (linearity has been verified), USP <81> chapter has been attached for reference. However, the method of analysis is not as per USP, For the cylinder-plate assay, each plate includes only two treatments, the reference treatment (median level standard, i.e., S3) and one of the other four concentrations of the standard (S1, S2, S4 and S5) or the sample

justification/clarification is required for using standard material for preparation of sample stock solution.	(U3). While, according to the submitted assay procedure each plate contains three treatments (S3, STANDARD and U3) which is not in accordance to USP. Firm submitted the revised analytical method in accordance with USP. Firm has submitted the reply that "it is a typo error, for sample preparation we use the test sample, accordingly worksheet has been revised and attached.
Validation of analytical procedures How the specificity of method has been verified without comparing the results of sample with standard and placebo, as in the submitted data sample solution has not been prepared.	Firm has submitted the reply that "Specificity was done comparatively with blank, standard and sample, results are compared, method found selective that was missed in the method verification report, method verification report has been revised and attached for ready reference". Method verification protocol submitted along with the reply reflects that the API manufacturer is M/s. Mac-Chem Products (India) Pvt. Ltd. while the CTD dossier submitted previously shows that the API manufacturer is M/s. Livzon Group Fuzhou Fuxing Pharmaceuticals, China.
Pharmaceutical equivalence should be established against the innovator/reference/comparator product of the same strength. Provide the comparison data with the reference product of same strength.	For comparative analysis against the reference-listed drug (RLD) COLOMYCIN Injection, we were only able to procure samples of COLOMYCIN 1MIU Injection and unable to arrange COLOMYCIN 2MIU due to international availability issues arising from ongoing pandemic situation. The literature data of reference-listed drug (Innovator product) revealed that, their product is ready-to-fill sterile powder injection and the formulation only contains API having no other excipients. The same has been confirmed on the testing of COLOMYCIN 1 MIU Injection at our end. The only difference between 1MIU & 2MIU injection is the fill weight, similarly we also used the same criteria for the development of our products i.e. weight multiplication, and comparative analysis have been performed against COLOMYCIN 1MIU strength, that fulfil the requirements. We have developed LISTIM 2 MIU Injection against the reference listed drug (RLD) i.e. Colomycin 2 Million International Units (IU) Powder for solution for injection, infusion or inhalation.
Component of drug product: Formulation Development Provide detail of type and quantity of diluents used for reconstitution of applied product.	We have developed LISTIM 2 MIU Injection against the reference listed drug (RLD) i.e. Colomycin 2 Million International Units (IU) Powder for solution for injection, infusion or

Inform about quantity of diluent used for reconstitution when the product is used for inhalation as nebulizer solution. Compatibility Provide compatibility studies data with its diluent Provide compatibility study data of drug product with its suitable diluent, after reconstitution as per the instructions provided in individual label of the drug product	inhalation. Quantity and type of diluents used are as under; BOLUS INJECTION: 4ml of water for injection or 0.9% sodium chloride INFUSION: Reconstituted vial will be further diluted in 50 ml 0.9% sodium chloride solution INTRATHECAL AND INTRAVENTRICULAR: Not more than 1 ml of water for injection or 0.9% sodium chloride will be used for reconstitution INHALATION AS NEBULIZER SOLUTION: 4ml of water for injection or saline (0.9% sodium chloride solution) for reconstitution when the product is used for inhalation as nebulizer solution. Before opening: 3 years. Reconstituted solutions: Hydrolysis of Colistimethate is significantly increased when reconstituted and diluted below its critical micelle concentration of about 80,000 IU per ml. Solutions below this concentration should be used immediately For solutions for bolus injection or nebulization, the chemical and physical in-use stability of reconstituted solution in the original vial, with a concentration ≥ 80,000 IU/mL, has been demonstrated for 24 hours at 2 to 8°C. From a microbiological point of view, unless the method of opening/ reconstitution/ dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of user. Solutions for infusion, which have been diluted beyond the original vial volume and / or with a concentration < 80,000 IU/mL should be used immediately. For solutions for intrathecal and intraventricular administration, the reconstituted product should be used immediately.
Analytical procedure: Sample stock solution has been prepared in distilled water while as per the reference product, water for injection or 0.9% sodium chloride should be used as diluent for "Colistimethate for injection". Justification is required for using distilled water for preparation of sample solution.	Firm stated that "it was the typo error we actually use water for injection for reconstitution of sample. The method has been revised and attached".
The median concentration i.e. U3 of Colistimethate sodium should be 1mcg/ml as per USP, while the submitted assay method indicate that the median concentration U3	Firm Stated that USP allows to adjust the Median conc. to optimize the zone sizes if the data remain in the linear range (linearity has been verified), USP <81> chapter has been attached for reference.

was 5mcg/ml. Clarification is required in this regard.	However, the method of analysis is not as per USP, For the cylinder-plate assay, each plate includes only two treatments, the reference treatment (median level standard, i.e., S3) and one of the other four concentrations of the standard (S1, S2, S4 and S5) or the sample (U3). While, according to the submitted assay procedure each plate contains three treatments (S3, STANDARD and U3) which is not in accordance to USP. Firm submitted the revised analytical method in accordance with USP.
Provide assay method for the infusion and inhalation route of administration, as the amount of diluent will be varying accordingly for the preparation of sample stock solution.	Firm stated that the constitution volume for both infusion and inhalation route of administration is same i.e. 2ml of water for injection or 0.9 % saline, therefore same method will be applied Volume of diluent used for reconstitution is different for intrathecal/intraventricular route of administration and for infusion and according to USP monograph for sample preparation "Constitute Colistimethate for Injection in a volume of water, accurately measured, corresponding to the volume of diluent specified in the labeling."
Analytical verification report reflects that weight of sample used for sample solution is 240mg instead of 160mg (content per vial) justification/clarification required in this regard. How the specificity of method has been verified without comparing the results of sample with standard and placebo, as in the submitted data sample solution has not been prepared.	Firm stated that It was typo graphical error, the amount of standard used was 240 mg and the vial of sample directly reconstituted with diluent. Revised method and report have been attached. Firm has submitted the reply that "Specificity was done compartively with blank, standard and sample, results are compared, method found selective that was missed in the method verification report, method verification report has been revised and attached for ready reference".
Acceptance criteria of assay is not as per labelled claimed of USP monograph of "Colistimethate for Injection". It is not clear that the given percentage is of colistin or Colistimethate sodium.	Firm has stated that results obtained by our calculation is labelled amount of Colistin according to USP.
Working standard supplied by MAC-chem Products (India) has been used while the drug substance manufacturer used USP reference standard. Justification is required for not using the primary standard or the working standard supplied by the drug substance manufacturer.	The material supplied by MAC-chem Products (India) was tested against reference standard and same lot is standardized against USP reference standard and use accordingly. However, the API manufacturer is M/s. Livzon Group Fuzhou Fuxing Pharmaceuticals, China as per the CTD dossier.
Provide in use stability data of reconstituted solution along with give the detail of proposed in-use storage statement and in-use shelf-life.	Firm has submitted the in-use stability data and the proposed in-use storage statement and in-use shelf life is as under: Store at 2-8°C for 24hours

	After 24hours of reconstitution the product found stable with respect to quality, strength and compatibility

Decision of 316th meeting of Registration Board:
Deferred for further deliberation regarding the label claim of Colistimethate sodium in line with the product approved in reference regulatory agencies and pharmacopeia.

Decision: Deferred for following clarification:

- **Manufacturing facility (lyophilized or dry powder filling) wherein the trial batches have been manufactured along with evidence of approval of required manufacturing facility from CLB.**
- **Applied label claim against the recommendations of USP monograph of Colistimethate for injection.**

295.	Name, address of Applicant / Marketing Authorization Holder	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.no. 13397 dated 18/05/2021
	Details of fee submitted	PKR 20,000/-: dated 28/07/2020 slip no.2031157
	The proposed proprietary name / brand name	Jawaflox 0.3% Ophthalmic Solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains Ciprofloxacin HCl e.q. Ciprofloxacin… 3mg (0.3%)
	Pharmaceutical form of applied drug	Cleared slightly Yellow colored solution for Ophthalmic use only
	Pharmacotherapeutic Group of (API)	Quinolone class of anti-bacterial
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Ciloxan 0.3% eye drops Alcon USA Approved
	For generic drugs (me-too status)	Ciloxan 0.3% Reg.no. 016754 Novartis Pharma Ltd.
	GMP status of the Finished product manufacturer	GMP certificate granted on 06/07/2020 Valid for 2 Years Ophthalmic section approved.

	Name and address of API manufacturer.	M/s Citi Pharma Pvt Ltd. Head Balloki Road, Phool Nagar, Kasur, Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of ciprofloxacin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity fluoroqinolonic acid, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Used factor as per ICH guidelines Batches: (T1, T2, T3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence.	Pharmaceutical Equivalence have been established against the ophthalmic solution (ciprofloxacin HCl) by performing quality tests (Identification, pH Assay)
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s Citi Pharma Pvt Ltd. Head Balloki Road, Phool Nagar, Kasur, Pakistan
API Lot No.	CPH1908055
Description of Pack (Container closure system)	White opaque LDPE bottle with polypropylene nozzle and high-density polyethylene (HDPE) cap.1 x 1`s
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH Used factor of water loss as per ICH guidelines

Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9, 12, 18, 24 (Months)		
Batch No.	T-1	T-2	T-3
Batch Size	3L (600 bottles)	3L (600 bottles)	3L (600 bottles)
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	05-02-2020	06-02-2020	07-02-2020
No. of Batches	03		

	Administrative Portion	
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. K0708 issued by CFDA valid till 27/11/2023
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Comply
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Ophthalmic general section has not been mentioned in CGMP certificate issued dated 06-07-2020 and in Renewal letter of Drug manufacturing License issued dated 17th July, 2019.Section approval letter of ophthalmic solution is required.	Firm has submitted the grant of additional section letter specified that firm has ophthalmic (general) section issued dated 25, June,2019 vide letter no. F.1-38/91-Lic (Vol-I).
Control of Drug Substance Analytical procedures Provide detailed analytical procedures for the testing of drug substance.	Firm has submitted the analytical procedure for testing of drug substance according to USP monograph.
Validation of analytical procedures Provide analytical Method Verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Firm has submitted the method verification studies of drug substance performed by the drug product manufacturer. However, the solution preparation methods are not in accordance with USP, as in the USP mobile phase has been used for the preparation

	of sample and standard solution while firm used distilled water first and then make up the volume with mobile phase for preparation of solution.
Component of drug product: Formulation Development Acceptance limit of pH of ciprofloxacin ophthalmic solution as per USP is 3.5-5.5 while pharmaceutical equivalence table reflect that the pH of applied and reference drug product is 6.76 and 6.8 respectively. Justification/clarification is required in this regard.	Firm has submitted the revised pharmaceutical equivalence data in which the pH of both the applied and innovator drug product is in the range recommended by USP i.e. 3.5-5.5, but the reference product used for equivalence study is vigamox ophthalmic solution which is the innovator brand of moxifloxacin hydrochloride.
Microbiological Attributes Formulation contain preservative, so preservative effectiveness studies to be performed as per recommendations of pharmacopoeia and shall be submit.	Firm has submitted the preservative efficacy studies data. But how the firm performed preservative efficacy test prior the manufacturing of stability batches, as the stability batches were manufactured in the month of feb,2020, while the batch used for preservative test was manufactured in dec,2019 and test date was jan,2020. Further, the test results of all the recent applied ophthalmic solution are similar.
Control of Drug Product Analytical procedure for the determination of pH, sterility and bacterial endotoxin limit and osmolality/osmolarity of ophthalmic solution has not been provided.	Firm has submitted the analytical procedure for the determination of pH, sterility and bacterial endotoxin limit and osmolality/osmolarity of drug product.
Batch analysis The copies of complete analysis of at least two batches shall be provided.	Firm has provided the batch analysis report of three batches.
Validation of analytical procedures Justification of performing specificity parameter without determining placebo/diluent to demonstrate the absence of interference with the elution of analyte. According to ICH Q2 R1 guidelines for repeatability a minimum of 9 determinations covering the specified range for the procedure (e.g., 3 concentrations/3 replicates each); or a minimum of 6 determinations at 100% of the test concentration are used. Justification is required for using five determinants along with provide the detail of concentration of test sample used to assessed the repeatability parameter. Elaborate following for the performance of accuracy parameter: Preparation of standard solution Preparation of sample solution Preparation of placebo solution preparation Concentration range of sample solution used to determine the percentage recovery.	Firm has submitted the revised analytical method verification studies of drug product which is also not in accordance with USP monograph in terms of method of preparation of solutions (sample and standard solutions). As per USP monograph sample and standard solutions has been prepared in water while the submitted studies evident the solution has been prepared in mobile phase. Submitted chromatograms did not mention the date of requisition and processing of sample.

Stability Provide raw data sheet reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content. How percentage of water loss has been calculated at zero-time point during stability studies. Provide the detail calculation performed to obtained the water loss using the factor 3 and 1.8 at the initial time point.	Firm has submitted revised stability study data of 3 batches of drug product at both accelerated as well as real time conditions. Revised stability study shows that at zero-time point percentage water loss is 0% and result of osmolarity has been included in the stability data sheet. Firm has not submitted the raw data sheet reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.
Water loss study performed for LDPE container as per the Asian Guidelines on stability study of drug product under the recommended condition of temperature and humidity i.e. 40℃/25% (factor 3.0) and 30℃/35% (factor 1.8) have same results of % water loss for all the applied ophthalmic solution, justification/clarification is required in the regard.	Firm stated that "as our all ophthalmic products has same manufacturing method and water based, placed on same stability conditions and same semi-preamble packaging (LDPE Bottles). So, our water loss results have variations in points. We have already attached the data logger of stability data in dossier which shows that same conditions applied which cause same results of water loss studies with just points variations".
Executed Production Documents: Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.	Firm has submitted copy of BMR of three stability batches. However, the following discrepancies has been observed in the submitted BMR: Justification is required for autoclaving of bulk solution in the glass container for all three stability batches. Bulk solution is autoclaved in closed Glass container before filing because ophthalmic solutions are filled in LDPE vials which cannot be sterilized by terminal sterilization. Sterilization by Filtration is also done by 0.2µm and 0.45µm filters. LDPE plastic vials for ophthalmic solution filling are received as sterilized. Not every Solution is sterilized by autoclave before filling. Evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of large capacity. Volume of HCL/NaOH has been used for the adjustment of pH of the ophthalmic solution was not mentioned in all three BMRs. pH of the solution was adjusted by using 1N HCl. Quantity of 1N HCl solution used for adjusting pH of the solution was 1.0ml
Decision of 316th meeting of Registration Board: Deferred for the submission of following:	

Justification for reporting Pharmaceutical equivalence studies of Ciprofloxacin against the innovator brand of moxifloxacin HCl i.e. Vigamox.
Justify, how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave, and provide evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of such large capacity.
Scientific justification for using an entirely different formula for calculation of assay results of stability batches from that specified in USP monograph and rationale of the results reported on basis of this calculation formula.
Scientific justification for variation in the sample & standard solution preparation method from that specified in the USP monograph of "Ciprofloxacin Ophthalmic solution".
Justification regarding, how the firm performed preservative efficacy test prior to manufacturing of stability batches.
Scientific justification for submitting same water loss study data in all applied ophthalmic solution products.

Reply of the Firm:

<table>
<tr><th>Sr.no.</th><th>Decision of 316th meeting of Registration Board</th><th>Reply of the Firm</th></tr>
<tr><td>1.</td><td>Justification for reporting Pharmaceutical equivalence studies of Ciprofloxacin against the innovator brand of moxifloxacin HCl i.e. Vigamox.</td><td>Firm claimed that only the name in heading of pharmaceutical equivalence report was mistakenly written as vigamox, otherwise the results are same as compared with innovator product.
However, the specifications and label claim of ophthalmic solution is not in accordance with USP monograph of ciprofloxacin ophthalmic solution.</td></tr>
<tr><td>2.</td><td colspan="2">Justify, how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave, and provide evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of such large capacity.
Firm claimed that they sterilized the container in which the bulk solution will be prepared prior manufacturing of bulk solution, further the bulk solution will be filter through 0.2µ filter paper and then the filling procedure will be done under aseptic condition.
Terminal sterilization of ophthalmic solution will not be done because the primary container of ophthalmic solution is LDPE bottle.</td></tr>
<tr><td>3.</td><td>Scientific justification for using an entirely different formula for calculation of assay results of stability batches from that specified in USP monograph and rationale of the results reported on basis of this calculation formula.</td><td>Firm submitted the revised assay testing procedure in accordance with USP monograph of ciprofloxacin ophthalmic solution.</td></tr>
<tr><td>4.</td><td>Scientific justification for variation in the sample & standard solution preparation method from that specified in the USP monograph of "Ciprofloxacin Ophthalmic solution".</td><td>Firm submitted the revised assay testing procedure in accordance with USP monograph of ciprofloxacin ophthalmic solution.</td></tr>
<tr><td>5.</td><td colspan="2">Justification regarding, how the firm performed preservative efficacy test prior to manufacturing of stability batches.
Firm submitted the revised preservative efficacy test report of all three trial batches, which is again performed prior manufacturing of each trial batches:
<table>
<tr><td>T-01</td><td>T-02</td><td>T-03</td></tr>
<tr><td>Mfg date:</td><td>Mfg date:</td><td>Mfg date:</td></tr>
</table></td></tr>
</table>

	05-02-2020	06-02-2020	07-02-2020
	Performance of preservative efficacy test in january-2020	Performance of preservative efficacy test in january-2020	Performance of preservative efficacy test in january-2020
6.	Scientific justification for submitting same water loss study data in all applied ophthalmic solution products. Firm submitted the reply that "We have already provided justification for same water loss study results (We had purchased LDPE bottles from Pak Nationals Limited which was used for all ophthalmic preparation's trial batches of the same batch. The temperature, humidity conditions was same for all preparations, even the preparation also done on oil base method which leads to same water loss results with changes in points."		

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of documents related to performance of next time point of long term stability studies as per USP monograph, Pharmaceutical equivalence studies performed against the innovator/reference/comparator product, preservative efficacy test performed in accordance with general guidance chapter of Pharmacoepias and updated water loss study alongwith fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

296.	Name, address of Applicant / Marketing Authorization Holder	M/s Jawa Pharmaceuticals Private Limited112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.no.13398 dated 18/05/2021
	Details of fee submitted	PKR 20,000/-: dated 19/10/2020 slip no. 2031169
	The proposed proprietary name / brand name	Jfenac 0.1% Ophthalmic solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains Diclofenac Sodium … 1mg (0.1%)
	Pharmaceutical form of applied drug	Clear and colorless solution for Ophthalmic use only
	Pharmacotherapeutic Group of (API)	NSAID

	Reference to Finished product specifications	Manufacturer's Specification
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA approved Voltarol Ophtha Thea Pharmaceuticals Ltd.
	For generic drugs (me-too status)	Oclonac 0.1% eye drops Barrett Hodgson (Reg.no.039728)
	GMP status of the Finished product manufacturer	GMP certificate granted on 06/07/2020 Valid for 2 Years Ophthalmic section approved.
	Name and address of API manufacturer.	M/s Henan Dongtai Pharma Co. Ltd China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Diclofenac Sodium is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A and related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Used factor as per ICH guidelines Batches: (T1, T2, T3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence.	Pharmaceutical Equivalence have been established against the brand leader that is Voltarol 0.1% eye drops by Thea Pharmaceutical by performing quality tests (Identification, pH and Assay)

	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Henan Dongtai Pharma Co. Ltd China		
API Lot No.		20190509		
Description of Pack (Container closure system)		White opaque LDPE bottle with polypropylene nozzle and high-density polyethylene (HDPE) cap. 1 x 1`s		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH Used factor as per ICH guidelines		
Time Period		Real time: 24 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9, 12, 18, 24 (Months)		
Batch No.		T-1	T-2	T-3
Batch Size		3L (600 bottles)	3L (600 bottles)	3L (600 bottles)
Manufacturing Date		02-2020	02-2020	02-2020
Date of Initiation		05-02-2020	06-02-2020	07-02-2020
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. HA20170001 issued by CFDA valid till 22/01/2022.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Already registered product Copy of letter No.8111/2020/DRAP-AD-CD(I&E) dated 11/12/2020		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Comply		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted		
Remarks OF Evaluator:				
Ophthalmic general section has not been mentioned in CGMP certificate issued dated		Firm has submitted the grant of additional section letter specified that firm has ophthalmic		

06-07-2020 and in Renewal letter of Drug manufacturing License issued dated 17th July, 2019.Section approval letter of ophthalmic solution is required.	(general) section issued dated 25, June,2019 vide letter no. F.1-38/91-Lic (Vol-I).
3.2S.4.2: Analytical procedures Provide detailed analytical procedures for the testing of drug substance.	Firm has submitted the analytical procedure for testing of drug substance according to BP monograph of Diclofenac Sodium in which the assay has been performed on potentiometer.
3.2S.4.3: Validation of analytical procedures Provide analytical Method Verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Firm has submitted the method verification studies of drug substance performed by the drug product manufacturer. However, the assay method is not as per the BP monograph for diclofenac sodium.
Batch analysis Provide results of analysis of relevant batches of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacture.	Firm has not submitted the results of analysis of relevant batches of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacture.
Description and Composition of the Drug Product Amount of diclofenac sodium used in the formulation is 1.1mg/ml as per reference product it is 1mg/ml. Scientific justification is required for using overage of active ingredient in the formulation.	Firm has not provided any justification regarding the overage of diclofenac sodium used in the formulation i.e. 1.1mg/ml, while as per reference product it is 1mg/ml.
Component of drug product: Drug substance Provide compatibility studies of the Drug Substance(s) with excipients as the qualitative composition of the formulation is not similar to innovator / reference product.	Firm has not submitted the compatibility studies of drug substance with excipient.
Microbiological Attributes Formulation contain preservative, so preservative effectiveness studies to be performed as per recommendations of pharmacopoeia and shall be submit.	Firm has submitted the preservative efficacy report of boric acid which has similar results as that of benzalkonium chloride report. Further, how the firm performed preservative efficacy test prior the manufacturing of stability batches, as the stability batches were manufactured in the month of feb,2020, while the batch used for preservative test was manufactured in dec,2019 and test date was jan,2020.
Control of Drug Product Analytical procedures Provided assay procedure is of diclofenac sodium injection as evident from the documents and only acceptance criteria of pH, sterility test and identification test has been given instead of detailed analytical	Firm has not submitted the analytical procedure used for quality test of drug product.

procedure. Provide detailed analytical procedure used for testing of applied product i.e. diclofenac sodium ophthalmic solution.	
Validation of analytical procedures Validation of assay procedure of diclofenac sodium injection has been performed as evident from the submitted documents. Provide validation study of analytical method of diclofenac ophthalmic solution.	Firm has submitted the analytical method validation studies of drug product but the detailed assay procedure including chromatographic condition has not been provided.
Reference Standards or Materials COA of raw material of Diclofenac sodium (Bromine free) BP2010 has been attached in 3.2.P.6 instead of COA of reference/working standard.	Firm has not submitted COA of reference standard against which quality of product has been tested.
Stability Provide raw data sheet reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content. How percentage of water loss has been calculated at zero time point during stability studies. Provide the detail calculation performed to obtained the water loss using the factor 3 and 1.8 at the initial time point.	Firm not submitted any response regarding both of these shortcomings.
Executed Production Documents: Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.	Firm has submitted copy of BMR of three stability batches. However, the following discrepancies has been observed in the submitted BMR: Justification is required for autoclaving of bulk solution in the glass container for all three stability batches. Volume of HCL/NaOH has been used for the adjustment of pH of the ophthalmic solution was not mentioned in all three BMRs In BMR the range of pH of ophthalmic solution was 7.5-8.5, while the finished product specification specify that the pH range of product should be 6.5-7.5.

Decision of 316th meeting of Registration Board:
Deferred for submission of following:
Clarification regarding how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave and provide evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of large capacity.
Scientific justification for using an entirely different formula for calculation of assay results of stability batches from that specified in USP monograph and rationale of the results reported on basis of this calculation formula.
Scientific justification for variation in the sample & standard solution preparation method from that specified in the USP monograph.
Submission of detailed analytical procedure of drug product as per BP monograph.
Submission of drug excipient compatibility studies as the qualitative composition of the formulation is not similar to innovator / reference product.

Scientific justification for submitting same data of preservative efficacy test for benzalkonium and boric acid.
Justification for performing preservative efficacy test prior to manufacturing of stability batches.
Scientific justification for submitting same water loss study data in all the applied ophthalmic solution products.
Provide raw data sheets reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.
Scientific justification for using overage of diclofenac sodium in the formulation.
Clarification regarding the variation of pH range observed in BMR from that specified in drug product specifications.

Response of the Firm:

Sr.no.	Decision of 316th meeting of Registration Board	Reply of the Firm
1.	Justify, how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave, and provide evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of such large capacity.	Firm claimed that they sterilized the container in which the bulk solution will be prepared prior manufacturing of bulk solution, further the bulk solution will be filter through 0.2µ filter paper and then the filling procedure will be done under aseptic condition. Terminal sterilization of ophthalmic solution will not be done because the primary container of ophthalmic solution is LDPE bottle.
2.	Scientific justification for using an entirely different formula for calculation of assay results of stability batches from that specified in USP monograph and rationale of the results reported on basis of this calculation formula.	Firm submitted the revised assay testing procedure of drug substance in accordance with BP monograph of Diclofenac Sodium along with clarification that the drug substance used is of BP grade.
3.	Scientific justification for variation in the sample & standard solution preparation method from that specified in the USP monograph.	Firm submitted the revised assay testing procedure of drug substance in accordance with BP monograph of Diclofenac Sodium along with clarification that the drug substance used is of BP grade.
4.	Submission of detailed analytical procedure of drug substance as per BP monograph.	Submitted
5.	Submission of drug excipient compatibility studies as the qualitative composition of the formulation is not similar to innovator / reference product.	Firm in their reply claimed that there the qualitative composition of both test product and innovator product is same therefore API-Excipient compatibility is not required.
6.	Scientific justification for submitting same data of preservative efficacy test for benzalkonium and boric acid. Justification for performing preservative efficacy test prior to manufacturing of stability batches.	Firm submitted the revised preservative efficacy test report of all three trial batches, which is again performed prior manufacturing of each trial batches:

T-01	T-02	T-03
Mfg date: 05-02-2020	Mfg date: 06-02-2020	Mfg date: 07-02-2020
Performance of preservative efficacy test	Performance of preservative efficacy test in january-2020	Performance of preservative efficacy test

		in january-2020		in january-2020
		Further the same preservative efficacy test report has been submitted in all the applied ophthalmic solution.		
7.	Scientific justification for using overage of diclofenac sodium in the formulation.	Firm in their reply that it was a typographical mistake and correct batch formula is submitted.		
8.	Scientific justification for submitting same water loss study data in all applied ophthalmic solution products. Firm submitted the reply that "We have already provided justification for same water loss study results (We had purchased LDPE bottles from Pak Nationals Limited which was used for all ophthalmic preparation's trial batches of the same batch. The temperature, humidity conditions was same for all preparations, even the preparation also done on oil base method which leads to same water loss results with changes in points."			
9.	Provide raw data sheets reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.	Submitted		
10.	Clarification regarding the variation of pH range observed in BMR from that specified in drug product specifications.	Firm has submitted the correct/revised copy of BMR without any clarification, in which acceptable range of pH is between 6.5-7.5.		

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Registration letter will be issued after submission of following documents:

- **Fee of Rs. 7500/- for correction/pre-approval change in product specifications of each strength as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Preservative efficacy studies, performed in accordance with general chapter of Pharmacopeias, performance of updated water loss studies and Pharmaceutical equivalence studies against the innovator/reference product**.

297.	Name, address of Applicant / Marketing Authorization Holder	M/s Jawa Pharmaceuticals Private Limited112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale

		☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.no.13400 dated 18/05/2021
	Details of fee submitted	PKR 20,000/-: dated 30/11/2020 slip no. 2031159
	The proposed proprietary name / brand name	Tbrix 0.3% Ophthalmic Solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains Tobramycin …. 3mg (0.3%)
	Pharmaceutical form of applied drug	Clear colorless solution for Ophthalmic use only
	Pharmacotherapeutic Group of (API)	Aminoglycosides
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Tobrex eye drops 0.3% Alcon USFDA Approved
	For generic drugs (me-too status)	Tobrex 0.3% Reg# 008249 Novartis Pharma Ltd
	GMP status of the Finished product manufacturer	GMP certificate granted on 06/07/2020 Valid for 2 Years Ophthalmic section approved.
	Name and address of API manufacturer.	M/s Livzon New North River Pharmaceuticals Co. Ltd Guangdong China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Tobramycin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Using factor as per ICH guidelines

		Batches: (T1, T2, T3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence.	Pharmaceutical Equivalence have been established against the brand leader that is Tobrex 0.3% by Novartis Pharma Ltd by performing quality tests (Identification, pH Assay)
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Livzon New North River Pharmaceuticals Co. Ltd Guangdong China		
API Lot No.	TB-19005		
Description of Pack (Container closure system)	White opaque LDPE bottle with polypropylene nozzle and high-density polyethylene (HDPE) cap. 1 x 1`s		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH Using factor as per ICH guidelines		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9, 12, 18, 24 (Months)		
Batch No.	T-1	T-2	T-3
Batch Size	3L (600 bottles)	3L (600 bottles)	3L (600 bottles)
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	24-02-2020	25-02-2020	27-02-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP inspection report of M/s. Livzon New North River Pharmaceuticals (Co.) Ltd. Guangdong China Certificate No.20190944 valid uptill 31/01/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of Letter No.5337/2020/DRAP-AD-CD(I&E) dated 20/01/2020 submitted

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Comply
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Approval of manufacturing facility of API by regulatory body of country and validity. Provide Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin.	Firm has submitted the Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin.
Control of Drug Substance 3.2S.4.2: Analytical procedures Provide detailed analytical procedures for the testing of drug substance.	Firm has submitted the copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance with the claimed that they followed USP specification.
3.2S.4.3: Validation of analytical procedures Provide analytical Method Verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Firm has submitted the method verification studies of drug substance performed by the drug product manufacturer. However, the assay method verification studies did not include the system suitability determination which is the part of assay in USP. Specificity parameter has not been performed as per international guidelines Recovered active content obtained in Accuracy parameter is in percentage, while the formula given in USP monograph is for Calculate the quantity, in µg/mg, of tobramycin. Firm did not submit the raw data sheets which reflect the preparation of solutions.
Batch analysis Provide results of analysis of relevant batches of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacture.	Firm has not submitted the results of analysis of relevant batches of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacture.
Microbiological Attributes Formulation contain preservative, so preservative effectiveness studies to be performed as per recommendations of pharmacopoeia and shall be submit.	Firm has not submitted preservative efficacy report.
Validation of analytical procedures	Firm has submitted the revised analytical method verification studies of drug product without

Justification of performing specificity parameter without determining placebo/diluent to demonstrate the absence of interference with the elution of analyte. According to ICH Q2 R1 guidelines for repeatability a minimum of 9 determinations covering the specified range for the procedure (e.g., 3 concentrations/3 replicates each); or a minimum of 6 determinations at 100% of the test concentration are used. Justification is required for using five determinants along with provide the detail of concentration of test sample used to assessed the repeatability parameter. Elaborate following for the performance of accuracy parameter: Preparation of standard solution Preparation of sample solution Preparation of placebo solution preparation Concentration range of sample solution used to determine the percentage recovery	submitting the raw data sheets and chromatogram. One-page raw data sheet submitted by the firm reflects that the preparation of solutions for verification of assay method was not as per USP.
Batch analysis Justification for not performing osmolality and osmolarity test of ophthalmic solution is required.	Firm has not provided any justification for not performing the test of osmolality and osmolarity at the time of batch release, as the said test is the part of USP monograph and the critical attributes for ophthalmic solutions.
Reference Standards or Materials Re-standardization date on the submitted COA of working standard was 04-09-2020 while the stability study of drug product was continued till 21-12-2020 as per the date mentioned on chromatograms. So, the documented evidence is required that either the standardization of working standard has been performed before the due date.	Firm has submitted an undertaking which stated that the firm has purchased new working standard TB-1090613 and claimed that they submitted raw data sheets reflecting that the new working standard has been used for testing of drug product. But the raw data sheets are not being submitted by the firm.
Stability Provide raw data sheet reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content. How percentage of water loss has been calculated at zero-time point during stability studies. Provide the detail calculation performed to obtained the water loss using the factor 3 and 1.8 at the initial time point. Water loss study performed for LDPE container as per the Asian Guidelines on stability study of drug product under the recommended condition of temperature and humidity i.e. 40℃/25% (factor 3.0) and 30℃/35% (factor 1.8) have same results of % water loss for all the applied ophthalmic	Firm has submitted the table of water loss study of all three stability batches but the values specified in the said table is different from the values of water loss initially submitted in the stability data and the values mentioned in the water loss study submitted in section 3.2. P.2.4. Firm has not provided any justification regarding the same data of water loss study of all the applied ophthalmic solutions.

solution, justification/clarification is required in the regard.	
Executed Production Documents: Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.	Firm has submitted copy of BMR of three stability batches. However, the following discrepancies has been observed in the submitted BMR: Justification is required for autoclaving of bulk solution in the glass container for all three stability batches. Bulk solution is autoclaved in closed Glass container before filing because ophthalmic solutions are filled in LDPE vials which cannot be sterilized by terminal sterilization. Sterilization by Filtration is also done by 0.2µm and 0.45µm filters. LDPE plastic vials for ophthalmic solution filling are received as sterilized. Not every Solution is sterilized by autoclave before filling. Evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of large capacity. Volume of HCL/NaOH has been used for the adjustment of pH of the ophthalmic solution was not mentioned in all three BMRs. pH of the solution was adjusted by using 1N HCl. Quantity of 1N HCl solution used for adjusting pH of the solution was 1.0ml

Decision of 316th meeting of Registration Board:
Deferred for submission of following:
Justification for not performing the verification studies of drug substance in accordance with relevant guidelines. Further, the verified method did not include the system suitability studies.
Justify, how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave, and provide evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of large capacity.
Provide batch analysis report of drug substance performed by drug product manufacturer, for relevant batch used in the production of drug product stability batches.
Preservative efficacy test data as the formulation contains preservative.
Scientific justification for submitting same water loss study data in all the applied ophthalmic solution products.
Raw data sheets reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.
Scientific justification for not performing osmolality and osmolarity test of ophthalmic solution at the time of batch release, despite the test is included in the USP monograph.

Sr. no.	Decision of 316th meeting of Registration Board	Reply of the Firm
1.	Justify, how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave, and provide evidence of availability of large capacity closed glass containers for autoclaving of	Firm claimed that they sterilized the container in which the bulk solution will be prepared prior manufacturing of bulk solution, further the bulk solution will be filter through 0.2µ filter paper and then the filling procedure will be done under aseptic condition.

<table>
<tr><td></td><td>commercial batches and autoclave of such large capacity.</td><td>Terminal sterilization of ophthalmic solution will not be done because the primary container of ophthalmic solution is LDPE bottle.</td></tr>
<tr><td>2.</td><td>Justification for not performing the verification studies of drug substance in accordance with relevant guidelines. Further, the verified method did not include the system suitability studies.</td><td>In the reply firm has submitted the verification report of drug product instead of drug substance.</td></tr>
<tr><td>3.</td><td>Raw data sheets reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.</td><td>Submitted</td></tr>
<tr><td>4.</td><td>Provide batch analysis report of drug substance performed by drug product manufacturer, for relevant batch used in the production of drug product stability batches.</td><td>Firm submitted the batch analysis report by drug product manufacturer and COA of API of same batch i.e. batch no. TB-190052</td></tr>
<tr><td>5.</td><td colspan="2">Scientific justification for submitting same water loss study data in all applied ophthalmic solution products.
Firm submitted the reply that “We have already provided justification for same water loss study results (We had purchased LDPE bottles from Pak Nationals Limited which was used for all ophthalmic preparation’s trial batches of the same batch. The temperature, humidity conditions was same for all preparations, even the preparation also done on oil base method which leads to same water loss results with changes in points.”</td></tr>
<tr><td>6.</td><td colspan="2">Preservative efficacy test data as the formulation contains preservative.
Firm submitted the revised preservative efficacy test report of all three trial batches, which is again performed prior manufacturing of each trial batches:
<table>
<tr><th>T-01</th><th>T-02</th><th>T-03</th></tr>
<tr><td>Mfg date:
24-02-2020</td><td>Mfg date:
25-02-2020</td><td>Mfg date:
26-02-2020</td></tr>
<tr><td>Performance of preservative efficacy test in january-2020</td><td>Performance of preservative efficacy test in january-2020</td><td>Performance of preservative efficacy test in january-2020</td></tr>
</table>
Further the same preservative efficacy test report has been submitted in all the applied ophthalmic solution.</td></tr>
</table>

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications of each strength as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Registration letter will be issued after submission of analytical method verification report of drug substance by drug product manufacturer, preservative efficacy test report performed in accordance with general guidance chapter of Pharmacoepias and performance report of revised water loss study.**

298.	Name, address of Applicant / Marketing Authorization Holder	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.no. 13399 dated 18/05/2021
	Details of fee submitted	PKR 20,000/-: dated 28/07/2020 slip no. 2031158
	The proposed proprietary name / brand name	Mox-Q 0.5% Ophthalmic solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains Moxifloxacin HCL e.q. to Moxifloxacin … 5mg (0.5%)
	Pharmaceutical form of applied drug	Clear and light-yellow solution for Ophthalmic use only
	Pharmacotherapeutic Group of (API)	Quinolone Anti-infective
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Vigamox 0.5% eye drops Alcon USFDA Approved
	For generic drugs (me-too status)	Vigamox 0.5% eye drops Reg # 039897 Novartis Pharma Ltd
	GMP status of the Finished product manufacturer	GMP certificate granted on 06/07/2020 Valid for 2 Years Ophthalmic section approved.
	Name and address of API manufacturer.	M/s Mankind Pharma Ltd New Delhi India 110020 Shree Jee Laboratories Pvt Ltd.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.

	Module III (Drug Substance)	Official monograph of Moxifloxacin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Used factor as per ICH guidelines Batches: (T1, T2, T3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence.	Pharmaceutical Equivalence have been established against the brand leader that is Vigamox 0.1% eye drops by Novartis Pharma Ltd by performing quality tests (Identification, pH and Assay)
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Mankind Pharma Ltd New Delhi India 110020 Shree Jee Laboratories Pvt Ltd.		
API Lot No.	10000565		
Description of Pack (Container closure system)	White opaque LDPE bottle with polypropylene nozzle and high-density polyethylene (HDPE) cap. 1 x 1`s		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH Used factor as per ICH Guidelines		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9, 12, 18, 24 (Months)		
Batch No.	T-1	T-2	T-3
Batch Size	3L (600 bottles)	3L (600 bottles)	3L (600 bottles)
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	03-02-2020	04-02-2020	05-02-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. DC-I/A-I/WHO/GMP/2019/203 issued by Drug Controller Rajasthan, Jaipur valid till 26/01/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of Letter No. 1936/2020/DRAP-AD-CD(I&E) dated 31/01/2020 submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Complied
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Ophthalmic general section has not been mentioned in CGMP certificate issued dated 06-07-2020 and in Renewal letter of Drug manufacturing License issued dated 17th July, 2019.Section approval letter of ophthalmic solution is required.	Firm has submitted the grant of additional section letter specified that firm has ophthalmic (general) section issued dated 25, June,2019 vide letter no. F.1-38/91-Lic (Vol-I).
Manufacture According to the submitted documents Mankind Pharma Limited 208, Okhla Ind. Estate, Phase-3, Delhi is the license holder and Manufacturing site is Shree Jee Laboratory Private Limited (A subsidiary of Mankind Pharma Limited) C-24 &25, Riico Industrial Area, Sotanala, Behror Rajasthan. Provide the licensing status of Mankind Pharma issued by relevant regulatory authority of country of origin.	Firm has not submitted any document which clarify the licensing status of Mankind Pharma in the country of origin.
Control of Drug Substance 3.2S.4.2: Analytical procedures Provide detailed analytical procedures for the testing of drug substance.	Firm has submitted the analytical procedure for testing of drug substance according to USP monograph of moxifloxacin hydrochloride.
3.2S.4.3: Validation of analytical procedures Provide analytical Method Verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Firm has submitted the method verification studies of drug substance performed by the drug product manufacturer. However, the solution preparation methods are not in accordance with USP, as in the USP specific diluent has been used for the preparation

	sample and standard solution while firm used distilled water for the preparation of both solutions.
3.2.P.2: provide preservative efficacy test as the boric acid has been used as preservative in ophthalmic solution.	Firm has submitted the preservative efficacy report of Benzalkonium chloride instead of boric acid.
Control of Drug Product Analytical procedure for the determination of pH, sterility and bacterial endotoxin limit and osmolality/osmolarity of ophthalmic solution has not been provided.	Firm has submitted the analytical procedure for the determination of pH, sterility and bacterial endotoxin limit and osmolality/osmolarity of drug product.
Batch analysis Justification for not performing osmolality and osmolarity test of ophthalmic solution is required.	Firm has not provided any justification for not performing the test of osmolality and osmolarity at the time of batch release, as the said test is the part of USP monograph and the critical attributes for ophthalmic solutions.
Validation of analytical procedures Justification of performing specificity parameter without determining placebo/diluent to demonstrate the absence of interference with the elution of analyte. According to ICH Q2 R1 guidelines for repeatability a minimum of 9 determinations covering the specified range for the procedure (e.g., 3 concentrations/3 replicates each); or a minimum of 6 determinations at 100% of the test concentration are used. Justification is required for using five determinants along with provide the detail of concentration of test sample used to assessed the repeatability parameter. Elaborate following for the performance of accuracy parameter: Preparation of standard solution Preparation of sample solution Preparation of placebo solution preparation Concentration range of sample solution used to determine the percentage recovery Run time of HPLC should be of 42 min as per the USP monograph of moxifloxacin while the chromatogram provided along with the dossier shows that the run time was 3min, justification is required in this regard.	Firm has submitted the revised analytical method verification studies of drug product which is also not in accordane with USP monograph in terms of method of preparation of solutions (sample and standard solutions). Further, firm has not provided any justification for run time of 3min instead of 42 min as recommended by the USP.
Reference Standards or Material The submitted COA reflects that the product is API of Moxifloxacin Hydrochloride instead of primary or secondary reference standard. Clarification is required in this regard.	Firm has submitted the COA of working standard of compendial reference European pharmacopeia, since the drug product is of USP specification.
Stability Provide raw data sheet reflecting the method of preparation of standard solution,	Firm has submitted revised stability study data of 3 batches of drug product at both accelerated as well as real time conditions.

sample solution, formula for calculation of assay content, calculation for determination of water loss content. How percentage of water loss has been calculated at zero time point during stability studies. Provide the detail calculation performed to obtained the water loss using the factor 3 and 1.8 at the initial time point. Water loss study performed for LDPE container as per the Asian Guidelines on stability study of drug product under the recommended condition of temperature and humidity i.e. 40℃/25% (factor 3.0) and 30℃/35% (factor 1.8) have same results of % water loss for all the applied ophthalmic solution, justification/clarification is required in the regard.	Revised stability study shows that at zero time point percentage water loss is 0% and result of osmolarity has been included in the stability data sheet. Firm has not submitted the raw data sheet reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content. Firm has not provided any justification regarding the same data of water loss study of all the applied ophthalmic solutions.
Executed Production Documents: Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.	Firm has submitted copy of BMR of three stability batches. However, the following discrepancies has been observed in the submitted BMR: According to the BMR, glass container has been sterilized in the autoclave, while the drug product is packed in LDPE bottles. How much volume of HCL/NaOH has been used for the adjustment of pH of the ophthalmic solution was not mentioned in all three BMRs.

Decision of 316th meeting of Registration Board:
Deferred for submission of following:
Justification regarding how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave, and provide evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of large capacity.
Submission of drug-excipient compatibility studies as the qualitative composition of the formulation is not similar to innovator / reference product.
Justification for submitting the preservative efficacy test of benzalkonium instead of boric acid.
Justification for performing preservative efficacy test prior to manufacturing of stability batches.
Scientific justification for submitting the same water loss study data in all the applied ophthalmic solution products.
Provide raw data sheets reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.
Scientific justification for applying an entirely different formula for calculation of assay results in verification studies from that specified in USP monograph and rationale of the results reported on basis of this calculation formula
Scientific justification for variation in the sample & standard solution preparation method applied in verification studies, from that specified in the USP monograph.

Reply of the Firm

Sr. no.	Decision of 316th meeting of Registration Board	Reply of the Firm
1.	Justify, how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave, and provide evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of such large capacity.	

<table>
<tr><td></td><td colspan="2">Firm claimed that they sterilized the container in which the bulk solution will be prepared prior manufacturing of bulk solution, further the bulk solution will be filter through 0.2µ filter paper and then the filling procedure will be done under aseptic condition.
Terminal sterilization of ophthalmic solution will not be done because the primary container of ophthalmic solution is LDPE bottle.</td></tr>
<tr><td>2.</td><td>Submission of drug-excipient compatibility studies as the qualitative composition of the formulation is not similar to innovator / reference product.</td><td>Firm in their reply stated that excipient do not show any interaction with the API which was evident from the stability data in which all the specifications of drug product were within limit.</td></tr>
<tr><td>3.</td><td>Raw data sheets reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.</td><td>Submitted</td></tr>
<tr><td>4.</td><td>Scientific justification for applying an entirely different formula for calculation of assay results in verification studies from that specified in USP monograph and rationale of the results reported on basis of this calculation formula</td><td>Firm submitted the revised analytical procedure of drug product which is in accordance with USP monograph of moxifloxacin ophthalmic solution.</td></tr>
<tr><td>5.</td><td>Scientific justification for variation in the sample & standard solution preparation method applied in verification studies, from that specified in the USP monograph.</td><td>Firm submitted the revised analytical procedure of drug product which is in accordance with USP monograph of moxifloxacin ophthalmic solution.</td></tr>
<tr><td>6.</td><td>Scientific justification for not performing osmolality and osmolarity test of ophthalmic solution at the time of batch release, despite the test is included in the USP monograph.</td><td>Firm has not submitted the reply of this observation.</td></tr>
<tr><td>7.</td><td>Provide batch analysis report of drug substance performed by drug product manufacturer, for relevant batch used in the production of drug product stability batches.</td><td>Firm submitted the batch analysis report by drug product manufacturer and COA of API of same batch i.e. batch no. TB-190052</td></tr>
<tr><td>8.</td><td colspan="2">Scientific justification for submitting same water loss study data in all applied ophthalmic solution products.
Firm submitted the reply that “We have already provided justification for same water loss study results (We had purchased LDPE bottles from Pak Nationals Limited which was used for all ophthalmic preparation’s trial batches of the same batch. The temperature, humidity conditions was same for all preparations, even the preparation also done on oil base method which leads to same water loss results with changes in points.”</td></tr>
<tr><td>9.</td><td colspan="2">Preservative efficacy test data as the formulation contains preservative.
Firm submitted the revised preservative efficacy test report of all three trial batches, which is again performed prior manufacturing of each trial batches:
<table>
<tr><td>T-01</td><td>T-02</td><td>T-03</td></tr>
<tr><td>Mfg date:
24-02-2020</td><td>Mfg date:
25-02-2020</td><td>Mfg date:
26-02-2020</td></tr>
<tr><td>Performance of preservative efficacy test in january-2020</td><td>Performance of preservative efficacy test in january-2020</td><td>Performance of preservative efficacy test in january-2020</td></tr>
</table>
Further the same preservative efficacy test report has been submitted in all the applied ophthalmic solution.</td></tr>
</table>

Decision: Approved.

	• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration letter will be issued after submission of performance of next time point of long term stability studies as per USP monograph, Pharmaceutical equivalence studies performed against the innovator/reference/comparator product, preservative efficacy test performed in accordance with general guidance chapter of Pharmacoepias and updated water loss study alongwith fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	
299.	Name, address of Applicant / Marketing Authorization Holder	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid e Azam Industrial Area Kot Lakhpat Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.no. 17948 dated 28/06/2021
	Details of fee submitted	PKR 20,000/-: dated 19/10/2020 slip no.2031168
	The proposed proprietary name / brand name	Jentacin 0.3% Ophthalmic solution
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains Gentamicin (as Sulphate) …… 3mg (0.3%)
	Pharmaceutical form of applied drug	Clear slightly yellow color solution for Ophthalmic use only
	Pharmacotherapeutic Group of (API)	Aminoglycosides anti-infective
	Reference to Finished product specifications	USP
	Proposed Pack size	1×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Genoptic 0.3% Ophthalmic solution Allegan Australia Pvt Ltd
	For generic drugs (me-too status)	Optagen 0.3% eye drops Reg # 011261 Remington Pharma

	GMP status of the Finished product manufacturer	GMP certificate granted on 06/07/2020 Valid for 2 Years Ophthalmic section approved.
	Name and address of API manufacturer.	Fuan Pharmaceuticals Group, Yantai Justaware Pharmaceutical Co. Ltd
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Gentamicin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Using factor as per ICH guidelines Batches: (T1, T2, T3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence.	Pharmaceutical Equivalence have been established against the brand leader that is Optagen 0.3% eye drops by Remington Pharmaceuticals by performing quality tests (Identification, pH and Assay)
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Fuan Pharmaceuticals Group, Yantai Justaware Pharmaceutical Co. Ltd
API Lot No.	181211016
Description of Pack (Container closure system)	White opaque LDPE bottle with polypropylene nozzle and high-density polyethylene (HDPE) cap. 1 x 1`s

Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH Used factor as per ICH guidelines		
Time Period	Real time: 12 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 ,9, 12 (Months)		
Batch No.	T-1	T-2	T-3
Batch Size	3L (600 bottles)	3L (600 bottles)	3L (600 bottles)
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	20-02-2020	21-02-2020	22-02-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate No. SD20190963 issued by CFDA valid till 16.07.2024
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Already Registered Product • Copy of letter No.8822/2019/DRAP-AD-CD(I&E) dated 07/07/2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Approval of manufacturing facility of API by regulatory body of country and validity. Provide Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin.	Firm submitted the GMP certificate of M/s. Fuan Pharmaceutical Group Yantai Justaware Pharmaceutical Co. Ltd. valid till 16-07-2024.
Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2. P.8.3.	Firm submitted the Batch manufacturing record which reflects that the filling of ophthalmic solution has been performed under aseptic condition and prior filling ophthalmic solution has filtered through 0.2µm filter.

	But the BMR did not reflect the salt adjustment calculation of Gentamicin sulphate.
• Provide detailed analytical procedures for the testing of drug substance. • Provide analytical Method Verification studies including specificity, accuracy and repeatability performed by the Drug Product manufacturer.	Firm submitted the analytical procedure and verification studies of drug substance performed by drug product manufacturer.
Provide results of analysis of relevant batches of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance manufacture.	Firm submit the batch analysis report of drug substance batch no. 181211016.
Provide compatibility studies of the Drug Substance(s) with excipients as the qualitative composition of the formulation is not similar to innovator / reference product.	Firm submitted the formulation optimization study instead compatibility studies with excipient.
Formulation contain preservative, so preservative effectiveness studies to be performed as per recommendations of pharmacopoeia and shall be submit.	Firm has submitted the preservative efficacy studies data. But how the firm performed preservative efficacy test prior the manufacturing of stability batches, as the stability batches were manufactured in the month of feb,2020, while the batch used for preservative test was manufactured in dec,2019 and test date was jan,2020. Further, the test results of all the recent applied ophthalmic solution are similar.
You have claimed USP specifications for the drug product and have used drug substance complying BP specifications. Justification is required in this regard.	Firm replied that our drug substance complied with BP specifications and we had chosen USP for our product. USP specifications define a wide range of assay percentage (90-135%) with comparison to BP (90-120%). It allowed us to lock an accurate formulation for safety of the product.
Submit detailed microbial assay procedure for quantification of content of gentamicin as per USP along with detail of media, inoculum, sample preparation procedure of standard and test solution, concentration of median solution, incubation temperature and duration and calculation of potency.	Firm submitted the microbiological assay procedure of drug product which is not in accordance with USP <81>.
Submitted verification report reflects that the verification studies have been done on identification method while as per the CTD guidance document *"officially recognized compendial methods for assay are required to be verified and verification shall include a demonstration of specificity, repeatability (method precision) and accuracy".*	Firm submitted the verification studies of microbial assay which is not in accordance with USP.

Reference Standards or Materials Submit COA of primary / secondary reference standard including source and lot number, since the submitted COA is of raw material of gentamicin sulphate	Firm submitted the COA of working standard supplied by API manufacturer, Batch no.181217266.
Stability • Provide raw data sheet reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content. • How percentage of water loss has been calculated at zero-time point during stability studies, provide the detail calculation performed to obtained the water loss using the factor 3 and 1.8 at the initial time point. • As per the submitted stability data sheet, stability has been performed at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH, while data logger record reflects the maintenance of temperature and humidity at 40°C/25% and 30°C/35%. Justification is required in this regard.	Firm submitted the one pager raw data sheet reflect only the procedure along with calculation formula which is also not in accordance with USP. Firm submitted the revised stability data sheet which shows that at zero-time point water loss has not occurred. Firm submitted the revised data logger record which reflects that temperature and humidity maintained at 30°C ± 2°C / 65% ± 5%RH and 40°C ± 2°C / 75% ± 5%RH.

Decision of 316th meeting of Registration Board

Deferred for the submission of following:

- Clarification regarding the sterilization method of ophthalmic solution with respect to the BMR, whether the filling has been done under aseptic condition or the bulk solution was sterilized in autoclave.
- Drug-excipient compatibility studies as the qualitative composition of the formulation is not similar to innovator / reference product.
- Justification is required for applying different microbial assay procedure for analysis of both drug substance and drug product from that specified in relevant USP monograph.
- Justification for submitting the preservative efficacy test for benzalkonium instead of boric acid.
- Justification for performing preservative efficacy test prior to manufacturing of stability batches.
- Scientific justification for submitting the same water loss study data in all the applied ophthalmic solution products.
- Raw data sheets reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.
- Differential fee of Rs. 10,000/- as the application for registration had been submitted after the notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

Reply of the Firm:

Sr. no.	Decision of 316th meeting of Registration Board	Reply of the Firm
1.	Justify, how the bulk ophthalmic solution of commercial batches will be sterilized in the autoclave, and provide evidence of availability of large capacity closed glass containers for autoclaving of commercial batches and autoclave of such large capacity.	Firm claimed that they sterilized the container in which the bulk solution will be prepared prior manufacturing of bulk solution, further the bulk solution will be filter through 0.2µ filter paper and then the filling procedure will be done under aseptic condition.

<table>
<tr><td></td><td colspan="2">Terminal sterilization of ophthalmic solution will not be done because the primary container of ophthalmic solution is LDPE bottle.</td></tr>
<tr><td>2.</td><td>Submission of drug-excipient compatibility studies as the qualitative composition of the formulation is not similar to innovator / reference product.</td><td>Firm in their reply stated that excipient do not show any interaction with the API which was evident from the stability data in which all the specifications of drug product were within limit.</td></tr>
<tr><td>3.</td><td>Justification is required for applying different microbial assay procedure for analysis of both drug substance and drug product from that specified in relevant USP monograph.</td><td>Submitted only the analytical procedure in accordance with USP. Analytical method verification needs to be submitted.</td></tr>
<tr><td>4.</td><td>Raw data sheets reflecting the method of preparation of standard solution, sample solution, formula for calculation of assay content, calculation for determination of water loss content.</td><td>Firm submitted the raw data sheets.</td></tr>
<tr><td>5.</td><td colspan="2">Scientific justification for submitting same water loss study data in all applied ophthalmic solution products.
Firm submitted the reply that “We have already provided justification for same water loss study results (We had purchased LDPE bottles from Pak Nationals Limited which was used for all ophthalmic preparation’s trial batches of the same batch. The temperature, humidity conditions was same for all preparations, even the preparation also done on oil base method which leads to same water loss results with changes in points.”</td></tr>
<tr><td>6.</td><td colspan="2">Preservative efficacy test data as the formulation contains preservative.
Firm submitted the revised preservative efficacy test report of all three trial batches, which is again performed prior manufacturing of each trial batches:
<table>
<tr><td>T-01</td><td>T-02</td><td>T-03</td></tr>
<tr><td>Mfg date:
20-02-2020</td><td>Mfg date:
21-02-2020</td><td>Mfg date:
22-02-2020</td></tr>
<tr><td>Performance of preservative efficacy test in january-2020</td><td>Performance of preservative efficacy test in january-2020</td><td>Performance of preservative efficacy test in january-2020</td></tr>
</table>
Further the same preservative efficacy test report has been submitted in all the applied ophthalmic solution.</td></tr>
<tr><td>7.</td><td colspan="2">Differential fee of Rs. 10,000/- as the application for registration had been submitted after the notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.
Firm submitted the differential fee of Rs. 10,000/- DATED 24-05-2022 as the application for registration had been submitted after the notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.</td></tr>
</table>

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of performance of next time point of long term stability studies as per USP monograph, Pharmaceutical equivalence studies performed against the innovator/reference/comparator product, preservative efficacy test performed in accordance with general guidance chapter of Pharmacoepias and updated water loss study alongwith fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**

300.	Name, Address Of Applicant / Marketing Authorization Holder	M/s Bio-Labs (Pvt). Ltd Plot No. 145industrial Triangle Kahuta road Islamabad.
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt). Ltd Plot No. 145industrial Triangle Kahuta road Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 2811 dated 28-01-22
	Details of fee submitted	PKR 30,000/-: dated 26-11-2021
	The proposed proprietary name / brand name	Cetol 100ml infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Paracetamol ……..10mg
	Pharmaceutical form of applied drug	Infusion
	Pharmacotherapeutic Group of (API)	Analgesic
	Reference to Finished product specifications	In-House
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	US FDA
	For generic drugs (me-too status)	Provas infusion by sami Pharma.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conduct 23-4-2019, valid upto 22-04-2022.
	Name and address of API manufacturer.	Hebei jiheng (Group) Pharmaceutical Co.,Ltd Xijingming Village Donganzhuang Township Shenzhou Country Hengshui City,Hebei Province,053800 China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product.

	Module III (Drug Substance)	Firm has submitted detailed data of drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at $30^{O}C \pm 2^{O}$ C / 65% ± 5% RH for 60 months. (31106015,31106016,31106017)
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against the comparator i.e. Provas 100ml infusion.
	Analytical method validation/verification of product	Firm has submitted report of validation of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	Hebei jiheng(Group) Pharmaceutical Co., Ltd Xijingming Village Donganzhuang Township Shenzhou Country Hengshui City, Hebei Province,053800 China.		
API Lot No.	W32002004		
Description of Pack (Container closure system)	Glass vial filled with clear colorless sterile solution, with blue colored flip-off seal.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	CET 21 -41	CET 21 -42	CET 21 -43
Batch Size	250 Vials	250 Vials	250 Vials
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	05-05-21	05-05-21	05-05-21
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empaglif 10mg tablet
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP Certificate.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of Form 6 "License to import drugs for clinical trial, examination, test or analysis. The license was issued on 20-03-20 with Invoice No. 2002ZP26.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail and HPLC CFR Compliance record.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Evaluation by PEC:

Sr. no.	Observations/Deficiencies/ Short-comings	Reply of the Firm
1.	Justify why the pharmaceutical equivalence was studied against comparator product instead of using innovator / reference product.	Firm in their reply stated that "As that Paracetamol infusion is short in the pharma market due to current pandemic situation of COVID-1& Dengue. So, innovator packs weren't available in the local market of Pakistan. That is the reason the comparative study has been done against local leading brand".
2.	Submit COA of reference standard actually used in the analysis of drug substance in section 3.2. S.5.	The requisite documents regarding reference standard are attached.
3.	Scientific justification is required for not using antioxidant in the applied formulation since the innovator brand used cysteine as an antioxidant because paracetamol is susceptible to degradation by oxidation.	In order to avoid degradation, bio-oxidation and to purging was done during manufacturing that reduces the oxidation and stabilize the formulation. However the executed BMR did not mentioned any kind of purging while filling of vials.
4.	Scientific justification is required for not performing test of osmolality while batch release of trial batches of drug product, since the test has included in drug product specification of innovator brand.	Osmolarity test has been performed on the finished formulation, however, as it was additional test to check the stability of product. So it wasn't included in the final report.

	Justify the acceptance limit of pH below 5.5. ,since the innovator brand describe the pH value of infusion solution about 5.5.	
5.	As per the CTD guidance document the minimum batch size for injectable should be atleast 2 batches of minimum 2000 batch size OR At least 3 batches having scientifically rational batch size, sufficient enough to perform complete testing till the claimed shelf life, while you have manufactured three trial batches with batch size of 250 vial each. Justify, the batch size of trial batches in light of guidance document approved by DRAP.	The batch size was design to perform the stability testing as the batch size 250 infusion fulfil the requirement of samples for stability testing. So this was selected.
6.	BMR formulation sheet reflect that you have used injectable grade paracetamol but the COA of API did not reveal that the paracetamol is of injectable grade, clarification is required in this regard.	The injectable grade of Paracetamol has been used in the formulation. However, it wasn't mentioned on the COA.

Decision of 320th meeting of Registration Board:

Deferred for;

- Justification for the acceptance limit of pH below 5.5 for the applied product, since the innovator brand describe the pH value of infusion solution about 5.5.
- Submission of finished product specification mentioning Osmolality test.
- Scientific justification is required for not using antioxidant in the applied formulation since the innovator brand used cysteine as an antioxidant because paracetamol is susceptible to degradation by oxidation.

Response of the firm:

Sr.no.	Shortcomings/deficiencies	Response of the Firm
1.	Justification for the acceptance limit of pH below 5.5 for the applied product, since the innovator brand describe the pH value of infusion solution about 5.5.	Firm replied that Teva PHARMA ,Netherland Product have pH between 4.5-7.5 and MHRA approved product of Fresenius Kabi has set pH range between 5-7,so their product pH range i.e. below 5 is well within specified range.
2.	Submission of finished product specification mentioning Osmolality test.	Revised specification of drug product has been submitted by the Firm.
3.	Scientific justification is required for not using antioxidant in the applied formulation since the innovator brand used cysteine as an antioxidant because paracetamol is susceptible to degradation by oxidation.	Firm claimed that they used same qualitative composition as of MHRA registered product.

Decision: Approved.

Registration Board further decided that registration letter will be issued after submission of clarification that specification of which innovator brand will be adapted for quality testing of

drug product and accordingly submit the performance report of all quality parameters on next time point of stability.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Previously Deferred cases of Form-5

301.	Name and address of manufacturer /Applicant	The Searle company limited F-39 Site Karachi Pakistan.
	Brand Name +Dosage Form + Strength	Frutum tablets
	Composition	Each tablet contains: Zinc Oxide eq. to Zinc…..22.5mg Vitamin A acetate eq. to Vitamin A…..5000IU Vitamin B1……2.25mg Vitamin B2……2.6mg Vitamin B6…….3mg Vitamin B12…….9mcg Vitamin C……90mg Vitamin D……..400IU Vitamin E Acetate 50% eq. to Vitamin E……30IU Nicotinamide…….20mg Biotin…….150mcg Calcium…..162mg Phosphorus…….125mg Copper…..3mg Folic Acid…..400mcg Ferrous Fumarate eq. to Iron……18mg Potassium Iodide eq. to Iodine….150mcg Magnesium Oxide eq. to Magnesium…..100mg Manganese Sulphate monohydrate eq.to Manganese……7.5mg Calcium-D Pantothenate eq. to Pantothenic Acid..10mg Potassium Sulphate eq. to Potassium…….7.5mg
	Diary No. Date of R& I & fee	Dy. No.170; 27-1-2017; Rs.20,000/- (26-1-2017)
	Pharmacological Group	Vitamin & minerals
	Type of Form	Form-5
	Finished product Specification	Inhouse
	Pack size & Demanded Price	30’s, As per DPC
	Approval status of product in Reference Regulatory Authorities.	Provided Reference could not be confirmed.
	Me-too status	Provided Reference could not be confirmed
	GMP status	Last inspection report 30-01-2019, with the conclusion that the firm for continuous improvement and people met, it is concluded that the firm is operating at a Good level of GMP compliance.
	Remarks of the Evaluator.	International Reference in RRA and me-too status could not be confirmed.

	Previous Decision (279th)	Registration Board in its 279th meeting decided as under: Deferred for following: • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Previous Decision and Response of the firm	Registration in its 295th meeting decided as under: Deferred for the evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. Firm submitted revised formulation along with fee of Rs. 20,000/- dated 05-01-2021 Dy. No. 703, according to the formulation of Me-Too registered in Pakistan Theragran Ultra Tablet (Reg.no. 033732) by M/s. Glaxo Smith Kline Pakistan. Revised formulation is as under: Vitamin A ….4000IU Beta Carotene….1000IU Vitamin D ….400IU Vitamin E ….30IU Vitamin C ….90mg Vitamin B1….3mg Vitamin B2….3.4mg Vitamin B6….3mg Vitamin B12….9mcg Pantothenic Acid….10mg Folic Acid ….0.4mg Biotin….30mcg Niacin ….20mg Iron ….27mg Calcium…40mg Phosphorus ...31mg Iodine ….150mcg Magnesium….100mg Copper….2mg Zinc….15mg Manganese ……5mg Selenium….10mcg Molybdenum ….15mcg Chromium….15mcg Potassium……7.5mg Chloride ….7.5mg
	Previous Decision (297th meeting)	Decision of 297th meeting of Registration Board Deferred, as the quantity of Iodine used in the composition is above upper tolerable intake level (UL). Furthermore, clarification/justification is required from M/s. Glaxo smith Kline Pakistan regarding the quantity of iodine used in the Theragran Ultra Tablet, as it is above the UL level.

	Remarks of the Evaluator	M/s. Glaxo Smith Kline Pakistan Ltd. Submitted an additional pack approval letter dated 19-03-2015 according to that quantity of iodine used in the Theragran ultra is 150mcg, which is within UL limit and same quantity has been used in the applied formulation.
Decision: Approved.		
302.	Name and address of manufacturer / Applicant	M/s. Kanel Pharmaceuticals, Plot No.6, Road SS-3 National Industrial Zone, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Kortel-D DS Tablets
	Diary No. Date of R& I & fee	(Original Dossier) Dy. No.7038 dated 13/07/2012 Rs.8,000/- Differential fee (Original) of Rs.12,000/- submitted on 26/01/2016 Dy.No.570
	Composition	Each Film coated Tablet contains Artemether…… 80mg Lumefantrine …….480 mg
	Pharmacological Group	Antimalarial
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack Size & Demanded Price	As per S.R. O
	Approval Status of Product in Reference Regulatory Authorities	WHO prequalified drug
	Me-too Status	Marlin DS Tablet M/s Jupiter Pharma Plot # 25, St# S6 RCCI, Rawat Islamabad (Reg.no. 081928)
	GMP Status	Certificate of GMP issued dated 04th June,2020 vide certificate no.F.3-52/2020-Addl.Dir. (QA&LT-I) by QA&LT Division and valid for two years. Following sections are mentioned on the GMP certificate: Tablet (General) Capsule (General) Cream/Ointment Topical Lotion Capsule (Cephalosporin) Dry Suspension (Cephalosporin) Dry vial Injection (Cephalosporin)
	Remarks of the Evaluator.	• Firm applied with manufacturers' specification while the official monograph of applied formulation is present in IP. • Reference product is uncoated tablet while the firm applied for film coated tablet.
	Decision of 312th meeting of Registration Board: Deferred for revision of applied formulation in line with reference product i.e. uncoated tablet alongwith submission of requisite fee, revised Form-5, master formulation & manufacturing method.	
	Firm submitted the revised formulation in line with reference product i.e. uncoated tablet alongwith submission of requisite fee (fee of 7,500/- paid vide challan no. 56003611041 dated28-06-2022), revised Form-5, master formulation & manufacturing method.	
	Decision: Approved. Firm will deposit Rs.30,000/- for revision of applied formulation in line with reference product.	
303.	Name and address of manufacturer / Applicant	M/s. Kanel Pharmaceuticals, Plot No.6, Road SS-3 National Industrial Zone, Rawat, Rawalpindi

	Brand Name +Dosage Form + Strength	Kenkast 5mg Tablet
	Diary No. Date of R& I & fee	(Original Dossier) Dy. No.7065 dated 13/07/2012 Rs.8,000/- Differential fee (Original) of Rs.12,000/- submitted on 26/01/2016 Dy.No.571
	Composition	Each film coated tablet contains: Montelukast sodium eq to Montelukast ……. 5 mg
	Pharmacological Group	Bronchodilator and antiasthmatic agent
	Type of Form	Form 5
	Finished Product Specification	USP Specification
	Pack Size & Demanded Price	As per S.R. O
	Approval Status of Product in Reference Regulatory Authorities	SINGULAIR 5-mg Chewable Tablets (USFDA)
	Me-too Status	Trilukas 5mg chewable Tablet, Trillium Pharmaceuticals, Reg. No. 096678.
	GMP Status	Certificate of GMP issued dated 04th June,2020 vide certificate no.F.3-52/2020-Addl.Dir. (QA&LT-I) by QA&LT Division and valid for two years. Following sections are mentioned on the GMP certificate: Tablet (General) Capsule (General) Cream/Ointment Topical Lotion Capsule (Cephalosporin) Dry Suspension (Cephalosporin) Dry vial Injection (Cephalosporin)
	Remarks of the Evaluator.	• Initially, firm used Methylene chloride as a coating solvent which is a banned excipient, later firm submitted revise formulation without methylene chloride. Requisite fee for pre-registration variation has not been submitted by the firm. • Firm applied with manufacturers' specification, later change the specification to USP without the requisite fee. • Firm applied for film coated tablet while the reference product is chewable tablet.
	Decision of M-312: Deferred for submission of following: • Provide either evidence of approval of reference product as film coated tablet or otherwise revision of applied formulation in line with reference product i.e. chewable tablet alongwith submission of requisite fee, revise Form-5, master formulation & manufacturing method. • Change of specification from in-house to USP. • Revision of formulation in order to remove methylene chloride as a coating solvent.	
	Firm submitted the revised formulation in line with reference product i.e. chewable tablet alongwith submission of requisite fee(fee of 7,500/- paid vide challan no. 71459906687 dated28-06-2022), revise Form-5, revise specification, master formulation & manufacturing method.	

	Decision: Approved. Firm will deposit Rs.30,000/- for revision of applied formulation in line with reference product.	
304.	Name and address of manufacturer / Applicant	M/s. Maple Pharmaceuticals (Pvt.) Ltd., 147/23, Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form+ Strength	Skelet tablets 2mg
	Diary No. Date of R& I & fee	(Duplicate Dossier) dy.no.Rs.8,000/-(Photocopy) dated 23-2-2011 Differential fee (Yellow slip) Rs.12,000/- submitted on 21-10-2015 Receipt of application has verified from R&I
	Composition	Each tablet contains: Tizanidine Hydrochloride.....2mg
	Pharmacological Group	Skeletal muscle relaxant
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	10's/ As per PAC/PRC
	Approval Status of Product in Reference Regulatory Authorities	USFDA approved as uncoated tablets
	Me-too Status	Tizadin 2mg Tablets Global Pharmaceuticals, Islamabad.
	GMP Status	Grant of GMP certificate based on inspection conducted on 20-12-2019 concluded with the remarks of Good compliance
	Remarks of the Evaluator.	▪ Firm revised the master formulation and remove the overage. ▪ Revision of applied composition as in reference regulatory authorities the approved drug is "Tizanidine as HCl", while the applied drug is "Tizanidine HCl". ▪ The official monograph for the applied formulation is available in USP.
	Decision of M-308: Deferred the case for revision of formulation as the reference product contains Tizanidine as HCl…2mg while the applied formulation contains Tizanidine HCl…2mg along with submission of revised Form 5, master formulation and requisite fee.	
	Firm submit the revised formulation in line with reference product i.e. Tizanidine as HCl…2mg along with submission of revised Form 5, master formulation and requisite fee(fee of Rs.7,500/- submitted vide challan no. 2967386323 dated 15-10-2021).	
	Decision: Approved. Firm will deposit Rs.30,000/- for revision of applied formulation in line with reference product.	
305.	Name and address of manufacturer / Applicant	M/s. Maple Pharmaceuticals (Pvt.) Ltd., 147/23, Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form+ Strength	Skelet tablets 4mg
	Diary No. Date of R& I & fee	(Duplicate Dossier) dy.no. Rs. 8,000/-(Photocopy) dated 23-2-2011 Differential fee (Yellow slip) Rs. 12,000/- submitted on 21-10-2015 Receipt of application has verified from R&I
	Composition	Each tablet contains: Tizanidine Hydrochloride.....4mg

	Pharmacological Group	Skeletal muscle relaxant
	Type of Form	Form 5
	Finished Product Specification	USP
	Pack Size & Demanded Price	10's/ As per PAC/PRC
	Approval Status of Product in Reference Regulatory Authorities	USFDA approved as uncoated tablets
	Me-too Status	Musidin 4mg Tablet by M/s Martin Dow
	GMP Status	Grant of GMP certificate based on inspection conducted on 20-12-2019 concluded with the remarks of Good compliance
	Remarks of the Evaluator.	▪ Firm revised the master formulation and remove the overage. ▪ Revision of applied composition as in reference regulatory authorities the approved drug is "Tizanidine as HCl", while the applied drug is "Tizanidine HCl". ▪ The official monograph for the applied formulation is available in USP.
	Decision of M-308: Deferred the case for revision of formulation as the reference product contains Tizanidine as HCl…4mg while the applied formulation contains Tizanidine HCl…4mg along with submission of revised Form 5, master formulation and requisite fee.	
	Firm submit the revised formulation in line with reference product i.e. Tizanidine as HCl…4mg along with submission of revised Form 5, master formulation and requisite fee(fee of Rs.7,500/- submitted vide challan no. 2638920487 dated 15-10-2021).	
	Decision: Approved. Firm will deposit Rs.30,000/- for revision of applied formulation in line with reference product.	

Item No. VI: Agenda of Evaluator-V (Mst. Iqra Aftab)

Case No. 01: Registration applications of Local Cases.
Deferred Cases

306.	Name and address of manufacturer / Applicant	"M/s Friends Pharma Pvt Ltd. 31-km, Ferozepur Road, Lahore, Pakistan"
	Brand Name +Dosage Form + Strength	Ketafend Injection 500mg
	Composition	"Each 10ml Contains: Ketamine HCl Eq To Ketamine…500mg
	Diary No. Date of R& I & fee	Dy.No 13121 dated 06-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	General anaesthetics
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per SRO, Glass ampoule 10ml.
	Approval status of product in Reference Regulatory Authorities.	USFDA approved in Vial .
	Me-too status	Ketarol of Global

	GMP status	GMP inspection 08-03-2019 General Liquid section (Vial and Ampoule)
	Remarks of the Evaluator V	• Revision of master formulation as per innovator is required i.e. "50 mg ketamine base (equivalent to 57.67 mg ketamine hydrochloride" along with submission of requisite fee. • Availability of applied product in ampoule. **Evaluation** • Initially, the firm has applied for ampoule now the firm has changed the container closure system to vial without submitting relevant documents as per Form 5. • Evidence of SVP couldn't be confirmed from section letter and panel inspection report. • Firm has corrected the master formulation with submission of Rs 7500/- dated 17-03-2022.

Decision of 320th Meeting: Deferred for the following reasons:

- Submission of evidence of approval of SVP section by the Central Licensing Board or panel inspection report for renewal of DML verifying the section.
- Firm shall submit the full fee of Rs. 30,000/- for correction/pre-approval change in composition (correction of salt form of the drug substance) and change of container closure system, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

Submission of evidence of approval of SVP section by the Central Licensing Board or panel inspection report for renewal of DML verifying the section.	
Firm shall submit the full fee of Rs. 30,000/- for correction/pre-approval change in composition (correction of salt form of the drug substance) and change of container closure system, as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	Firm has submitted the full fee Rs. 30,000/- dated 03-11-2022.

Decision of 322nd meeting: Approved.

30	Name and address of manufacturer / Applicant	"M/s Max Pharmaceuticals,Plot # 12, St. No. N-7, National Industrial Zone, Rawat, Islamabad"
	Brand Name +Dosage Form + Strength	Maxibest Capsules 500mg
	Composition	"Each Capsule Contains: Azithromycin…500mg"
	Diary No. Date of R& I & fee	Dy.No 41724 dated 07-12-2018 Rs.20,000/- 06-12-2018
	Pharmacological Group	Macrolides ATC Code: J01FA10
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	1x10's, As per PRC.
	Approval status of product in Reference Regulatory Authorities.	Could not be confirmed.
	Me-too status	071422; Brand Name: Azithromycin 500mg Capsules Manufacturer Name: Unipharma (Pvt) Ltd.,

	GMP status	26-06-2019 Conclusion: The company is working at good level of GMP and record of raw material was found maintained along with SOP's the clearance of API's for imported sources are attached as of today. GMP is a continuous process of up gradation, the firm the advise to continue with up gradation and purchase the desired equipments are advised.
	Remarks of the Evaluator	Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/ approved by the Registration Board in its 275th meeting.
	Decision of 295th Meeting: Deferred for evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.	
	Firm's reply: Firm has revised their formulation from Azithromycin Capsule to Azithromycin Tablet.	
	Name and address of manufacturer / Applicant	"M/s Max Pharmaceuticals,Plot # 12, St. No. N-7, National Industrial Zone, Rawat, Islamabad"
	Brand Name +Dosage Form + Strength	Maxibest Tablet 500mg
	Composition	"Each film coated tablet contains: Azithromycin…500mg"
	Diary No. Date of R& I & fee	Dy.No 30822 dated 31-10-2022 Rs.30,000/- 31-10-2022
	Pharmacological Group	Macrolides ATC Code: J01FA10
	Type of Form	Form 5
	Finished product Specification	USP
	Pack size & Demanded Price	As per PRC.
	Approval status of product in Reference Regulatory Authorities.	TGA Approved.
	Me-too status	Registration Number: 067514 Zezot Tablet by M/s Bosch
	GMP status	26-06-2019 Conclusion: The company is working at good level of GMP and record of raw material was found maintained along with SOP's the clearance of API's for imported sources are attached as of today. GMP is a continuous process of up gradation, the firm the advise to continue with up gradation and purchase the desired equipments are advised.
	Remarks of the Evaluator	
	Decision: Approved.	

Case No. 02: Registration applications of CTD Cases.

New Cases

308.	Name, address of Applicant / Marketing Authorization Holder	M/s Genix Pharma (pvt.) Ltd. 44-45B Korangi creek road, Karachi.
	Name, address of Manufacturing site.	M/s Genix Pharma (pvt.) Ltd. 44-45B Korangi creek road, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 9894 dated 30/04/2021
	Details of fee submitted	PKR 50,000/-: dated 30/11/2020
	The proposed proprietary name / brand name	Carlep 200mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Eslicarbazepine acetate……200mg
	Pharmaceutical form of applied drug	Oblong, White colored, biconvex core tablet plain from both sides
	Pharmacotherapeutic Group of (API)	Anti-epileptic
	Reference to Finished product specifications	Inhouse Specification
	Proposed Pack size	10's, 20's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	APTIOM tablets 200mg by Sunovion Pharmaceuticals Inc. USFDA Approved.
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	**GMP inspection : 28/10/2019** Tablet (General & Psychotropic) section approved.
	Name and address of API manufacturer.	Ami Lifesciences Pr,t. Limited Plot No. 8218, ECP channel Road At & post Karakhadi, Dist. Vadodara -391 450 State Gujarat, INDIA Phone: +9 | -2662-27 3 40 | I 27 33 12 Fax: * 9l-2662-273401
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and

		its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Batches: (ECA/50030515, ECA/50040515, ECA/50050515) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (ECA/50020111, ECA/50030111 ECA/50040111)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Aptiom 200mg tablet by Sunovion Pharmaceuticals Inc.by performing quality tests (Appearance, Identification, DT ,Assay, Dissolution). CDP has been performed against the same brand that is Aptiom 200mg tablet by Sunovion Pharmaceuticals Inc in 0.1N HCL, Acetate buffer 4.5 and Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity & Range, robustness, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Ami Lifesciences Pr,t. Limited Plot No. 8218, ECP channel Road At & post Karakhadi, Dist. Vadodara -391 450 State Gujarat, INDIA		
API Lot No.	ECA/50010117		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (10's, 20's & 30's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 1,2,3,4 & 6 (months) Real Time: 0, 3, 6 (Months)		
Batch No.	19SB-159-01	19SB-160-02	19SB-161-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	08-2019	08-2019	08-2019
Date of Initiation	08-2021	08-2021	08-2021

No. of Batches		03
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	A Panel Inspection for the verification of authenticity of Stability Data of product on Form-5D "Wymly Tablet 25mg" for Tablet Section has been conducted on 06 April, 2018. Inspection Report included in the 281th DRB meeting held on 11-13th April, 2018.. The firm has 21CFR compliant system and adequate monitoring and control for stability chamber.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 19041306 issued by FOOD AND DRUG CONTROL ADMINISTRATION valid till 24/04/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Form 6 Dated:27/04/2017 is submitted, wherein the permission to import API Eslicarbazepine acetate for the purpose of test/analysis and stability studies is granted. • Invoice No & Date: EXP/A/007/2017-18 dated 13/04/2017. • Batch No:ECA/50010117
4.	Data of stability batches will be supported by attested respective documents like chromatograms,Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S. No	Sections	Observations/Deficiencies/ Short-comings	Reply
1.	1.3.5.	Evidence of approval of relevant section from Licensing Authority is required as you have provided approval of master layout plan.	Firm has provided grant of additional/revised section Tablet (General) – Revised letter dated 30 Sep 2021.
2.	2.3.S.6	The container closure system mentions material of construction as food grade quality material ,clarification is required.	Firm has used food grade LDPE as primary packing material for drug substance.
3.	2.3.P.2.2.1	Provide Summary of the results of comparative dissolution profile.	The summary of CDP is of Carlep 400mg.
4.	2.3.P.3.2	Provide List of all components of the Drug	First trail batch of 1000 tablets were manufactured and parameters found unsatisfactory.

		Product to be used in the manufacturing process and their amounts per proposed commercial batch as provided data is of Trial batch. Moreover, the batch size mentioned in this section is 1000 tablets and BMR mentions batch size of 1500 Tablets. The quantity of individual components per tablet mentioned in Trail batch formula is different than stability batch formula.	In order to obtain best and optimized product formulation was designed with change in quantitative composition that is Trail 2 in which all physical and chemical parameters were found satisfactory. As per CTD guidelines three stability batch sizes 1500 Tablet as mentioned in BMR with same formulation were manufactured as that of passed trail 2.
5.	2.3.P.5.6	Provide justification of specifications for all the tests specified in section 2.3.P.5.1.	Justification for specification not provided only inhouse has been mentioned.
6.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	BMR has not been signed.
7.	3.2.S.4.4	A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer like residual solvents.	**Firms Response** We follow suppliers COA for residual solvents.
8.	3.2.P.3.3	The maximum holding time for bulk product prior to final packaging shall be stated.	Firm has submitted the SOP for withholding time.
9.	3.2.P.5.1	The innovator proposes two point dissolution according to chemistry review.	**Firms Response** We have set our specification single point in 15 minutes.
10.	3.2.P.5.2	Dissolution testing conducted by test 1 or test 2 of USP monograph by Drug product manufacturer.	**Firms Response** USP Type II Paddle apparatus are used.
11.	3.2.P.8.3	The formulation was previously applied on Form 5 D which was rejected in 289th meeting wherein 7kg API was imported vide invoice dated 27-04-2017 and 3kg vide invoice dated 24-02-2017 for manufacturing of trial batches of Carlep 200mg, 400mg and 800mg.	**Firms Response** **Provided at the end of 800mg strength.**

		Approximately, 6.4 kg was consumed in manufacturing of trial batches. Now, you have applied same formulation on Form 5 F wherein the submitted commercial invoice is same dated 27-04-2017. Please justify/clarify the quantity of API in manufacturing of current trial batches of **Carlep 200mg, 400mg and 800mg** applied on Form-5F.	

309.	Name, address of Applicant / Marketing Authorization Holder	M/s Genix Pharma (pvt.) Ltd. 44-45B Korangi creek road, Karachi.
	Name, address of Manufacturing site.	M/s Genix Pharma (pvt.) Ltd. 44-45B Korangi creek road, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 9893 dated 30/03/2021
	Details of fee submitted	PKR 50,000/-: dated 30/11/2021
	The proposed proprietary name / brand name	Carlep 400mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Eslicarbazepine acetate……400mg
	Pharmaceutical form of applied drug	Oblong shape, white color, biconvex tablet, engraved 'GENIX" on one side and plain on other side.
	Pharmacotherapeutic Group of (API)	Anti-epileptic
	Reference to Finished product specifications	Inhouse Specification
	Proposed Pack size	10's, 20's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	APTIOM tablets 400mg by Sunovion Pharmaceuticals Inc. USFDA Approved.
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	GMP granted on 28/10/2019 Tablet (General & Psychotropic) section approved.

	Name and address of API manufacturer.	Ami Lifesciences Pr,t. Limited Plot No. 8218, ECP channel Road At & post Karakhadi, Dist. Vadodara -391 450 State Gujarat, INDIA Phone: +9 | -2662-27 3 40 | I 27 33 12 Fax: * 9l-2662-273401
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 72 months Batches: (ECA/50030515, ECA/50040515, ECA/50050515) Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (ECA/50020111, ECA/50030111 ECA/50040111)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Aptiom 400mg tablet by Sunovion Pharmaceuticals Inc.by performing quality tests (Appearance, Identification, DT ,Assay, Dissolution). CDP has been performed against the same brand that is Aptiom 200mg tablet by Sunovion Pharmaceuticals Inc in 0.1N HCL, Acetate buffer 4.5 and Buffer (pH 6.8). The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity & Range, robustness, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Ami Lifesciences Pr,t. Limited Plot No. 8218, ECP channel Road At & post Karakhadi, Dist. Vadodara -391 450 State Gujarat, INDIA		
API Lot No.	ECA/50010117		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (10's, 20's & 30's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 1,2,3,4 & 6 (months) Real Time: 0, 3, 6 (Months)		
Batch No.	19SB-162-01	19SB-163-02	19SB-164-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	08-2019	08-2019	08-2019
Date of Initiation	10-09-2019	10-09-2019	10-09-2019
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	A Panel Inspection for the verification of authenticity of Stability Data of product on Form-5D "Wymly Tablet 25mg" for Tablet Section has been conducted on 06 April, 2018. Inspection Report included in the 281th DRB meeting held on 11-13th April, 2018.. The firm has 21CFR compliant system and adequate monitoring and control for stability chamber.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 19041306 issued by FOOD AND DRUG CONTROL ADMINISTRATION valid till 24/04/2022
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Form 6 Dated:27/04/2017 is submitted, wherein the permission to import API Eslicarbazepine acetate for the purpose of test/analysis and stability studies is granted. • Invoice No & Date: EXP/A/007/2017-18 dated 13/04/2017.
4.	Data of stability batches will be supported by attested respective documents like chromatograms,Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of	Submitted

	stability chambers (real time and accelerated)		
Remarks OF Evaluator:			
S. No	Sections	Observations/Deficiencies/ Short-comings	Reply
1.	1.3.5.	Evidence of approval of relevant section from Licensing Authority is required as you have provided approval of master layout plan.	Firm has provided grant of additional/revised section Tablet (General) – Revised letter dated 30 Sep 2021.
2.	2.3.S.6	The container closure system mentions material of construction as food grade quality material ,clarification is required.	Firm has used food grade LDPE as primary packing material for drug substance.
3.	2.3.P.3.2	Provide List of all components of the Drug Product to be used in the manufacturing process and their amounts per proposed commercial batch as provided data is of Trial batch. Moreover, the batch size mentioned in this section is 1000 tablets and BMR mentions batch size of 1500 Tablets. The quantity of individual components per tablet mentioned in Trail batch formula is different than stability batch formula.	First trail batch of 1000 tablets were manufactured and parameters found unsatisfactory . In order to obtain best and optimized product formulation was designed with change in quantitative composition that is Trail 2 in which all physical and chemical parameters were found satisfactory. As per CTD guidelines three stability batch sizes 1500 Tablet as mentioned in BMR with same formulation were manufactured as that of passed trail 2.
4.	2.3.P.5.6	Provide justification of specifications for all the tests specified in section 2.3.P.5.1.	Justification for specification not provided only inhouse has been mentioned.
5.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	BMR has not been signed.
6.	3.2.S.4.4	A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer like residual solvents.	Firms Response We follow suppliers COA for residual solvents.
7.	3.2.P.3.3	The maximum holding time for bulk product prior to final packaging shall be stated.	Firm has submitted the SOP for withholding time.
8.	3.2.P.5.1	The innovator proposes two point dissolution according to chemistry review.	Firms Response We have set our specification single point in 15 minutes.

9.	3.2.P.5.2	Dissolution testing conducted by test 1 or test 2 of USP monograph by Drug product manufacturer.	USP Type II Paddle apparatus are used.
10.	3.2.P.8.3	The formulation was previously applied on Form 5 D which was rejected in 289th meeting wherein 7kg API was imported vide invoice dated 27-04-2017 and 3kg vide invoice dated 24-02-2017 for manufacturing of trial batches of Carlep 200mg, 400mg and 800mg. Approximately, 6.4 kg was consumed in manufacturing of trial batches. Now, you have applied same formulation on Form 5 F wherein the submitted commercial invoice is same dated 27-04-2017. Please justify/clarify the quantity of API in manufacturing of current trial batches of **Carlep 200mg, 400mg and 800mg** applied on Form-5F.	**Firms Response** **Provided at the end of 800mg strength.**

310.	Name, address of Applicant / Marketing Authorization Holder	M/s Genix Pharma (pvt.) Ltd. 44-45B Korangi creek road, Karachi.
	Name, address of Manufacturing site.	M/s Genix Pharma (pvt.) Ltd. 44-45B Korangi creek road, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.9895 dated 30/03/2021
	Details of fee submitted	PKR 50,000/-: dated 30/11/2021
	The proposed proprietary name / brand name	Carlep 800mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Eslicarbazepine acetate……800mg

	Pharmaceutical form of applied drug	Oblong shape, white color, biconvex tablet, engraved 'GENIX" on one side and break line on other side.
	Pharmacotherapeutic Group of (API)	Anti-epileptic
	Reference to Finished product specifications	Inhouse Specification
	Proposed Pack size	10's, 20's & 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	APTIOM tablets 800mg by Sunovion Pharmaceuticals Inc. USFDA Approved.
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	GMP granted on 28/10/2019 Tablet (General & Psychotropic) section approved.
	Name and address of API manufacturer.	Ami Lifesciences Pr,t. Limited Plot No. 8218, ECP channel Road At & post Karakhadi, Dist. Vadodara -391 450 State Gujarat, INDIA Phone: +9 | -2662-27 3 40 | I 27 33 12 Fax: * 9l-2662-273401
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Batches: (ECA/50030515, ECA/50040515, ECA/50050515) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (ECA/50020111, ECA/50030111 ECA/50040111)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence	Pharmaceutical Equivalence have been established against the

	and comparative dissolution profile	brand leader that is Aptiom 800mg tablet by Sunovion Pharmaceuticals Inc.by performing quality tests (Appearance, Identification, DT ,Assay, Dissolution). CDP has been performed against the same brand that is Aptiom 200mg tablet by Sunovion Pharmaceuticals Inc in 0.1N HCL, Acetate buffer 4.5 and Buffer (pH 6.8). The values for f2 are in the acceptable range.		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity & Range, robustness, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		Ami Lifesciences Pr,t. Limited Plot No. 8218, ECP channel Road At & post Karakhadi, Dist. Vadodara -391 450 State Gujarat, INDIA		
API Lot No.		ECA/50010117		
Description of Pack (Container closure system)		Alu-Alu blister packed in unit carton (10's, 20's & 30's)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 1,2,3,4 & 6 (months) Real Time: 0, 3, 6 (Months)		
Batch No.		19SB-165-01	19SB-166-02	19SB-167-03
Batch Size		1500 tab	1500 tab	1500 tab
Manufacturing Date		08-2019	08-2019	08-2019
Date of Initiation		10-09-2019	10-09-2019	10-09-2019
No. of Batches		03		
Administrative Portion				
7.	Reference of previous approval of applications with stability study data of the firm (if any)	A Panel Inspection for the verification of authenticity of Stability Data of product on Form-5D "Wymly Tablet 25mg" for Tablet Section has been conducted on 06 April, 2018. Inspection Report included in the 281th DRB meeting held on 11-13th April, 2018.. The firm has 21CFR compliant system and adequate monitoring and control for stability chamber.		
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 19041306 issued by FOOD AND DRUG CONTROL ADMINISTRATION valid till 24/04/2022		
9.	Documents for the procurement of API with approval from DRAP (in case of import).	• Form 6 Dated:27/04/2017 is submitted, wherein the permission to import API Eslicarbazepine acetate for the purpose of test/analysis and stability studies is granted.		

		• Invoice No & Date: EXP/A/007/2017-18 dated 13/04/2017.	
10.	Data of stability batches will be supported by attested respective documents like chromatograms,Raw data sheets, COA, summary data sheets etc.	Submitted	
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted	
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted	
Remarks of Evaluator:			
S. No	Sections	Observations/Deficiencies/ Short-comings	Reply
1.	1.3.5.	Evidence of approval of relevant section from Licensing Authority is required as you have provided approval of master layout plan.	Firm has provided grant of additional/revised section Tablet (General) – Revised letter dated 30 Sep 2021.
2.	2.3.S.6	The container closure system mentions material of construction as food grade quality material ,clarification is required.	Firm has used food grade LDPE as primary packing material for drug substance.
3.	2.3.P.3.2	Provide List of all components of the Drug Product to be used in the manufacturing process and their amounts per proposed commercial batch as provided data is of Trial batch. Moreover, the batch size mentioned in this section is 1000 tablets and BMR mentions batch size of 1500 Tablets. The quantity of individual components per tablet mentioned in Trail batch formula is different than stability batch formula.	First trail batch of 1000 tablets were manufactured and parameters found unsatisfactory . In order to obtain best and optimized product formulation was designed with change in quantitative composition that is Trail 2 in which all physical and chemical parameters were found satisfactory. As per CTD guidelines three stability batch sizes 1500 Tablet as mentioned in BMR

			with same formulation were manufactured as that of passed trail 2.
4.	2.3.P.5.6	Provide justification of specifications for all the tests specified in section 2.3.P.5.1.	Justification for specification not provided only inhouse has been mentioned.
5.	2.3.R.1.2	Provide blank master production document / batch manufacturing record to be used during the commercial manufacturing of the applied product.	BMR has not been signed.
6.	3.2.S.4.4	A discussion and justification shall be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer like residual solvents.	Firms Response We follow suppliers COA for residual solvents.
7.	3.2.P.3.3	The maximum holding time for bulk product prior to final packaging shall be stated.	Firm has submitted the SOP for withholding time.
8.	3.2.P.5.1	The innovator proposes two point dissolution according to chemistry review.	Firms Response We have set our specification single point in 15 minutes.
9.	3.2.P.5.2	Dissolution testing conducted by test 1 or test 2 of USP monograph by Drug product manufacturer.	USP Type II Paddle apparatus are used.
10.	3.2.P.8.3	The formulation was previously applied on Form 5 D which was rejected in 289th meeting wherein 7kg API was imported vide invoice dated 27-04-2017 and 3kg vide invoice dated 24-02-2017 for manufacturing of trial batches of Carlep 200mg, 400mg and 800mg. Approximately, 6.4 kg was consumed in manufacturing of trial batches. Now, you have applied same formulation on Form 5 F wherein the submitted commercial invoice is same dated 27-04-2017. Please justify/clarify the quantity of API in manufacturing of current trial batches of **Carlep 200mg, 400mg and 800mg** applied on Form-5F.	

Carlep Tablets Range		
Eslicarbazepine Acetate		
API Consumption for Trial Batches		
API	Eslicarbazepine Acetate	
RM #	1912	
Potency	99.20 %	
Quantity Received	03 kg	
Carlep Tablets 200mg		
Potency Adjustment	Potency of Eslicarbazepine Acetate = 99.2 % Required Quantity = Standard Qty. x 100 / Potency = 200mg x 100/99.2 =201.6 mg/Tab	
Trail Batch	Trail Batch 01	Trail Batch 02
	1000 Tablets	1000 Tablets

	201.6 mg x 1000 Tablets = 201.6 g	201.6 mg x 1000 Tablets = 201.6 g
	Total = 201.6 g + 201.6 g = 403.2 g	
Carlep Tablets 400mg		
Potency Adjustment	Potency of Eslicarbazepine Acetate = 99.2 % Required Quantity = Standard Qty. x 100 / Potency = 400mg x 100/99.2 =403.2 mg/Tab	
Trail Batch	Trail Batch 01	Trail Batch 02
	1000 Tablets 403.2 mg x 1000 Tablets = 403.2 g	1000 Tablets 403.2 mg x 1000 Tablets = 403.2 g
	Total = 403.2 g + 403.2 g = 806.4 g	
Carlep Tablets 800mg		
Potency Adjustment	Potency of Eslicarbazepine Acetate = 99.2 % Required Quantity = Standard Qty. x 100 / Potency = 800mg x 100/99.2 =806.4 mg/Tab	
Trail Batch	Trail Batch 01	Trail Batch 02
	1000 Tablets 806.4 mg x 1000 Tablets = 806.4 g	1000 Tablets 806.4 mg x 1000 Tablets = 806.4 g
	Total = 806.4 g + 806.4 g = 1612.8 g	

Quantity used in trial batches = 403.2 g + 806.4 g + 1612.8 g = **2.8224 kg**
Quantity used in testing = 10.0 g
Total = 2.8324 kg

Carlep Tablets Range			
Eslicarbazepine Acetate			
API Consumption for Stability Batches			
API	Eslicarbazepine Acetate		
RM #	2108		
Potency	99.00 %		
Quantity Received	07 kg		
Carlep Tablets 200mg			
Potency Adjustment	Potency of Eslicarbazepine Acetate = 99.0 % Required Quantity = Standard Qty. x 100 / Potency = 200mg x 100/99.0 = 202 mg/Tab		
Stability Batch	Stability Batch 01	Stability Batch 02	Stability Batch 03
	1500 Tablets 202mg x 1500 Tablets = 303.0 g	1500 Tablets 202mg x 1500 Tablets = 303.0 g	1500 Tablets 202mg x 1500 Tablets = 303.0 g
	Total = 303.0 g + 303.0 g + 303.0 g = 909.0 g		
Carlep Tablets 400mg			
Potency Adjustment	Potency of Eslicarbazepine Acetate = 99.0 % Required Quantity = Standard Qty. x 100 / Potency		

	= 400mg x 100/99.0 = 404 mg/Tab		
Stability Batch	Stability Batch 01	Stability Batch 02	Stability Batch 03
	1500 Tablets 404 mg x 1500 Tablets = 606.0 g	1500 Tablets 404 mg x 1500 Tablets = 606.0 g	1500 Tablets 404 mg x 1500 Tablets = 606.0 g
	Total = 606.0 g + 606.0 g + 606.0 g = 1818.0 g		
Carlep Tablets 800mg			
Potency Adjustment	Potency of Eslicarbazepine Acetate = 99.0 % Required Quantity = Standard Qty. x 100 / Potency = 800mg x 100/99.0 = 808 mg/Tab		
Stability Batch	Stability Batch 01	Stability Batch 02	Stability Batch 03
	1500 Tablets 808mg x 1500 Tablets = 1212.0 g	1500 Tablets 808mg x 1500 Tablets = 1212.0 g	1500 Tablets 808mg x 1500 Tablets = 1212.0 g
	Total = 1212.0 g + 1212.0 g + 1212.0 g = 3636.0 g		
Quantity used in Stability batches = 909.0 g + 1818.0 g + 3636.0 g **= 6.363 kg** **Quantity used in testing = 10.0 g** **Total = 6.373 kg**			
Total consumption of API			
Trial Batches of Carlep Tablets Range + Q.C. Testing		**RM # 1912**	**2.8324 kg**
Stability Batches of Carlep Tablets Range + Q.C. Testing		**RM # 2108**	**6.373 kg**

Also note that:
Formulation applied on form 5-D in which all results meet as per pre-defined specifications and no out of trends results were found. Furthermore, all physical and chemical parameters found satisfactory. Therefore, same formulation applied on form 5-F.

Evaluation by PEC
The firm has changed the batch size and number of batches for product applied in M-289 to justify the quantity of API.

	Minutes 289 meeting Form 5 D			Firms Response		
Strength	Carlep Tablet 200mg	Carlep Tablet 400mg	Carlep Tablet 800mg	Carlep Tablet 200mg	Carlep Tablet 400mg	Carlep Tablet 800mg
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets	1000 Tablets	1000 Tablets	1000 Tablets
Batch No.	TR001	TR001	TR001	TR001	TR001	TR001
	TR002	TR002	TR002	TR002	TR002	TR002
	TR003	TR003	TR003			

Well along the firm further submitted on 30-12-2021.
"We request Evaluation cell to consider our product Carlep Tablet Range in Registration Board once we submit additional data of the product in support of already submitted data to registration board."
Evaluation by PEC

	Since 30-12-2021 firm has not submitted any additional data in order to support already submitted data .The Registration Board may decide accordingly.	
Decision of 322nd meeting: Deferred for the reconciliation record of the quantity drug substance imported against the quantity required for the manufacturing of stability batches of each strength.		
311.	Name, address of Applicant / Marketing Authorization Holder	M/s Reliance Pharma Plot # 8, Street No. S-8, RCCI, Industrial Estate, Rawat Islamabad-Pakistan
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt) Ltd Plot # 22-23, Industrial Triangle, Kahuta Road, Islamabad"
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10339 dated 22/04/2022
	Details of fee submitted	PKR 75,000/-: dated 30/03/2022
	The proposed proprietary name / brand name	Relimol Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 100ml Contains: Paracetamol …1000mg
	Pharmaceutical form of applied drug	Clear and colorless liquid filled in clear and colorless glass vials.
	Pharmacotherapeutic Group of (API)	Analgesics and antipyretics
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	1 glassVial (100ml)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Acetaminophen 1g/100ml Infusion by Baxter Healthcare Coporation (United states), FDA Approved.
	For generic drugs (me-too status)	Provas Infusion by Sami Pharmaceuticals (Pvt) Ltd. Reg No: 053223
	GMP status of the Finished product manufacturer	GMP certificate valid till 10/02/2022 New license Applied on 22/12/2021.
	Name and address of API manufacturer.	M/s HEBEI JIHENG PHARMACEUTICAL CO., LTD. No.1 Weiwu Street Industrial Park Hengshui City, Hebei Province, 053000 China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time 60months : 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated 6 months: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (011608001, 011608002 & 011608003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (Liquid particle count) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the reference product OFIRMEV Infusion by Mallinckrodt Pharmaceuticals. Batch No 1019689 by performing quality tests (Physical appearance, pH, Liquid Particle count, Percent assay). CDP is not applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**M/s HEBEI JIHENG PHARMACEUTICAL CO., LTD.** No.1 Weiwu Street Industrial Park Hengshui City, Hebei Province, 053000 China.		
API Lot No.	011803173		
Description of Pack (Container closure system)	Clear glass vial		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 36 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 & 36 (Months)		
Batch No.	0718801	0718802	0718803
Batch Size	5000 Vials	5000 Vials	5000 Vials
Manufacturing Date	07-2018	07-2018	07-2018

Date of Initiation	07-08-2018	15-08-2018	13-09-2018
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

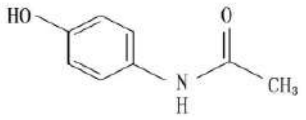
The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of drug production license certificate No. JI20150076 issued by Hebei Drug Administration valid till 30/08/2025 has been submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of clearance certificate dated 31-05-2018 is submitted .
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

REMARKS OF EVALUATOR

Sr. No.	Section	Observations/ Deficiencies	Response submitted by Firm and Evaluation
1	1.4.3	• Provide notarized copy of contract manufacturing agreement • Provide documents confirming number of approved sections of the applicant (DML holder) • Provide details of already registered drug products of contact giver on contract manufacturing,	• Notarized copy of Contact manufacturing agreement. Copy of agreement • Section approval letter of Applicant (DML holder) 4 sections • List of already registered drug products of contact giver on contract manufacturing. 6 Products

2	2.3.S.3.1	• Submit conclusion from the list of studies performed (e.g IR, UV, NMR, MS, Elemental analysis.)	• Based on the analysis of the Paracetamol samples produced in Hebei Jiheng Pharmaceutical Co. Ltd. , and with the comparison to results of the Paracetamol EP CRS (Batch No.: 4.1), we confirm that Paracetamol sample matches the chemical structure below,  which is defined as the structure of Paracetamol in EUR. Ph. 8. The crystal form of the product is identical with EP CRS Lot 4.1. the summary is provided in **ANNEXURE 2.**
3	2.3.S.4.4	• Submit discussion and justification for any incomplete analysis of the drug substance/API by drug product manufacturer. • The COA of API of DP manufacturer mentions reference of API manufacturer both USP and BP.	• Complete testing is performed and revised COA is attached in **ANNEXURE 3** Evaluation The COA mentions supplier/manufacturer as M/s Global pharmaceuticals. • We use <u>BP specification</u> as reference for testing; USP was only referred for verification purpose.
4	2.3.P.1	• The quantity of API per unit is 1020mg per 100ml whereas the applied strength is 1000mg/100ml. clarification is required with respect to composition of FPP.	• As per Standard for fill volume we go for the upper limit therefore the fill volume of paracetamol infusion is 102ml for which we use 1020mg of paracetamol API. Evaluation Submit scientific rationale for batch formula. The BMR mentions the Quantity of API 1000mg/100ml. Potency adjustment has not been done.
5	2.3.P.2.2.1	The pharmaceutical equivalence studies of applied formulation is with Orfimex 100ml infusion whose marketing status is discontinued as per USFDA database.	As we have already approved paracetamol infusion Brand Name: ACETAMOL 100ml INFUSION- manufacturer Vision Pharmaceuticals Pvt. Ltd. We will submit pharmaceutical equivalence with Brand leader as soon as possible.
6	2.3.P.5.1	The specification of drug Product does not include the test of osmolality which has been both determined by innovator and generic product the pH	We have now included the test for osmolality in our standard analytical procedures.

		of both generic and innovator product is between 5 – 7 whereas your claimed specification are pH 4 – 7.	The revised standard analytical procedure and COA is attached in **ANNEXURE 4**
7	2.3.P.5.6	Provide justification of specification of all the tests specified in section 2.3.P.5.1	Specification of product is as per Innovator specs.
8	3.2.S.4.2	Detailed analytical procedures for testing of drug substance shall be provided by the drug product manufacturer for API.	A detailed analytical procedure for testing of drug substance by the drug product manufacturer for API has been provided.
9	3.2.S.4.3	Analytical method verification studies including specificity, Accuracy and repeatability (method precision) performed by the drug product manufacturer shall be submitted for API.	Analytical method verification studies including specificity, Accuracy and repeatability (method precision) performed by the drug product manufacturer for API has been provided.
10.	3.2.S.4.4	A discussion and justification shall be provided for any incomplete analysis of the drug substance/ API by drug product manufacturer.	• Complete testing is performed and revised COA has been submitted. • We use BP specification as reference for testing; USP was only referred for verification purpose.

Decision of 320th Meeting: Deferred for;

- Justification for not performing pharmaceutical equivalence against the reference / innovator's product.
- Clarification regarding the specification of drug Product does not include the test of osmolality which has been both determined by innovator and generic product the pH of both generic and innovator product is between 5 – 7 whereas your claimed specification are pH 4 – 7.
- Clarification since potency adjustment has not been made.
- Submission scientific rationale for submitted batch formula.

Evaluation by PEC:

Decision	**Firms Response**
Justification for not performing pharmaceutical equivalence against the reference / innovator's product.	Firm has now performed pharmaceutical equivalence with Bofalgan Infusion 100ml.
Clarification regarding the specification of drug Product does not include the test of osmolality which has been both determined by innovator and generic product the pH of both generic and innovator product is between 5 – 7 whereas your claimed specification are pH 4 – 7.	Firm has updated the standard testing method by including the test of osmolality and also revised pH specifications.
Clarification since potency adjustment has not been made.	In fact, we are adjusting the potency but in current formulation already sent the potency of material 100%.
Submission scientific rationale for submitted batch formula.	We are calculating the active material as per 102ml , because USP recommends excess volume of 2 % for 100ml solution.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of analysis of stability batches as per revised limits of pH test.**

Item No. VII: Agenda of Evaluator-XVI (Mr. Akbar Ali)

Case No 1 : **Export Facilitation (out of que) Cases : (Human, Local, Form-5F)**
M/s Indus Pharma (Pvt) Ltd ,Karachi
Assistant Director PR-I / EFD vide its letter No. F.1-6/2019-PR-I (EFD) dated 6th October 2022 informed that as per decision of 133rd meeting of DRAP Authority wherein it was decided to grant registration on priority basis to the pharmaceutical i.e. one molecule for each 100,000 USD worth of export of medicine (to a maximum of 15 such molecules) during a financial year.
In compliance to the above decision M/s Indus Pharma (Pvt) Ltd ,Karachi have achieved benchmark of more than 100,000 USD and submitted their applications for priority consideration including following applications

312.	Name, address of Applicant / Marketing Authorization Holder	M/s **Indus Pharma (Pvt.) Ltd. Plots No. 26-27 & 63-67, sector-27 Korangi Industrial Area, Karachi – 74900, Pakistan**
	Name, address of Manufacturing site.	M/s **Indus Pharma (Pvt.) Ltd. Plots No. 26-27 & 63-67, sector-27 Korangi Industrial Area, Karachi – 74900, Pakistan**
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.12634 dated 24/06/2022
	Details of fee submitted	PKR 30,000/= Slip No. 4658125907 dated 27/04/2022
	The proposed proprietary name / brand name	Razan 10mg tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan Fumarate …….10mg

	Pharmaceutical form of applied drug	light yellow, oval shape, film-coated tablet with "Indus" engraved on one side and other side is plain.
	Pharmacotherapeutic Group of (API)	potassium-competitive acid blockers
	Reference to Finished product specifications	As per Innovator Product
	Proposed Pack size	7's, 14's, 28's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab tablets 10mg by Takeda Pharmaceuticals. PMDA Japan
	For generic drugs (me-too status)	Vonozan Tablet by M/s Getz Pharma (Pvt.) Ltd, Reg. No. 108570
	GMP status of the Finished product manufacturer	GMP renewed on 24/12/2021 Valid till: 17/12/2023
	Name and address of API manufacturer.	M/s Jiangxi Synargy Pharmaceutical Co., Ltd. Jiangxi Fengxin Industrial Park, Fengxin, 330700,Jiangxi Provence P.R. Chaina.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity (Impurity VOPZ-ZBB, VOPZ-ZBC, VOPZ-SJJ) & related substances specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(2190801BD,2190802BD,2190803BD,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic

		and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Vonozan 10mg Tablets (005FF8) by Getz Pharma (Pvt.) Ltd by performing quality tests (Identification, Assay, Dissolution, Disintegration). CDP has been performed against the same brand that is Vonozan 10mg Tablets by Getz Pharma (Pvt.) Ltd Pharma in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including System Suitability, Precision, Specificity, linearity, range, accuracy, robustness.

STABILITY STUDY DATA

Manufacturer of API	M/s Jiangxi Synargy Pharmaceutical Co., Ltd. Jiangxi Fengxin Industrial Park, Fengxin, 330700,Jiangxi Provence P.R. Chaina.		
API Lot No.	20210801BD		
Description of Pack	Alu. Alu. Blister strips of 2x5 Tablets packed in a final printed carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6,9,12,18,24 (Months)		
Batch No.	TR-1/ VNZ 10mg TAB	TR-2/ VNZ 10mg TAB	TR-3/ VNZ 10mg TAB
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	11-2021	12-2021	12-2021
Date of Initiation	6-12-2021	22-12-2021	22-12-2021
No. of Batches	03		

Administrative Portion

27.	Reference of previous approval of applications with stability study data of the firm (if any)	Canazin tablet 300mg Minutes of 289th Meeting of Registration Board (14-16 May,2019)
28.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. GAN 20160125 issued by Jiangxi Provincial Medical Products Administration (Sealed) valid till 03/11/2025.

29.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.3041/2021/DRAP-AD-CD(I&E) dated 11/5/2022 is submitted wherein the permission to import Vonoprazan Fumarate for the purpose of test/analysis and stability studies is granted.
30.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
31.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
32.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. #	Section #	Observation	Firm's Response vide dairy No.301655 dated 24-10-2022.
1.	**1.5.2**	The provided label claim mentioning strength/concentration of API per unit: Each film coated tablet contains: Vonoprazan fumarate……10 mg, Whereas the innovator is Vonoprazan (as Fumarate) ……. 10 mg, Clarification and resubmission is needed	Please note that the label claim provided in section 1.5.2 contains typographical error, the correct one is ***Each film coated tablet contains: Vonoprazan (as Fumarate) … 10mg***
2.	**2.3.S.1.3**	• The physical description of API is provided as, "White to almost white powder", whereas the innovator product literature mentions as "white to almost white crystals or crystalline powder". Clarification is needs where the applied API is crystalline powder or amorphous powder and justification in case of amorphous powder. • Melting point test is not conducted whereas melting point of innovator product API is 194.8 degree Celsius. • Pka value is different from the innovator reverence product.	• The physical description of API "white to almost white powder" was derived from the manufacturer specification as the Vonoprazan fumarate is a non-compendial API, however we have examined the API and found it to be crystalline. Also, in the DMF XRD spectrum of Vonoprazan Fumarate has been attached for crystal analysis which clearly indicating that the substance is in crystalline form and crystallization step is mentioned at the last stage of manufacturing procedure of API. (Attached • Melting point test is not conducted by API supplier for Identification. Instead of Melting Point API supplier have conducted IR and HPLC test whose results can be

			found API COAs attached. • Pka value mentioned in the section was a typographical error i.e 9.06 instead of 9.6. • Corrected one is attached with this document (Attachment-II).
3.	**3.2.P.5.1**	The Finished product release specification for dissolution test is mentioned as not less than Q of labelled amount of Vonoprazan in 30 minutes , whereas the innovator product has dissolution parameter of achieving Q within 15 minutes , clarification is needed.	The Limit for dissolution Test for Finished product was not mentioned as not less than Q of labelled amount of Vonoprazan in 15 minutes due to unavailability of any published literature for dissolution parameters at the time of initial development of the product. However according to CDP studies (already submitted) our product also releases > 85% within 15 minutes throughout the range of pH 1.2, 4.5 & 6.8. We hereby, commit to change the dissolution parameter to achieving Q within 15 minutes at the time of commercialization of product
4.	**3.2.P.8.3**	The firm has provided stability data up to three months' timeline for both accelerated and real time stability data , The stability study data up to 6 months' timeline is required for both accelerated and real time stability study data.	The stability data up to 6 months for both accelerated and real time stability study data has been attached with this Document (Attachment-III).

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Registration letter shall be issued after submission of applicable fee for pre-registration variation ,i-e 30000/= as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction in label claim..**

313.	Name, address of Applicant / Marketing Authorization Holder	M/s **Indus Pharma (Pvt.) Ltd. Plots No. 26-27 & 63-67, sector-27 Korangi Industrial Area, Karachi – 74900, Pakistan**
	Name, address of Manufacturing site.	M/s **Indus Pharma (Pvt.) Ltd. Plots No. 26-27 & 63-67, sector-27 Korangi Industrial Area, Karachi – 74900, Pakistan**
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.12635 dated 24/06/2022
	Details of fee submitted	PKR 30,000/-:1138595321 dated 09/05/2022
	The proposed proprietary name / brand name	Razan 20mg tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan Fumarate …….20mg
	Pharmaceutical form of applied drug	light yellow, oval shape, film-coated tablet with "Indus" engraved on one side and other side is plain.
	Pharmacotherapeutic Group of (API)	potassium-competitive acid blockers
	Reference to Finished product specifications	As per Innovator Product
	Proposed Pack size	7's, 14's, 28's, 30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab tablets 20mg by Takeda Pharmaceuticals.
	For generic drugs (me-too status)	Vonozan Tablet by M/s Getz Pharma (Pvt.) Ltd, Reg. No. 108571
	GMP status of the Finished product manufacturer	GMP renewed on 24/12/2021 Valid till: 17/12/2023
	Name and address of API manufacturer.	M/s Jiangxi Synargy Pharmaceutical Co., Ltd. Jiangxi Fengxin Industrial Park, Fengxin, 330700,Jiangxi Provence P.R. Chaina
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity (Impurity VOPZ-ZBB, VOPZ-ZBC, VOPZ-SJJ) & related substances specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance

	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(2190801BD,2190802BD,2190803BD,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Vonozan 20mg Tablets (004FF9) by Getz Pharma (Pvt.) Ltd by performing quality tests (Identification, Assay, Dissolution, Disintegration). CDP has been performed against the same brand that is Vonozan 20mg Tablets by Getz Pharma (Pvt.) Ltd Pharma in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including System Suitability, Precision, Specificity, linearity, range, accuracy, robustness.

STABILITY STUDY DATA

Manufacturer of API	M/s Jiangxi Synargy Pharmaceutical Co., Ltd. Jiangxi Fengxin Industrial Park, Fengxin, 330700,Jiangxi Provence P.R. Chaina		
API Lot No.	20210801BD		
Description of Pack (Container closure system)	Alu. Alu. Blister strips of 2x5 Tablets packed in a final printed carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6,9,12,18,24 (Months)		
Batch No.	TR-1/ VNZ 20mg TAB	TR-2/ VNZ 20mg TAB	TR-3/ VNZ 20mg TAB
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	11-2021	12-2021	12-2021
Date of Initiation	6-12-2021	22-12-2021	22-12-2021

No. of Batches		03
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Canazin tablet 300mg Minutes of 289th Meeting of Registration Board (14-16 May,2019)
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. GAN 20160125 issued by Jiangxi Provincial Medical Products Administration (Sealed) valid till 03/11/2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.3041/2021/DRAP-AD-CD(I&E) dated 11/5/2022 is submitted wherein the permission to import Vonoprazan Fumarate for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. #	**Section #**	**Observation**	**Firm's Response vide Dairy No.30164 dated 24-10-2022**
5.	**1.5.2**	The provided label claim mentioning strength/concentration of API per unit: Each film coated tablet contains: Vonoprazan fumarate……20 mg, Whereas the innovator is Vonoprazan (as Fumarate) ……. 20 mg, Clarification and resubmission is needed .	Please note that the label claim provided in section 1.5.2 contains typographical error, the correct one is ***Each film coated tablet contains: Vonoprazan (as Fumarate) … 20mg***
6.	**2.3.S.1.3**	• The physical description of API is provided as, "White to almost white powder", whereas the innovator product literature mentions as "white to almost white crystals or crystalline powder". Clarification is needs where the applied API is crystalline powder or amorphous powder and justification in case of amorphous powder. • Melting point test is not conducted whereas melting point of innovator	• The physical description of API "white to almost white powder" was derived from the manufacturer specification as the Vonoprazan fumarate is a non-compendial API, however we have examined the API and found it to be crystalline. Also, in the DMF XRD spectrum of Vonoprazan Fumarate has been attached for crystal analysis which clearly indicating that the substance is

		product API is 194.8 degree Celsius. • Pka value is different from the innovator reverence product.	in crystalline form and crystallization step is mentioned at the last stage of manufacturing procedure of API. (Attached • Melting point test is not conducted by API supplier for Identification. Instead of Melting Point API supplier have conducted IR and HPLC test whose results can be found API COAs attached. • Pka value mentioned in the section was a typographical error i.e 9.06 instead of 9.6. • Corrected one is attached with this document (Attachment-II).
7.	**3.2.P.5.1**	The Finished product release specification for dissolution test is mentioned as not less than Q of labelled amount of Vonoprazan in 30 minutes , whereas the innovator product has dissolution parameter of achieving Q within 15 minutes , clarification is needed.	The Limit for dissolution Test for Finished product was not mentioned as not less than Q of labelled amount of Vonoprazan in 15 minutes due to unavailability of any published
8.	**3.2.P.8.3**	The firm has provided stability data up to three months' timeline for both accelerated and real time stability data , The stability study data up to 6 months' timeline is required for both accelerated and real time stability study data.	The stability data up to 6 months for both accelerated and real time stability study data has been attached with this Document (Attachment-III).

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Registration letter shall be issued after submission of applicable fee for pre-registration variation ,i-e 30000/= as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction in label claim..**

314.	Name, address of Applicant / Marketing Authorization Holder	M/s **Indus Pharma (Pvt.) Ltd. Plots No. 26-27 & 63-67, sector-27 Korangi Industrial Area, Karachi – 74900, Pakistan**
	Name, address of Manufacturing site.	M/s **Nabiqasim Industries (Pvt) Ltd, 17/24, Korangi Industrial Area, Karachi, Pakistan**
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.792 dated 10/01/2022
	Details of fee submitted	PKR 75,000/-: sip No. 4585817201 dated 14/10/2021
	The proposed proprietary name / brand name	Vanco IV 500mg Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Vancomycin Hydrochloride USP equivalent to Vancomycin …….500mg (as lyophilized powder for injection)
	Pharmaceutical form of applied drug	A white to almost white color cake/powder on reconstitution form light tan color clear transparent liquid free from particles and fibers.
	Pharmacotherapeutic Group of (API)	Tricyclic glycopeptide antibiotics.
	Reference to Finished product specifications	As per USP Specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Product is registered and being marketed in USA & UK by Hospira and MYLAN LABS LTD.
	For generic drugs (me-too status)	Vanbact I.V. 500mg Injection by M/s Nabiqasim Industries (Pvt.) Ltd, Reg. No. 070682
	GMP status of the Finished product manufacturer	GMP renewed on 06/10/2020 Valid till: 19/09/2022
	Name and address of API manufacturer.	M/s Livzon Group Fuzhou Fixing Pharmaceutical Co, Ltd Jiangyin industrial zone Fuqing Fuzhou City Fujian Province, P.R. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity (Impurity B) & related substances specifications, analytical procedures and its

		verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 36 months Accelerated: 25°C ± 2°C / 60% ± 5% RH for 6 months Batches:(0905001,0905002,0905003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Vancomycin 500mg IV Injection by Abbott Laboratories by performing quality tests (description, pH, Assay, Microbial Limit).
	Analytical method validation/verification of product	Method verification studies have submitted including, Precision, Specificity, accuracy.

ABILITY STUDY DATA

Manufacturer of API	M/s Livzon Group Fuzhou Fixing Pharmaceutical Co, Ltd Jiangyin industrial zone Fuqing Fuzhou City Fujian Province, P.R. China.		
API Lot No.	HAF1910029		
Description of Pack (Container closure system)	Product will be supplied in Glass vial with 1 ampoule of 10ml sterile water for injection.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6,9,12,18,24 (Months)		
Batch No.	VIC001	VIC002	VIC003
Batch Size	21000 vials	21000 vials	21000 vials
Manufacturing Date	01-2020	03-2020	03-2020
Date of Initiation	02-2020	06-2020	06-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Esorid 40mg IV Injection Minutes of 370th Meeting of Registration Board

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. FJ200002 issued by (FIJIAN) FOOD AND DRUG ADMINISTRATION valid till 21/09/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of invoice No.FXIN2002251A dated 19-03-2020 cleared on 15/5/2020 is submitted wherein the permission to import Vancomycin Hydrochloride for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator

Sr. #	Section#	Observation	Response of firm vide dairy No.31105 dated 01-11-2022
1.	**3.2.S.4.2**	The claimed testing specifications of API , (Vancomycin Hcl) are USP specifications , however the provided method for conducting Microbial Assay/Potency of Vancomycin is different from USP method and justification is required to establish the provided formula for calculating Potency is equivalent to USP method as provided in Microbial Assay (81) of Antibiotics.	• Firm has submitted a declaration certificate issued by contract manufacturer, M/s Nabiqasim Industries (pvt) Ltd , Khi,dated 05-03-2020 stating that , " With reference to subjected matter, it is to inform you that except dilutions in the provided method all the parameters including reference standard, sample preparation , analytical technique(Gel diffusion method, culture, medium) are same as described in USP and as far as the dilution is concerned we have validated and verified analytical method. In addition to this firm now and onward the we have revised our monograph including dilutions as per current chapter of USP (81) Antibiotic-Microbial Assay. • Firm has also submitted revised Analytical specification of Vancomycin Hcl (API) pyrogen free mentioning analytical specifications and assay method. The document is issued by contract manufacturer and issued date is 29-10-2022 and effective date is 01-11-2022.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

• **Firm shall submit COA of API (Vancomycin) after conducting Antimicrobial Assay test as per pharmacopeia /USP method and results shall be calculated as per the given formula in USP method as provided in Microbial Assay (81) of Antibiotics.** • **Registration letter shall be issued after submission of applicable fee of 7500/=for pre-registration variation as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.** • **Capacity assessment of M/s Nabiqasim Industries, Karachi shall be conducted before issuance of Registration letter.**		
315.	Name, address of Applicant / Marketing Authorization Holder	M/s **Indus Pharma (Pvt.) Ltd. Plots No. 26-27 & 63-67, sector-27 Korangi Industrial Area, Karachi – 74900, Pakistan**
	Name, address of Manufacturing site.	M/s **Nabiqasim Industries (Pvt) Ltd, 17/24, Korangi Industrial Area, Karachi, Pakistan**
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 793 dated 10/01/2022
	Details of fee submitted	PKR 75,000/-: slip No. 7466843241 dated 14/10/2021
	The proposed proprietary name / brand name	VANCO IV 1g Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Vancomycin Hydrochloride USP equivalent to Vancomycin …….1g (as lyophilized powder for injection)
	Pharmaceutical form of applied drug	A white to almost white color cake/powder on reconstitution form light tan color clear transparent liquid free from particles and fibers.
	Pharmacotherapeutic Group of (API)	Tricyclic glycopeptide antibiotics.
	Reference to Finished product specifications	As per USP Specification
	Proposed Pack size	1’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Product is registered and being marketed in USA by Hospira (FDA approved)
	For generic drugs (me-too status)	Vanbact I.V. 1g Injection by M/s Nabiqasim Industries (Pvt.) Ltd, Reg. No. 070682
	GMP status of the Finished product manufacturer	GMP Dated 06/10/2020 Valid till: 19/09/2022
	Name and address of API manufacturer.	M/s Livzon Group Fuzhou Fixing Pharmaceutical Co, Ltd Jiangyin industrial zone Fuqing Fuzhou City Fujian Province, P.R. China

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity (Impurity B) & related substances specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 36 months Accelerated: 25°C ± 2°C / 60% ± 5% RH for 6 months Batches:(0905001,0905002,0905003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Vancomycin 1g IV Injection by Abbott Laboratories by performing quality tests (description, pH, Assay, Microbial Limit).
	Analytical method validation/verification of product	Method verification studies have submitted including, Precision, Specificity, accuracy.

STABILITY STUDY DATA	
Manufacturer of API	M/s Livzon Group Fuzhou Fixing Pharmaceutical Co, Ltd Jiangyin industrial zone Fuqing Fuzhou City Fujian Province, P.R. China
API Lot No.	HAF1910029
Description of Pack (Container closure system)	Product will be supplied in Glass vial with 1 ampoule of 10ml sterile water for injection.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9,12,18,24(Months)		
Batch No.	VBB006	VBC001	VBC002
Batch Size	111 L	111 L	111 L
Manufacturing Date	12-2019	01-2020	03-2020
Date of Initiation	01-2020	03-2020	06-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Esorid 40mg IV Injection Minutes of 370th Meeting of Registration Board
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. FJ200002 issued by (FIJIAN) FOOD AND DRUG ADMINISTRATION valid till 21/09/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of invoice No.FXIN2002251A dated 19-03-2020 cleared on 15/5/2020 is submitted wherein the permission to import Vancomycin Hydrochloride for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. #	Section#	Observation	Response of firm vide dairy No. 31105 dated 01-11-2022
1.	**3.2.S.4.2**	The claimed testing specifications of API , (Vancomycin Hcl) are USP specifications , however the provided method for conducting Microbial Assay/Potency of Vancomycin is different from USP method and justification is required to establish the provided formula for calculating Potency is equivalent to USP method as provided in Microbial Assay (81) of Antibiotics.	• Firm has submitted a declaration certificate issued by contract manufacturer, M/s Nabiqasim Industries (pvt) Ltd , Khi,dated 05-03-2020 stating that , " With reference to subjected matter, it is to inform you that except dilutions in the provided method all the parameters including reference standard, sample preparation , analytical technique(Gel diffusion method, culture, medium) are same as described in USP and as far as the dilution is concerned we have validated and verified analytical method. In addition to this firm now and onward the we have revised our monograph

			including dilutions as per current chapter of USP (81) Antibiotic-Microbial Assay. • Firm has also submitted revised Analytical specification of Vancomycin Hcl (API) pyrogen free mentioning analytical specifications and assay method. The document is issued by contract manufacturer and issued date is 29-10-2022 and effective date is 01-11-2022.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm shall submit COA of API (Vancomycin) after conducting Antimicrobial Assay test as per pharmacopeia /USP method and results shall be calculated as per the given formula in USP method as provided in Microbial Assay (81) of Antibiotics.**
- **Registration letter shall be issued after submission of applicable fee of 7500/=for pre-registration variation as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.**
- **Capacity assessment of M/s Nabiqasim Industries, Karachi shall be conducted before issuance of Registration letter.**

316.	Name, address of Applicant / Marketing Authorization Holder	M/s **Indus Pharma (Pvt.) Ltd. Plots No. 26-27 & 63-67, sector-27 Korangi Industrial Area, Karachi – 74900, Pakistan**
	Name, address of Manufacturing site.	M/s **Indus Pharma (Pvt.) Ltd. Plots No. 26-27 & 63-67, sector-27 Korangi Industrial Area, Karachi – 74900, Pakistan**
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10950 dated 30/04/2022
	Details of fee submitted	PKR 30,000/-: slip No. 2643439006 dated 18/03/2022
	The proposed proprietary name / brand name	Penol IR Tablets 75mg.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Tapentadol HCl eq to Tapentadol…..75mg

	Pharmaceutical form of applied drug	A light pink, round shape, film-coated tablet with "Indus" engraved on one side and other side is plain.
	Pharmacotherapeutic Group of (API)	Centrally Acting Analgesic
	Reference to Finished product specifications	As per Innovator Product
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	NUCYNTA immediate-release oral tablets by Janssen Ortho, LLC Gurabo, PR 00778 U.S. Food & Drug Administration
	For generic drugs (me-too status)	Tapento IR by M/s Sami Pharmaceuticals(Pvt) Ltd., F-95, SITE Karachi, Reg. No. 093064
	GMP status of the Finished product manufacturer	GMP renewed on 24/12/2021 Valid till: 17/12/2023
	Name and address of API manufacturer.	Ami Lifesciences Private Limited. Block No.82/B, ECP Road, AT & Post: Karakhadi391450, Taluka: Padra, District Vadodara Gujarat, INDIA.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(TPT/50111119,TPT/50121119,TPT/50131219,)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and

		controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Tapento IR Tablets 75mg (003G) by M/s Sami Pharmaceuticals (Pvt) Ltd. by performing quality tests (Identification, Assay, Dissolution, Disintegration). CDP has been performed against the same brand that is Tapento IR Tablets 75mg by M/s Sami Pharmaceuticals (Pvt) Ltd. in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including System Suitability, Precision, Specificity, linearity, range, accuracy, and repeatability.

STABILITY STUDY DATA

Manufacturer of API	Ami Life sciences Pvt. Ltd.		
API Lot No.	TPT/50010121		
Description of Pack (Container closure system)	Alu. Alu. Blister strips of 10x1 Tablets packed in a final printed carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9,12,18,24 (Months)		
Batch No.	TR-1/ TPD 75mg Tab	TR-2/ TPD 75mg Tab	TR-3/ TPD 75mg Tab
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	09-2021	09-2021	09-2021
Date of Initiation	25-10-2021	25-10-2021	25-10-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Canazin tablet 300mg Minutes of 289th Meeting of Registration Board (14-16 May,2019)
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 19041306 issued by Food & Drug Control Administration valid till 24/04/2022.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of Invoice No.EXP/1/21-22/0129 dated 21/06/2021 is submitted wherein the permission to import Tapentadol HCl for the purpose of test/analysis and stability studies is granted. • DRAP ADC attestation Date is 24-06-2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. #	Section#	Observation	Response of firm vide dairy No.30761 dated 31-10-2022
1.	**1.5.5**	Firm has mentioned Pharmacological class of API as, "Antidiarrheal". Clarification is needed.	It is a typo error, revised Pharmacological class of API as, "opioid Analgesic" is submitted.
2.	**2.3.P.3.4**	• Firm has mentioned Acceptance criteria for disintegration test NMT 15 minutes under compression step of Product manufacturing ,whereas under section 2.3.P.5.1 firm has mentioned specifications of Disintegration test as NMT 30 minutes, which needs clarification.	• We, Indus Pharma (Pvt.) Ltd., opted for acceptance criteria for disintegration test NMT 15 minutes in 3.P.3.4 which is under compression step (i.e. for Core tablet), whereas under section 2.3.P.5.1 specification for disintegration test is NMT 30 minutes (i.e. Film coated tablet) because as per the specified limits of Ph. Eur. monograph tablets (0478), the limit for disintegration test for Uncoated tablet is NMT 15minutes while for Film Coated is NMT 30minutes. The stated monographs are attached for your reference:
3.	**3.2.P.8.3**	The firm has provided stability data up to three months' timeline for both accelerated and real time stability data , The stability study data up to 6 months' timeline is required for both accelerated and real time stability study data.	Stability data up to 3rd month already submitted to you while remaining data of 6 month stability study is attached.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

- **Registration Board further decided that registration letter shall be issued after submission of applicable fee of 7500/=for pre-registration variation, as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.**

Case No 2: **Export Facilitation (out of que) Cases: (Human, Local, Form-5F)**
M/s NABIQASIM INDUSTRIES (PVT) LTD. Karachi
Assistant Director PR-I / EFD vide its letter No. F.1-6/2019-PR-I (EFD) dated 6th October 2022 informed that as per decision of 133rd meeting of DRAP Authority wherein it was decided to grant registration on priority basis to the pharmaceutical i.e. one molecule for each 100,000 USD worth of export of medicine (to a maximum of 15 such molecules) during a financial year.
In compliance to the above decision M/s M/s NABIQASIM INDUSTRIES (PVT) LTD.**,**Karachi have achieved benchmark of more than 100,000 USD and submitted their applications for priority consideration including following applications

317.	Name, address of Applicant / Marketing Authorization Holder	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762 E-mail address: info@nabiqasim.com
	Name, address of Manufacturing site.	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762 E-mail address: info@nabiqasim.com
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 2034 dated 21-01-2022
	Details of fee submitted	PKR 30,000/-:903391310 dated 23/12/2021
	The proposed proprietary name / brand name	VONTAB 20mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet: Vonoprazan Fumarate equivalent to Vonoprazan…20mg
	Pharmaceutical form of applied drug	Red colored, round shaped, film coated tablet, both sides plain oral tablet.
	Pharmacotherapeutic Group of (API)	Potassium-competitive acid blocker.
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	7's, 14's, 28's & 30's tablets
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab Tablets (Vonoprazan) is registered and being marketed by Takeda Pharmaceuticals

		(Approved by Pharmaceuticals and Medical Devices Agency, Japan).
	For generic drugs (me-too status)	Vonozan Tablet 20mg by M/s Getz Pharma Private Limited, Reg. No. 108571
	GMP status of the Finished product manufacturer	New GMP Certificate granted on 28/05/2022. Tablet (General & Antibiotic), Capsule (General & Cephalosporin), Dry Powder for Suspension (General Antibiotic &Cephalosporin), Oral Liquid (Syrup) (Non-Antibiotic & Antibiotic), Cream / Ointment / Lotion (Non-Antibiotic & Antibiotic & Steroids), Eye & Ear Drops (Non-Antibiotic & Antibiotic & Steroids), Liquid Enema (General), Sachet (General), Small Volume Lyophilized Injectable (Non-Antibiotic, Antibiotic), Gel & Tablet (Hormones) sections approved.
	Name and address of API manufacturer.	M/s Yibin Hongguang Pharmaceutical Co., Ltd. Luolong country NanxiDistrict,YibinCity,SichuanProvince, PC-644100,China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Monograph of Vonoprazan Fumarate is present is as per In-house (Manufacturer's) specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (Individual impurity, total impurity), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MS103201-190501, MS103201-190502, MS103201-190503)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers,

		description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Takecab Tablets (Vonoprazan) is registered and being marketed by Takeda Pharmaceuticals, by performing quality tests (Description, Identification, Dissolution and Assay). CDP has been performed against the same brand that is Vonozan Tablet 20mg (Vonoprazan) by Getz Pharma Private Limited, in Acid media (pH 1.2) & Phosphate Buffer (pH 4.5 & 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Yibin Hongguang Pharmaceutical Co., Ltd. Luolong country NanxiDistrict,YibinCity,SichuanProvince, PC-644100,China		
API Lot No.	MS103201-210501		
Description of Pack (Container closure system)	Alu-Alu blister 7's, 14's, 28's & 30's tablets packed in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	450DS01	450DS02	450DS03
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	23-08-2021	23-08-2021	23-08-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate issued by Yibin Association of Pharmaceutical Industry, Yibin, Sichuan, China valid till 16/03/2025. Firm has also provided copy of Drug Manufacturing License (valid up to(29-12-2025) issued by

		Sichuan Medical products Administration ,which is varied online.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of invoice no MC120210531-004 dated 31-05-2021 duly attested by Assistant Director, DRAP, Karachi on 21-08-2021 was provide.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Observations		**Firms response vide dairy NO.29738 dated 20-08-2022**
2.3.S.1.3	• Melting point test is not conducted whereas melting point of innovator product API is 194.8 degree Celsius. • Pka value is missing	•The melting point of innovator product API is 194.8 degree Celsius, we have revised our API testing specifications same has been attached in Annexure-A and also incorporated melting point test specifications on it for future QC release. •We also conducted melting point test on retention sample of Vonoprazan Fumarate API and found satisfactory results as mention below •The Pka value is 9.6

Serial No.	Test Specifications	Observed Re
01	Melting Point 194.8 °C.	Sample 1= 1 Sample 2 = 1 Sample 3 = 1 ***Average = 1***

3.2.P.5.1	• The finished product release specification for dissolution test is mentioned as not less than Q of labelled amount of Vonoprazan in 30 minutes, whereas the innovator product has dissolution parameter of achieving Q within 15 minutes, clarification is needed.	• Vonoprazan is a highly soluble drug substance, based on ICH Q6A, which states that the drug substance should be considered highly soluble if it meets following conditions: • "The dissolution profile of all strengths of the dosage form should be rapid i.e. Dissolution > 80% in 15 minutes at pH 1.2, 4.0 & 6.8." • Vonotab tablet 10 mg & 20mg as well as the reference product "Vonoget Tablets" by Getz Pharma releases more than 85% in all three mediums within 15 minutes at 50 RPM which is reflected by comparative dissolution profile studies. • As per USP general chapter<1092> "Dissolution Procedure: Development and Validation", Immediate release dosage form should release within 30 to 60 minutes. Therefore, we select the lowest time point i.e. 30 minutes for dissolution. • Moreover, Reference to the decision of "**Minutes of 294th Meeting of Registration Board"** case of Reference product "Vonoget 20mg Tablet" by M/s Getz Pharma(Pvt) Ltd. was approved having time interval for dissolution test at 30 minutes. (Attached in Annexure-B)
3.2.P.8.3	• The firm has provided stability data up to three months' timeline for both accelerated and real time stability data. The stability study data up to 6 months' time line is required for both accelerated and real-time stability data.	• we have already submitted 06 months' stability data on 11th March 2022, attached is the copy of receiving for ready reference.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration applicationRegistration Board further decided that,**
- **Registration Board further decided that, firm shall submit revised COA after setting dissolution test specification as NLT 85 % within 15 minutes before issuance of registration letter.**
- **Registration Board further decided that registration letter shall be issued after submission of applicable fee of 7500/= for pre-registration variation, as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.**

318.	Name, address of Applicant / Marketing Authorization Holder	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area, Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762 E-mail address: info@nabiqasim.com
	Name, address of Manufacturing site.	M/s NABIQASIM INDUSTRIES (PVT) LTD. 17 / 24, Korangi Industrial Area,

		Karachi – Pakistan. Telephone: + (21) 32213886, 32633590, UAN 111-742-762 E-mail address: info@nabiqasim.com
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.1654 dated 18-01-2022
	Details of fee submitted	PKR 30,000/-:31243049256 dated 23/12/2021
	The proposed proprietary name / brand name	VONTAB 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet: Vonoprazan Fumarate equivalent to Vonoprazan……..……10mg
	Pharmaceutical form of applied drug	Yellow colored, round shaped, film coated tablet, both sides plain oral tablet.
	Pharmacotherapeutic Group of (API)	Potassium-competitive acid blocker.
	Reference to Finished product specifications	Innovator's Specs.
	Proposed Pack size	7's, 14's, 28's & 30's tablets
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab Tablets (Vonoprazan) is registered and being marketed by Takeda Pharmaceuticals (Approved by Pharmaceuticals and Medical Devices Agency, Japan).
	For generic drugs (me-too status)	Vonozan Tablet 10mg by M/s Getz Pharma Private Limited, Reg. No. 108570
	GMP status of the Finished product manufacturer	New GMP Certificate granted on 28/05/2022. Tablet (General & Antibiotic), Capsule (General & Cephalosporin), Dry Powder for Suspension (General Antibiotic &Cephalosporin), Oral Liquid (Syrup) (Non-Antibiotic & Antibiotic), Cream / Ointment / Lotion (Non-Antibiotic & Antibiotic & Steroids), Eye & Ear Drops (Non-Antibiotic & Antibiotic & Steroids), Liquid Enema (General), Sachet (General), Small Volume Lyophilized Injectable (Non-Antibiotic, Antibiotic), Gel & Tablet (Hormones) sections approved.

	Name and address of API manufacturer.	M/s Yibin Hongguang Pharmaceutical Co., Ltd.Luolong country NanxiDistrict,YibinCity,SichuanProvince, PC-644100,China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Monograph of Vonoprazan Fumarate is present is as per In-house (Manufacturer's) specifications. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (Individual impurity, total impurity), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MS103201-190501, MS103201-190502, MS103201-190503)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Takecab Tablets (Vonoprazan) is registered and being marketed by Takeda Pharmaceuticals, by performing quality tests (Description, Identification, Dissolution and Assay). CDP has been performed against the same brand that is Vonozan Tablet 10mg (Vonoprazan) by Getz Pharma Private Limited, in Acid media (pH 1.2) & Phosphate Buffer (pH 4.5 & 6.8). The

		values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Yibin Hongguang Pharmaceutical Co., Ltd. Luolong country NanxiDistrict,YibinCity,SichuanProvince, PC-644100,China		
API Lot No.	MS103201-210501		
Description of Pack (Container closure system)	Alu-Alu blister 7's, 14's, 28's & 30's tablets packed in unit carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	451DS01	451DS02	451DS03
Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	23-08-2021	23-08-2021	23-08-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate issued by Yibin Association of Pharmaceutical Industry, Yibin, Sichuan, China valid till 16/03/2025. Firm has also provided copy of Drug Manufacturing License (valid up to(29-12-2025) issued by Sichuan Medical products Administration ,which is varied online.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of invoice no MC120210531-004 dated 31-05-2021 duly attested by Assistant Director, DRAP, Karachi on 21-08-2021 was provide.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks OF Evaluator:		

<table>
<tr><th colspan="2">Observations</th><th>Firms response vide dairy NO.29738 dated 20-08-2022</th></tr>
<tr><td>2.3.S.1.3</td><td>
Melting point test is not conducted whereas melting point of innovator product API is 194.8 degree Celsius.
Pka value is missing
</td><td>
The melting point of innovator product API is 194.8 degree Celsius, we have revised our API testing specifications same has been attached in Annexure-A and also incorporated melting point test specifications on it for future QC release.
We also conducted melting point test on retention sample of Vonoprazan Fumarate API and found satisfactory results as mention below
<table>
<tr><th>Serial No.</th><th>Test Specifications</th><th>Observed Resu</th></tr>
<tr><td>01</td><td>Melting Point 194.8 °C.</td><td>Sample 1= 194
Sample 2 = 19
Sample 3 = 19
Average = 194</td></tr>
</table>
The Pka value is 9.6
</td></tr>
<tr><td>3.2.P.5.1

3.2.P.8.3</td><td>
The finished product release specification for dissolution test is mentioned as not less than Q of labelled amount of Vonoprazan in 30 minutes, whereas the innovator product has dissolution parameter of achieving Q within 15 minutes, clarification is needed.
The firm has provided stability data up to three months' timeline for both accelerated and real time stability data. The stability study data up to 6 months' time line is required for both accelerated and real-time stability data.
</td><td>
Vonoprazan is a highly soluble drug substance, based on ICH Q6A, which states that the drug substance should be considered highly soluble if it meets following conditions:
"The dissolution profile of all strengths of the dosage form should be rapid i.e. Dissolution > 80% in 15 minutes at pH 1.2, 4.0 & 6.8."
Vonotab tablet 10 mg & 20mg as well as the reference product "Vonoget Tablets" by Getz Pharma releases more than 85% in all three mediums within 15 minutes at 50 RPM which is reflected by comparative dissolution profile studies.
As per USP general chapter<1092> "Dissolution Procedure: Development and Validation", Immediate release dosage form should release within 30 to 60 minutes. Therefore, we select the lowest time point i.e. 30 minutes for dissolution.
Moreover Reference to the decision of "Minutes of 294th Meeting of Registration Board" case of Reference product "Vonoget 20mg Tablet" by M/s Getz Pharma(Pvt) Ltd. was approved having time interval for dissolution test at 30 minutes.(Attached in Annexure-B)
We have already submitted 06 months stability data on 11th March 2022, attached is the copy of receiving for ready reference.
</td></tr>
<tr><td colspan="3">Decision: Approved with innovator's specifications.</td></tr>
</table>

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration applicationRegistration Board further decided that,**
- **Registration Board further decided that, Firm shall submit revised COA after setting dissolution test specification as NLT 85 % within 15 minutes before issuance of registration letter.**
- **Registration Board further decided that registration letter shall be issued after submission of applicable fee of 7500/=for pre-registration variation, as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.**

Case No 3 : **Export Facilitation (out of que) Cases: (Human, Local, Form-5F)**

M/s M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan

Assistant Director PR-I / EFD vide its letter No. F.1-6/2019-PR-I (EFD) dated 6th October 2022 informed that as per decision of 133rd meeting of DRAP Authority wherein it was decided to grant registration on priority basis to the pharmaceutical i.e. one molecule for each 100,000 USD worth of export of medicine (to a maximum of 15 such molecules) during a financial year.

In compliance to the above decision M/s AGP Limited, B-23-C, S.I.T.E., Karachi, have achieved benchmark of more than 100,000 USD and submitted their applications for priority consideration including following applications

319.	Name, address of Applicant / Marketing Authorization Holder	M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan
	Name, address of Manufacturing site.	M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10618 dated 26/04/2022
	Details of fee submitted	PKR 30,000/-: 68187020357dated 26/11/2021
	The proposed proprietary name / brand name	**Vonocid 10mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan (as Vonoprazan Fumarate)… 10mg
	Pharmaceutical form of applied drug	Film coated Table
	Pharmacotherapeutic Group of (API)	Potassium competitive acid blocker
	Reference to Finished product specifications	In-House
	Proposed Pack size	3×10's
	Proposed unit price	As per DRAP Approved Price
	The status in reference regulatory authorities	Tekecab Tablet 10mg M/s Takeda Pharmaceutical Company Limited, PMDA Approved.

	For generic drugs (me-too status)	Vonozan 10mg Tablet by M/s Getz Pharma Pakistan (Pvt) (Reg no. 108570)
	GMP status of the Finished product manufacturer	New GMP granted on 17/06/2021.
	Name and address of API manufacturer.	M/s Jiangxi Synergy Pharmaceutical Co., Ltd, Jiangxi Fengxin Industrial Park , Jiangxi Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Monograph of Vonoprazan Fumarate is according to Manufacturer's Specification. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20190801BD, 20190802BD and 20190803BD)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Takecab 10mg Tablet by Takeda Pharmaceutical Company Limited by performing quality tests CDP has been performed against the same brand that is Takecab 10mg Tablet by Takeda Pharmaceutical Company Limited in Acid media

		(pH 1.0-1.2) , Acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.	
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificty.	
STABILITY STUDY DATA			
Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co., Ltd, Jiangxi Fengxin Industrial Park , Jiangxi Province, China		
API Lot No.	20190803BD		
Description of Pack (Container closure system)	Alu/PVC/PVDC blister of 3 x 10's tablets		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 12 months (will be continued till shelf life of 24 months) Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	TR-616	TR-617	TR-618
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	16-07-2020	16-07-2020	16-07-2020
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empag Tablets 25mg by M/s AGP Limited, Karachi. Approved in **Minutes of 295th Meeting of Registration Board (8-11 June, 2020)**	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate issued by Jiangxi API Engineering Technology Research Centre valid till 11/03/2025. Firm has also submitted copy of Drug Manufacturing license No. GAN20160125 valid up to 26-11-2025 ,issued by Jiangxi Provincial Medical Product Administration ,China.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• License no. 1573 dated 09/06/2020 to import APIs Vonoprazan Fumarate for the purpose of test/analysis and stability studies is granted. • Invoice no. JXSG200409 , dated 09-06-2020	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliant	

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided

Remarks OF Evaluator:

S. No.	Section	Observations	Firms Response vide dairy No.31363 dated 02-11-2022
01.	2.3.S.1.3	• The physical description of API is provided as, "White to almost white powder", whereas the innovator product literature mentions as "white to almost white crystals or crystalline powder". Clarification is needed where the applied API is crystalline powder or amorphous powder and justification in case of amorphous powder. • Melting point test is not conducted whereas melting point of innovator product API is 194.8 degree Celsius. • pKa value is not provided.	• "White to almost white powder" is a general physical description given by API manufacturer while material is white to almost white crystalline powder. DMF reflects crystal characteristics of API: Crystal Analysis / Polymorphism "The polymorphic form of our product is stable confirm with X-ray spectra". Melting point is a physical test, not available in the manufacturer specification; hence not performed. • PKa value is updated in the Product Development Report (copy enclosed)
02.	3.2.S.4.4 .1	• Certificate of analysis of imported API Batch No. BD2009003 conducted by M/s AGP Limited has mentioned assay of Fumaric Acid as 25% and the value is taken from CoA of API manufacturer as mentioned on CoA. Clarification is required regarding skipping of test of Fumaric Acid.	• Fumaric acid test for fumarate salt; its quantitation is for information purpose only which is performed in 2nd analysis report (Batch No. 20190803BD), which is already provided in 3.2.S.4.4.1. (copy enclosed)
03.	3.2.P.3.2	Firm has mentioned batch formula with composition and label claim as under: **Vonoprazan fumarate…….. 10 mg**, Whereas the innovator is **Vonoprazan (as Fumarate) ..... 10 mg** Clarification and resubmission is needed.	It is a typographical error, the correct label claim is as under: **Vonoprazan (as Fumarate) ... 10 mg** Revised section 3.2.P.3.2 is enclosed
04.	3.2.P.5.1	• The finished product dissolution test parameter are mentioned as apparatus's; i.e. USP type 2 (paddle) with speed of paddle 75 rpm and time 15 minutes. Where are the process validation protocol and Pharmaceutical Development Report mentioning analytical specifications for dissolution of film coated tablet	• It is a typographical error, the revised Product Development Report and Process Validation Protocols are enclosed.

		mentions limit as "Not less than 80%Q in 30 minutes". • Clarification/ revision is needed regarding the dissolution time limit also speed of paddle as innovator product dissolution parameter mentioned paddle speed of 50 rpm.	• Parameters are not available in FDA dissolution database or in any assessment report. Time & rpm referred from WHO CDP guideline of very rapidly dissolving product; as no less than 85% of the labelled amount of the API dissolves in 15 minutes at 37°C using a paddle apparatus at 75 rpm in a volume of 900mL.
05.	3.2.P.8.3	• Firm is required to submit Stability Data Sheet of trial batches of finished product as per the format given in CTD guidance document. • Compliance record of HPLC software 21CFR & audit trail report on product testing. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	• Stability Data Sheets of trial batches are already provided in section 3.2.P.8.3. Data Sheets are also enclosed for your reference. • Compliance Record of HPLC software 21CFR is enclosed. Audit trail report is mentioned on each chromatogram. (Sample is enclosed for your reference). • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is already provided in section 3.2.P.8.3. Data is enclosed for your reference.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Registration letter shall be issued after submission of applicable fee for pre-registration variation, i-e 30000/= as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction in label claim.**
- **Firm shall submit revised COA after setting dissolution test specification as NLT 85 % within 15 minutes before issuance of registration letter**

320.	Name, address of Applicant / Marketing Authorization Holder	M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan
	Name, address of Manufacturing site.	M/s AGP Limited, B-23-C, S.I.T.E., Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 10619 dated 26/04/2022
	Details of fee submitted	PKR 30,000/-:240164904 dated 26/11/2021
	The proposed proprietary name / brand name	**Vonocid 20mg Tablet**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan (as Vonoprazan Fumarate)… 20mg
	Pharmaceutical form of applied drug	Film coated Tablet
	Pharmacotherapeutic Group of (API)	Potassium competitive acid blocker
	Reference to Finished product specifications	In-House
	Proposed Pack size	3×10's
	Proposed unit price	As per DRAP Approved Price
	The status in reference regulatory authorities	Tekecab Tablet 20mg M/s Takeda Pharmaceutical Company Limited, PMDA Approved.
	For generic drugs (me-too status)	Vonozan 20mg Tablet by M/s Getz Pharma Pakistan (Pvt) (Reg no. 108571)
	GMP status of the Finished product manufacturer	New GMP granted on 17/06/2021
	Name and address of API manufacturer.	M/s Jiangxi Synergy Pharmaceutical Co., Ltd, Jiangxi Fengxin Industrial Park , Jiangxi Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Monograph of Vonoprazan Fumarate is according to Manufacturer's Specification. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (20190801BD, 20190802BD and

		20190803BD)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Takecab 20mg Tablet by Takeda Pharmaceutical Company Limited by performing quality tests CDP has been performed against the same brand that is Takecab 20mg Tablet by Takeda Pharmaceutical Company Limited in Acid media (pH 1.0-1.2) , Acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA			
Manufacturer of API	M/s Jiangxi Synergy Pharmaceutical Co., Ltd, Jiangxi Fengxin Industrial Park , Jiangxi Province, China		
API Lot No.	20190803BD		
Description of Pack (Container closure system)	Alu/PVC/PVDC blister of 3 x 10's tablets		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 12 months (will be continued till shelf life of 24 months) Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	TR-613	TR-614	TR-615
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	15-07-2020	15-07-2020	15-07-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Empag Tablets 25mg by M/s AGP Limited, Karachi. Approved in **Minutes of 295th Meeting of Registration Board (8-11 June, 2020)**

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate issued by Jiangxi API Engineering Technology Research Centre valid till 11/03/2025. Firm has also submitted copy of Drug Manufacturing license No. GAN20160125 valid up to 26-11-2025 ,issued by Jiangxi Provincial Medical Product Administration ,China.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• License no. 1573 dated 09/06/2020 to import APIs Vonoprazan Fumarate for the purpose of test/analysis and stability studies is granted. • Invoice no. JXSG200409 , dated 09-06-2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided

Remarks OF Evaluator:

S. No.	Section	Observations	AGP Reply
01.	2.3.S.1.3	• The physical description of API is provided as, "White to almost white powder", whereas the innovator product literature mentions as "white to almost white crystals or crystalline powder". Clarification is needed where the applied API is crystalline powder or amorphous powder and justification in case of amorphous powder. • Melting point test is not conducted whereas melting point of innovator product API is 194.8 degree Celsius. • pKa value is not provided.	• "White to almost white powder" is a general physical description given by API manufacturer while material is white to almost white crystalline powder. DMF reflects crystal characteristics of API: Crystal Analysis / Polymorphism "The polymorphic form of our product is stable confirm with X-ray spectra". Melting point is a physical test, not available in the manufacturer specification; hence not performed. • PKa value is updated in the Product Development Report (copy enclosed)
02.	3.2.S.4.4.1	• Certificate of analysis of imported API Batch No. BD2009003 conducted by M/s AGP Limited has mentioned assay of Fumaric Acid as 25% and the value is taken from CoA of API manufacturer as mentioned on CoA. Clarification is required regarding skipping of test of Fumaric Acid.	• Fumaric acid test for fumarate salt; its quantitation is for information purpose only which is performed in 2nd analysis report (Batch No. 20190803BD), which is already provided in 3.2.S.4.4.1. (copy enclosed)

03.	3.2.P.3.2	Firm has mentioned batch formula with composition and label claim as under: **Vonoprazan fumarate…... 20 mg**, Whereas the innovator is **Vonoprazan (as Fumarate) ..... 20 mg** Clarification and resubmission is needed.	It is a typographical error, the correct label claim is as under: **Vonoprazan (as Fumarate) ... 20 mg** Revised section 3.2.P.3.2 is enclosed
04.	3.2.P.5.1	• The finished product dissolution test parameter are mentioned as apparatus's; i.e. USP type 2 (paddle) with speed of paddle 75 rpm and time 15 minutes. Where are the process validation protocol and Pharmaceutical Development Report mentioning analytical specifications for dissolution of film coated tablet mentions limit as "Not less than 80%Q in 30 minutes". • Clarification/ revision is needed regarding the dissolution time limit also speed of paddle as innovator product dissolution parameter mentioned paddle speed of 50 rpm.	• It is a typographical error, the revised Product Development Report and Process Validation Protocols are enclosed. • Parameters are not available in FDA dissolution database or in any assessment report. Time & rpm referred from WHO CDP guideline of very rapidly dissolving product; as no less than 85% of the labelled amount of the API dissolves in 15 minutes at 37°C using a paddle apparatus at 75 rpm in a volume of 900mL.
05.	3.2.P.8.3	• Firm is required to submit Stability Data Sheet of trial batches of finished product as per the format given in CTD guidance document. • Compliance record of HPLC software 21CFR & audit trail report on product testing. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	• Stability Data Sheets of trial batches are already provided in section 3.2.P.8.3. Data Sheets are also enclosed for your reference. • Compliance Record of HPLC software 21CFR is enclosed. Audit trail report is mentioned on each chromatogram. (Sample is enclosed for your reference). • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is already provided in section 3.2.P.8.3. Data is enclosed for your reference.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

- **Registration letter shall be issued after submission of applicable fee for pre-registration variation, i-e 30000/= as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction in label claim.**
- **Firm shall submit revised COA after setting dissolution test specification as NLT 85 % within 15 minutes before issuance of registration letter**

Case No 4: Export Facilitation (out of que) Cases: (Human, Local, Form-5F)
M/s Pharmedic Laboratories (Pvt.) Ltd.Lahore
Assistant Director PR-I / EFD vide its letter No. F.1-6/2019-PR-I (EFD) dated 6th October 2022 informed that as per decision of 133rd meeting of DRAP Authority wherein it was decided to grant registration on priority basis to the pharmaceutical i.e. one molecule for each 100,000 USD worth of export of medicine (to a maximum of 15 such molecules) during a financial year.
In compliance to the above decision M/s Pharmedic Laboratories (Pvt.) Ltd.Lahore have achieved benchmark of more than 100,000 USD and submitted their applications for priority consideration including following applications

321.	Name, address of Applicant / Marketing Authorization Holder	**Name:** Pharmedic Laboratories (Pvt.) Ltd. **Address:** 16km Multan Road, Lahore-Pakistan **Contact details: Tel: +92** 42 37511861-65 **Fax:** (042) 37511396-37510498 **Email:** info@pharmedic.com
	Name, address of Manufacturing site.	**Name:** Pharmedic Laboratories (Pvt.) Ltd. **Address:** 16km Multan Road, Lahore-Pakistan **Contact details: Tel: +92** 42 37511861-65 **Fax:** (042) 37511396-37510498 **Email:** info@pharmedic.com
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 177730 dated 17/06/2022
	Details of fee submitted	PKR 75000, Slip No. 844595626 dated 02/06/2022
	The proposed proprietary name / brand name	Vonov 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Vonoprazan fumarate equivalent to Vonoprazan……10mg
	Pharmaceutical form of applied drug	white colored, round shaped, biconvex film coated tablets with both sides plain.
	Pharmacotherapeutic Group of (API)	Antacids, Antireflux Agents & Antiulcerants Belongs to the class of potassium-competitive acid blocker.
	Reference to Finished product specifications	In-House (Innovator Specification)

	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab Tablets 10 mg, Takeda Pharmaceutical Company Limited, Japan.
	For generic drugs (me-too status)	Vonozan 10mg Tablet by M/s Getz Pharma, Reg. No. 108570
	GMP status of the Finished product manufacturer	Last GMP was granted on 09/06/2020 GMP is in Renewal Process
	Name and address of API manufacturer.	**Name:** Jiangxi Synergy Pharmaceutical Co., Ltd. **Address:** Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi Province, P.R.China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Vonoprazan fumarate is present in USP and BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, Test for Impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (VON-10/TR001, VON10-TR002, VON10-TR003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative	Pharmaceutical Equivalence have been

	dissolution profile	established against the brand leader that is Vonozan 10mg tablet by Getz Pharma (Pvt) Ltd. by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Vonozan 10mg tablet by Getz Pharma (Pvt) Ltd….. in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including Specificity, linearity, reproducibility accuracy, precision (repeatability), Limit of Detection, Limit of Quantification, Robustness.

STABILITY STUDY DATA			
Manufacturer of API	Jiangxi Synergy Pharmaceutical Co., Ltd		
API Lot No.	20210801BD		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24(Months)		
Batch No.	VON-10/TR001	VON-10/TR002	VON-10/TR003
Batch Size	750 tab	750 tab	750 tab
Manufacturing Date	12-2021	12-2021	12-2021
Date of Initiation	04-01-2022	04-01-2022	04-01-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate issued by Jiangxi API Engineering Technology Research Centre valid till 11/03/2025. Firm has also submitted copy of Drug Manufacturing license No. GAN20160125 valid up to 26-11-2025 ,issued by Jiangxi Provincial Medical Product Administration ,China.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.15439/2021DRAP-AD (I&E) dated 14/10/2021 is submitted wherein the permission to import Vonoprazan Fumarate for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms,	Submitted

	Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. #	Section#	Observation	Firms Response vide dairy No .2703 (PEC DRAP) dated 3-11-2022
1.	**2.3.S.1.3**	• The physical description of API is provided as, "White to almost white powder", whereas the innovator product literature mentions as "white to almost white crystals or crystalline powder". Clarification is needs where the applied API is crystalline powder or amorphous powder and justification in case of amorphous powder. • Melting point test is not conducted whereas melting point of innovator product API is 194.8 degree Celsius. • Pka value is not provided.	We, Jiangxi Synergy Pharmaceutical Co., Ltd., hereby certify that as for our product Vonoprazan Fumarate, the appearance is white to almost white crystalline powder ***Reference attached*** **Melting point：199.5~199.8℃** **(Both API manufacture and Finished product manufacturer has conducted Identification tests of Vonoprazan Fumarate (Batch No. 202110801BD) through HPLC and FTIR** **pKa：6.74±0.50**
2.	**3.2.S.4.4 .1**	• Certificate of analysis of imported API Batch Conducted by M/s Pharmedic Labortories has mentioned assay of Fumaric acid as 25 % and the value is taken from COA of API manufacturer as mentioned on COA. Clarification is required regarding skipping of test of Fumaric acid	• Regarding testing of fumaric acid, it was performed on raw material and its value is 25% but due to some clerical mistake / typographical error in COA, it was interpreted as taken from supplier COA. (Reference attached).
3.	**3.2.P.5.1**	• Justification of specification of Content uniformity test as 85 -115 (%) in light of compendia requirements. (See USP general chapter requirements of content uniformity test). • The Finished product release specification for dissolution test is mentioned as not less than Q of labelled amount of Vonoprazan in 30 minutes , whereas the innovator product has dissolution parameter of achieving Q within 15 minutes , clarification is needed.	Firm is using in-house alternative method Firm has submitted revised batch release specifications for dissolution test as NLT 80 % (Q) within 15 minutes.

4.	**3.2.S.7.3**	• Stability study data sheet of 3 batches of API (Vonoprazan Fumarate) conducted and displayed by API manufacturer.	Submitted
5.	**3.2.P.8.3**	• The firm has provided stability data up to three months' timeline for both accelerated and real time stability data, the stability study data up to 6 months' timeline is required for both accelerated and real time stability study data. • Stability study data does not mentioned testing of content uniformity test and impurities /degradation product test , Clarification is needed.	Attached Currently we are not conducting impurity/stress testing at method development and validation/verification report and as uniformity of content is not a stability indicating parameter (trial batches) and as it was performed at the time of trial manufacturing so this may not be required at each stability testing point.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Firm shall submit revised COA after conducting content uniformity test as per USP general chapter <905>UNIFORMITY OF DOSAGE UNITS, before issuance of registration**
- **Registration Board further decided that registration letter shall be issued after submission of applicable fee for pre-registration variation ,i-e 7500/=as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction of finished product specifications.**

322.	Name, address of Applicant / Marketing Authorization Holder	**Name:** Pharmedic Laboratories (Pvt.) Ltd. **Address:** 16km Multan Road, Lahore-Pakistan **Contact details: Tel: +92** 42 37511861-65 **Fax:** (042) 37511396-37510498 **Email:** info@pharmedic.com
	Name, address of Manufacturing site.	**Name:** Pharmedic Laboratories (Pvt.) Ltd. **Address:** 16km Multan Road, Lahore-Pakistan **Contact details: Tel: +92** 42 37511861-65 **Fax:** (042) 37511396-37510498 **Email:** info@pharmedic.com
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 17331 dated 17/06/2022
	Details of fee submitted	PKR 750,00/-:60336078057 dated 02/06/2022
	The proposed proprietary name / brand name	Vonov 20mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Vonoprazan fumarate equivalent to Vonoprazan…….20mg
	Pharmaceutical form of applied drug	white colored, round shaped, biconvex film coated tablets with both sides plain.
	Pharmacotherapeutic Group of (API)	Antacids, Antireflux Agents & Antiulcerants Belongs to the class of potassium-competitive acid blocker.
	Reference to Finished product specifications	In-House (Innovator Specification)
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab Tablets 20 mg, Takeda Pharmaceutical Company Limited, Japan.
	For generic drugs (me-too status)	Vonozan 20mg Tablet by M/s Getz Pharma, Reg. No. 108571
	GMP status of the Finished product manufacturer	Last GMP was granted on 09/06/2020 GMP is in Renewal Process
	Name and address of API manufacturer.	**Name:** Jiangxi Synergy Pharmaceutical Co., Ltd. **Address:** Jiangxi Fengxin Industrial Park, Fengxin, Jiangxi Province, P.R.China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Vonoprazan fumarate is present in USP and BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, Test for Impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24

		months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (VON-20/TR001, VON20-TR002, VON20-TR003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Vonozan 20mg tablet by Getz Pharma (Pvt) Ltd. by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Vonozan 20mg tablet by Getz Pharma (Pvt) Ltd….. in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including Specificity, linearity, reproducibility accuracy, precision (repeatability), Limit of Detection, Limit of Quantification, Robustness.

STABILITY STUDY DATA

Manufacturer of API	Jiangxi Synergy Pharmaceutical Co., Ltd		
API Lot No.	20210801BD		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24(Months)		
Batch No.	VON-20/TR001	VON-20/TR002	VON-20/TR003
Batch Size	750 tab	750 tab	750 tab
Manufacturing Date	12-2021	12-2021	12-2021
Date of Initiation	04-01-2022	04-01-2022	04-01-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No.2020002 issued by Jiangxi API Engineering Technology Research Centre valid till 11/03/2025. Firm has also submitted copy of Drug Manufacturing license No. GAN20160125 valid up to 26-11-2025 ,issued by Jiangxi Provincial Medical Product Administration ,China.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of letter No.15439/2021DRAP-AD (I&E) dated 14/10/2021 is submitted wherein the permission to import Vonoprazan Fumarate for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. #	Section#	Observation	Firms Response vide dairy No .2703 (PEC DRAP) dated 3-11-2022
1.	**2.3.S.1.3**	• The physical description of API is provided as, "White to almost white powder", whereas the innovator product literature mentions as "white to almost white crystals or crystalline powder". Clarification is needs where the applied API is crystalline powder or amorphous powder and justification in case of amorphous powder. • Melting point test is not conducted whereas melting point of innovator product API is 194.8 degree Celsius. • Pka value is not provided.	We, Jiangxi Synergy Pharmaceutical Co., Ltd., hereby certify that as for our product Vonoprazan Fumarate, the appearance is white to almost white crystalline powder ***Reference attached*** **Melting point：199.5~199.8℃** **(Both API manufacture and Finished product manufacturer has conducted Identification tests of Vonoprazan Fumarate (Batch No. 202110801BD) through HPLC and FTIR** **pKa：6.74±0.50**
2.	**3.2.S.4.4 .1**	• Certificate of analysis of imported API Batch Conducted by M/s Paramedic Labortories has mentioned assay of Fumaric acid as 25 % and the value is taken from COA of API manufacturer as mentioned on COA. Clarification is required regarding skipping of test of Fumaric acid	• Regarding testing of fumaric acid, it was performed on raw material and its value is 25% but due to some clerical mistake / typographical error in COA, it was interpreted as taken from supplier COA. (Reference attached).

3.	**3.2.P.5.1**	• Justification of specification of Content uniformity test as 85 -115 (%) in light of compendia requirements. (See USP general chapter requirements of content uniformity test). • The Finished product release specification for dissolution test is mentioned as not less than Q of labelled amount of Vonoprazan in 30 minutes , whereas the innovator product has dissolution parameter of achieving Q within 15 minutes , clarification is needed.	Firm is using in-house alternative method Firm has submitted revised batch release specifications for dissolution test as NLT 80 % (Q) within 15 minutes
4.	**3.2.S.7.3**	• Stability study data sheet of 3 batches of API (Vonoprazan Fumarate) conducted and displayed by API manufacturer.	Submitted
5.	**3.2.P.8.3**	• The firm has provided stability data up to three months' timeline for both accelerated and real time stability data, the stability study data up to 6 months' timeline is required for both accelerated and real time stability study data. • Stability study data does not mentioned testing of content uniformity test and impurities /degradation product test , Clarification is needed.	Attached Currently we are not conducting impurity/stress testing at method development and validation/verification report and as uniformity of content is not a stability indicating parameter (trial batches) and as it was performed at the time of trial manufacturing so this may not be required at each stability testing point.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Firm shall submit revised COA after conducting content uniformity test as per USP general chapter <905>UNIFORMITY OF DOSAGE UNITS, before issuance of registration**
- **Registration Board further decided that registration letter shall be issued after submission of applicable fee for pre-registration variation ,i-e 7500/=as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction of finished product specifications.**

Case No 05: Caliph Pharmaceuticals (Pvt) Ltd. Plot No 17, Special Industrial Zone (EPZ), Risalpur

In light of the Decision made in Authority Meeting dated 15th September 2022" as under

"This has reference to the aforementioned subject and decision made in the last Authority Meeting

dated 15th September 2022, to ensure continuous supply of Paracetamol Tablets and to incentivize

manufacturer thereon in form of out-of-queue consideration of application of 1 generic (Me-too) molecule on manufacturing and immediate distribution of atleast 15,000 packs of Paracetamol Tablets
with pack size of 200 Tablets.:

It is therefore submitted that in line with the decision of DRAP Authority, M/s Caliph Pharmaceuticals (Pvt) Ltd. Plot No 17, Special Industrial Zone (EPZ), Risalpur have immediately manufactured and distributed 18,000 packs of their already registered product Cepmol 500mg Tablet (Paracetamol). The details of the manufactured batches of Cepmol 500mg Tablet is as under:

Sr. No	Batch No.	Batch Size	Packs	Mfg. Date	Exp. Date
1	2010	400,000	2000	09-2022	08-2024
2	2017	800,000	4000	09-2022	08-2024
3	2032	800,000	4000	09-2022	08-2024
4	2033	400,000	2000	09-2022	08-2024
5	2034	400,000	2000	09-2022	08-2024
6	2047	800,000	4000	10-2022	09-2024
Total		**3,600,000**	**18,000**		

Accordigly following 01 molecule (Vonoprazan Tablet) is considered out of queue as per the decision of DRAP Authority. Details of our applications of this molecule is as under:

Sr. No	Brand Name	Composition	Date of R&I submission in DRAP
1	Vonocal 10mg Tablet	Each Film Coated Tablet Contains: Vonoprazan Fumarate Eq. to Vonoprazan…10mg	12-05-2022
2	Vonocal 20mg Tablet	Each Film Coated Tablet Contains: Vonoprazan Fumarate Eq. to Vonoprazan…20mg	12-05-2022

Following documents are also attached.

a) Copy of Batch Manufacturing Record of 6 batches of Cepmol 500mg Tablet.
b) Copy of Invoices and delivery challan as evidence of distribution of the manufactured stock.
c) Copy of R&I receiving of our applied product i.e. Vonocal 10mg Tablet and Vonocal 20mg Tablet.

323.	Name, address of Applicant / Marketing Authorization Holder	Caliph Pharmaceuticals (Pvt) Ltd. Plot No 17, Special Industrial Zone (EPZ), Risalpur
	Name, address of Manufacturing site.	Caliph Pharmaceuticals (Pvt) Ltd. Plot No 17, Special Industrial Zone (EPZ), Risalpur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.11462 dated 12/05/2022
	Details of fee submitted	PKR 30,000/-:Slip No.5146720245 dated 26-4-2022
	The proposed proprietary name / brand name	VONOCAL 10MG TABLET

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan fumarate eq to Vonoprazan ……10mg
	Pharmaceutical form of applied drug	White colored, round, biconvex, film-coated tablets with bisectional line on one side containing Vonoprazan Fumarate as active ingredient
	Pharmacotherapeutic Group of (API)	Proton pump inhibitors
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab 10mg Tablet by Takeda Pharmaceutical Company Limited, PMDA Japan Approved.
	For generic drugs (me-too status)	Vonozan Tablet 10mg of Getz Pharma
	GMP status of the Finished product manufacturer	GMP certificate granted on 02-03-2021. Inspection was conducted on 02-03-2021
	Name and address of API manufacturer.	Ami Lifesciences Pvt. Ltd., Block No.82/B, ECP Road, At & Post. Karakhadi, Tal - Padra, Karakhadi - 391 450, Vadodara, Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (VPF/RD/31800819, VPF/RD/31810819, VPF/RD/31820819)
	Module-III (Drug Product):	The firm has submitted detail of product development, manufacturers, description of manufacturing process and controls, impurities,

		specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovators product Takecab 10mg Tablet manufactured by Takeda Pharmaceutical Company Limited by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form etc). CDP has been performed against the innovators product Takecab 10mg Tablet manufactured by Takeda Pharmaceutical Company Limited in Acid media (pH 1.2), Acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted for API and method validation studies for finished product.

STABILITY STUDY DATA

Manufacturer of API	Ami Lifesciences Pvt. Ltd., Block No.82/B, ECP Road, At & Post. Karakhadi, Tal - Padra, Karakhadi - 391 450, Vadodara, Gujarat, India.		
API Lot No.	VPF/30020821M		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2500 tablet	2500 tablet	2500 tablet
Manufacturing Date	11-2021	11-2021	12-2021
Date of Initiation	20-11-2021	30-11-2021	11-12-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Product specific inspection for Dexcal (Dexlansoprazole) 30mg and 60mg Capsule was conducted by the panel on 1st June, 2021 and the report was presented in 308th meeting of Registration Board held on 21-22nd June 2021.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 19041306 issued by Food and Drug Control Administration Gujrat State India valid till 24/04/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• ADC attested invoice is submitted cleared on 09-09-2021. 0.5Kg Vonoprazan Fumarate is imported from Ami Life Sciences
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Complete record of testing of all batches along with chromatograms and raw data sheets is attached.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not available
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted.

Remarks of Evaluator:

Sr. #	Section#	Observation	Firms response vide dairy No. 29608 dated 18-10-22 and 31566 dated 03-11-2022
1.	**3.2.S.1.3**	Melting point of Vonoprazan API is mentioned as 206 degrees Celsius whereas melting point of innovator product API (Vonoprazan) is 194.8 degree Celsius. Clarification is needed.	It was a typographical error in our dossier, as identified by your good office we have also rechecked and identified our mistake. the melting point of Vonoprazan fumarate API is 194.8.
2.	**3.2.S.4.4**	Batch Analysis report of imported API Batch No .VPF/3002082 conducted locally by Finished product manufacturer does not mention LOD test, water content test , Residual on ignition , heavy metal test , as well as impurity tests and residual solvent test , moreover the COA does not bear signature on analysist and QC in charge.	Or specification of the drug substance includes the test of appearance, solubility, identification, loss on drying, assay of Vonoprazan and assay of Fumaric acid we have also performed all these on the imported lot of API and we are also mentioned in the COA report. For rest of the tests we rely on the results of API manufacturer as our practice, signed COA is attached
3.	**3.2.P.1**	The submitted master formulation of finished tablet mentioned 5.2 % of Croscarmellose Sodium(USP) per tablet , and method used is direct compression , which is more than the recommended quantity of Croscarmellose sodium per tablet , Justification is required.	The recommended concentration of Croscarmellose sodium is 2—5 %, however during formulation development trials we get ideal dissolution using 5.2 % Croscarmellose sodium. the dissolution results in CDP studies also evident the release profile of the drug ,however before commercial manufacturing after importing bulk quantity of API we will again perform some trials and make some minor adjustment in the formulation and will

			only use recommended percentage of Croscarmellose sodium .
4.	**3.2.P.5.3**	Analytical method validation study report is incomplete with reference System suitability test, Specificity test and Robustness .Moreover the provided report is not signed by analyst and QC In charge.	We have performed system suitability test and robustness during the validation studies. The signed copy of complete validation sstudies is attached.
5.	**3.2.P.8.3**	• The firm has provided stability data up to three months' timeline for both accelerated and real time stability data, the stability study data up to 6 months' timeline is required for both accelerated and real time stability study data. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing is missing, which is required. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is missing , which is required.	• Stability study data up to 6-month time for accelerated and real time stability study is submitted. • Audit trial report for the product testing for vonocol tablets is not available since the HPLC system was not 21 CFR complaint. • Digital record of data logger of both chamber is provided.

Decision: Approved with Innovator's specifications.

- **Registration Board directed the firm to optimize the formulation for quantity of excipients within permissible limits as per Handbook of Pharmaceutical excipients/recommendations of reference regulatoruy authorities, for commercial batches.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter wil be issued upon submission of complete analytical method validation studies report including test of specificity and robusteness.**

324.	Name, address of Applicant / Marketing Authorization Holder	Caliph Pharmaceuticals (Pvt) Ltd. Plot No 17, Special Industrial Zone (EPZ), Risalpur
	Name, address of Manufacturing site.	Caliph Pharmaceuticals (Pvt) Ltd. Plot No 17, Special Industrial Zone (EPZ), Risalpur
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No.11463 dated 12/05/2022
	Details of fee submitted	PKR 30,000/-: Slip No.89634230928 dated 26-04-2022
	The proposed proprietary name / brand name	VONOCAL 20MG TABLET
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan fumarate eq to vonoprazan ……20mg
	Pharmaceutical form of applied drug	White colored, round, biconvex, film-coated tablets with bisectional line on one side containing Vonoprazan Fumarate as active ingredient
	Pharmacotherapeutic Group of (API)	Proton pump inhibitors
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab 20mg Tablet by Takeda Pharmaceutical Company Limited, PMDA Japan Approved.
	For generic drugs (me-too status)	Vonozan Tablet 20mg of Getz Pharma
	GMP status of the Finished product manufacturer	GMP certificate granted on 02-03-2021. Inspection was conducted on 02-03-2021
	Name and address of API manufacturer.	Ami Lifesciences Pvt. Ltd., Block No.82/B, ECP Road, At & Post. Karakhadi, Tal - Padra, Karakhadi - 391 450, Vadodara, Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months

		Batches: (VPF/RD/31800819, VPF/RD/31810819, VPF/RD/31820819)
	Module-III (Drug Product):	The firm has submitted detail of product development, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovators product Takecab 20mg Tablet manufactured by Takeda Pharmaceutical Company Limited by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form etc). CDP has been performed against the innovators product Takecab 20mg Tablet manufactured by Takeda Pharmaceutical Company Limited in Acid media (pH 1.2), Acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted for API and method validation studies for finished product.

STABILITY STUDY DATA			
Manufacturer of API	Ami Lifesciences Pvt. Ltd., Block No.82/B, ECP Road, At & Post. Karakhadi, Tal - Padra, Karakhadi - 391 450, Vadodara, Gujarat, India.		
API Lot No.	VPF/30020821M		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	2500 tablet	2500 tablet	2500 tablet
Manufacturing Date	12-2021	12-2021	12-2021
Date of Initiation	17-12-2021	24-12-2021	31-12-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Product specific inspection for Dexcal (Dexlansoprazole) 30mg and 60mg Capsule was conducted by the panel on 1st June, 2021 and the report was presented in 308th meeting

		of Registration Board held on 21-22nd June 2021.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 19041306 issued by Food and Drug Control Administration Gujrat State India valid till 24/04/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• ADC attested invoice is submitted cleared on 09-09-2021. 0.5Kg Vonoprazan Fumarate is imported from Ami Life Sciences
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Complete record of testing of all batches along with chromatograms and raw data sheets is attached.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not available
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submiited.

Remarks of Evaluator:

Sr. #	Section#	Observation	Firms response vide dairy No. 29608 dated 18-10-22 and 31566 dated 03-11-2022	2
1.	**3.2.S.1.3**	Melting point of Vonoprazan API is mentioned as 206 degrees Celsius whereas melting point of innovator product API (Vonoprazan) is 194.8 degree Celsius. Clarification is needed.	It was a typographical error in our dossier, as identified by your good office we have also rechecked and identified our mistake. the melting point of Vonoprazan fumarate API is 194.8.	
2.	**3.2.S.4.4**	Batch Analysis report of imported API Batch No .VPF/3002082 conducted locally by Finished product manufacturer does not mention LOD test, water content test , Residual on ignition , heavy metal test , as well as impurity tests and residual solvent test , moreover the COA does not bear signature on analysist and QC in charge.	Or specification of the drug substance includes the test of appearance, solubility, identification, loss on drying, assay of Vonoprazan and assay of Fumaric acid we have also performed all these on the imported lot of API and we are also mentioned in the COA report. For rest of the tests we rely on the results of API manufacturer as our practice, signed COA is attached	
3.	**3.2.P.1**	The submitted master formulation of finished tablet mentioned 5.2 % of Croscarmellose Sodium(USP) per tablet , and method used is direct compression , which is more than the recommended quantity of Croscarmellose sodium per tablet , Justification is required.	The recommended concentration of Croscarmellose sodium is 2—5 %, however during formulation development trails we get ideal dissolution using 5.2 % Croscarmellose sodium. the dissolution results in CDP studies also evident the release profile of the drug ,however before commercial manufacturing after importing bulk quantity of API we will again perform	

			some trials and make some minor adjustment in the formulation and will only use recommended percentage of Croscarmellose sodium .	
4.	**3.2.P.5.3**	Analytical method validation study report is incomplete with reference System suitability test, Specificity test and Robustness .Moreover the provided report is not signed by analyst and QC In charge.	We have performed system suitability test and robustness during the validation studies. The signed copy of complete validation 9studies is attached.	
5.	**3.2.P.8.3**	• The firm has provided stability data up to three months' timeline for both accelerated and real time stability data, the stability study data up to 6 months' timeline is required for both accelerated and real time stability study data. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing is missing, which is required. • Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is missing , which is required.	• Stability study data up to 6-month time for accelerated and real time stability study is submitted. • Audit trial report for the product testing for vonocol tablets is not available since the HPLC system was not 21 CFR complaint. • Digital record of data logger of both chamber is provided.	• Stability stu time for ac stability stud

Decision: Approved with Innovator's specifications.

- **The Registration Board directed the firm to optimize the formulation for quantity of excipients within permissible limits as per Handbook of Pharmaceutical excipients/recommendations of reference regulatoruy authorities, for commercial batches.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration Board further decided that registration letter wil be issued upon submission of complete analytical method validation studies report including test of specificity and robusteness.**

B: Human(New) (Local) FORM-5 F

325.	Name, address of Applicant / Marketing Authorization Holder	**M/s Novamed Pharmaceuticals(Pvt.) Ltd Lahore**
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals(Pvt.) Ltd ., 28km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28454 dated 15/10/2021
	Details of fee submitted	PKR 30,000/-: dated 08/10/2021
	The proposed proprietary name / brand name	**Empozin 10mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated Tablet Contains: Empagliflozin……10mg
	Pharmaceutical form of applied drug	Film coated tablet
	Pharmacotherapeutic Group of (API)	**(1)Empagliflozin** is an inhibitor of SGLT2
	Reference to Finished product specifications	In-House
	Proposed Pack size	10's, 14's 20's, 28's.
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	**Jardiance 10mg tablet** Boehringer Ingelheim Limited USA
	For generic drugs (me-too status)	**Empator 10mg** by Horizon Pharma Reg no. 098822
	GMP status of the Finished product manufacturer	License granted on 08/04/2006 and renewed on 08/04/2021 General tablet section approved and GMP certificate on 31/08/2021.
	Name and address of API manufacturer.	**(1) Empagliflozin;** **API manufacturer Name:**Jiangsu Yong'an Pharmacy CompanyLimited **Address:** No.18 ,237 Proviancial, Road ,Economic Development Zone, Huai'an Jiangsu,China,
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for

		impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Emphagliflozin Batches:(130701,130702,130801)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Jardiance 10mg tablet** by performing quality tests (Identification, Assay, Dissolution, pH). **CDP** was applicable and has been submitted.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity, robustness and Limit of Quantification.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin;** **Name:**Jiangsu Yong'an Pharmacy Company Limited **Address:** No.18 ,237 Proviancial, Road ,Economic Development Zone, Huai'an Jiangsu,China,		
API Lot No.	**Emphagliflozin:** 4500-202003001		
Description of Pack (Container closure system)	Alu-PVC blisters, each containing White colour, Oval shaped biconvex, film coated tablets having breaking line on upper side & lower side is plain. One side of blister is printed with labeling specification. After primary packing blister is packed in specific hard card unit carton along with Patient information leaflet		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	**RD/PR21-058/T1/S1**	**RD/PR21-058/T1/S2**	**RD/PR21-058/T1/S3**

Batch Size	2000 tablets	2000 tablets	2000 tablets
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	05-05-2021	05-05-2021	05-05-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted copy of Last inspection Report conducted on 24/01/2018 (Daclatasvir), 06/03/2017 (Sofosbuvir)
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Emphagliflozin**: Copy of GMP certificate issued by CFDA,People's republic of china HUAI'AN JIANGSU valid till 14/01/2024
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Emphagliflozin** AD Attested invoice ZY20052001G/W Dated.09/06/2020 and
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks Of Evaluator:

Sr. #	Section #	Observation
1.	1.1.5	Legible copy of GMP certificate of manufacturing Site of API ,(Empagliflozin).
2.	3.2.S.2.1	The system suitability conditions set my API manufacturer is detection of API through HPLC with UV detector at 224 nm , same as innovator product , i-e Jardiance whereas under 3.2.S.4.3 validation /verification of analytical procedure by drug product manufacturer significantly varied , including UV detection at 205 nm, which needs clarification.
3.	3.2.S.2.1	Content Uniformity test conducted to establish pharmaceutical equivalence during comparative dissolution ,L1 value is not calculated to meet the specifications as per Pharmacopeia General chapter for content uniformity testing.
4.	3.2.P.2.2 .1	• Justification for setting of Dissolution time specification while conducting Comparative dissolution with reference product was set as 30 minutes whereas the innovator product has mentioned specification for dissolution time as 15 minutes. • In comparative dissolution the RPM for USP type 2 (Paddle Apparatus) is set to be 50 RPM whereas innovator Tab Jardiance has conducted same at 75 RPM which needs clarification.
5.	3.2.P.5.3	• The specificity test for conducting validation of analytical method is conducted without the presence of other components like impurities,

		excipients and matrix compounds which is necessary to establish the specificity of testing method. • Intermediate precision is conducting without comparing the result of separate or different analyst on same apparatus.
6.	3.2.P.8.3	• Stability data of three batches for 6th month for both accelerated and real time stability is missing which is required. • Content uniformity test for Empagliflpzin 10 mg is not mentioned in finished product specification nor it is part of stability batches data / COA, which needs clarification. • Documents for the procurement of API with approval from DRAP (in case of import).

Decision: Registration Board has deferred the case for submission of the reply for above cited shortcomings within six (6) months.

326.	Name, address of Applicant / Marketing Authorization Holder	M/s Helix Pharma (Pvt)., Ltd. A-56, S.I.T.E, Karachi.
	Name, address of Manufacturing site.	Same as above
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.31528 dated : 15/11/2021
	Details of fee submitted	PKR 30,000/- Slip No. 90975244 dated 02/09/2021
	The proposed proprietary name / brand name	YOFERA TABLETS 10mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin……10 mg (Innovator's Specification)
	Pharmaceutical form of applied drug	Tablet (Oral) ; Yellow round slight biconvex film coated tablets
	Pharmacotherapeutic Group of (API)	Anti-Diabetics ; sodium-glucose co-transporter 2 (SGLT2) inhibitors (Drugs used in diabetes, Other blood glucose lowering drugs, excl. insulins)
	Reference to Finished product specifications	Helix Pharma follow the Innovator's Specification
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Jardiance tablet 10mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc., USFDA Approved.

	For generic drugs (me-too status)	Diampa Tablets 10mg by M/s Getz Pharma; Empozin Tablets 10mg by M/s Macter ; Xenglu Tablets 10mg by M/s Hilton ; Empaa Tablets 10mg by M/s Horizon
	GMP status of the Finished product manufacturer	DML # 000030; Renewal on 24.04.2022 Tablet (General) section approved. GMP routine inspection conducted on 09/02/2022 GMP Certificate issued on 25/01/2021 on basis of inspection conducted on 29/10/2020 ;valid upto 28/10/2022
	Name and address of API manufacturer.	M/s CHIFENG ARKER PHARMACEUTICAL CO.LTD CHINA ; Address: No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng , Inner Mongolia, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	In-house monograph of Empagliflozin. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A,B & C & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (**EGF20151201**, **EGF20151202**, **EGF20151203**)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Diampa Tablets 25mg ; Batch # **016FB5** manufactured by Getz Pharma Pakistan by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Diampa Tablets 10mg manufactured by Getz Pharma Pakistan in Acid media (pH 1.2 HCl & pH 4.5 Acetic Acid) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity etc.

STABILITY STUDY DATA			
Manufacturer of API	M/s CHIFENG ARKER PHARMACEUTICAL CO.LTD CHINA ; Address: No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng , Inner Mongolia, China		
API Lot No.	D89-200401		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2 x7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 1,2,3,6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TR-004	TR-005	TR-006
Batch Size	2000 Tablets	2000 Tablets	2000 Tablets
Manufacturing Date	09-2020	09-2020	09-2020
Date of Initiation	02.11.2020	02.11.2020	02.11.2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred the DRB 312th meeting Minutes for approval of new molecule "ZALPO (VONOPRAZAN) TABLETS 10mg & 20mg which were approved on basis of onsite inspection for another product of same dosage form. The said DRB Meeting minutes has mentioned that: □ The HPLC is 21CFR Compliant. □ Audit trail on the testing reports of "ZALPO Tablet 10mg & 20mg" were available.

		□ Adequate monitoring & control are available for stability chamber. The firm has installed software for recording temperature/Humidity of the chamber (for real time stability software V5.7T Thermo, India & Accelerated Stability studies, software is Logit Chrt; Technoman; Pakistan) & the data can been verified for 01 year.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. NM20150062 issued by CFDA
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm submitted the Form-6 & invoice dully attested by AD DRAP Karachi on 19/05/2020 , confirming the import of API "Empagliflozin" Qty: 560 gms ; Batch # D89-200401
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted complete compliance record of HPLC software 21CFR & audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	submitted

Remarks of Evaluator:

Sr. #	Section	Observation	Firms response vide dairy No.30445 dated 27-10-2022
1.	1.1.5	GMP certificate of manufacturing site of API is required ,i-e M/s CHIFENG ARKER PHARMACEUTICAL CO.LTD CHINA ; Address: No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng , Inner Mongolia, China	Submitted.
2.	3.2.S.4	Under the heading of "Control of Drug Substance", the manufacturer mentioned HPLC with UV detector assay of product at 225 nm wave length , however the assay of applied product is conducted at 230 nm whereas the innovator product Jardiance (USFDA) is conducted at 224 nm , clarification in this regard is required.	Please note that the selection of wavelength was carried out by preparing empagliflozin standard solution and all process impurities in diluent at the specification limit. The prepared solution injected into the HPLC system with PDA detector and spectra was recorded. The chromophoric structure of all the compounds almost similar and all compounds were found to have optimum UV absorption at 230 nm. Therefore, the 230 nm wavelength

			was chosen for the study and quantification of Empagliflozin and its impurities. We also conducted the test by using both wave lengths i.e : 225nm & 230nm & found no difference in retention time (Working sheet along with chromatograms are enclosed herewith for your ready reference)
3.	3.2.P.5 .1	Dissolution specification of applied product does not mentioned the time of dissolution for Finished product for batch release specification.	Revised submitted, Internal control limit for dissolution as NLT 80 % within 30 minutes While for shelf life limit as NLT 80% within 15 minutes.
4.	3.2.P.2 .2.1	Justification for setting of Dissolution time specification while conducting Comparative dissolution with reference product was set as 30 minutes whereas the innovator product has mentioned specification for dissolution time as 15 minutes.	Please note that we have conducted Comparative Dissolution Profile (CDP) up to 30minutes as per our internal control specification whereas the set product batch release dissolution specification is NLT 80% in 15minutes
5.	3.2.P.8	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Firm shall submit revised COA after setting dissolution test specification as NLT 85 % within 15 minutes before issuance of registration letter.**
- **Registration letter shall be issued after submission of applicable fee for pre-registration variation ,i-e 7500/=as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction of finished product specifications.**

327.	Name, address of Applicant / Marketing Authorization Holder	M/s Helix Pharma (Pvt)., Ltd. A-56, S.I.T.E, Karachi.
	Name, address of Manufacturing site.	Same as above
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.31527 dated : 15/11/2021
	Details of fee submitted	PKR 30,000/-: dated 03/09/2021
	The proposed proprietary name / brand name	YOFERA TAB LETS 25mg

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin……25 mg (Innovator's Specification)
	Pharmaceutical form of applied drug	Tablet (Oral) ; Yellow elliptical slight biconvex film coated tablets with H logo on one side and break line on other side.
	Pharmacotherapeutic Group of (API)	Anti-Diabetics ; sodium-glucose co-transporter 2 (SGLT2) inhibitors (Drugs used in diabetes, Other blood glucose lowering drugs, excl. insulins)
	Reference to Finished product specifications	Helix Pharma follow the Innovator's Specification
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Jardiance tablet 25mg by M/s Boehringer Ingelheim Pharmaceuticals, Inc., USFDA Approved.
	For generic drugs (me-too status)	Diampa Tablets 25mg by M/s Getz Pharma; Empozin Tablets 25mg by M/s Macter ; Xenglu Tablets 25mg by M/s Hilton ; Empaa Tablets 25mg by M/s Horizon
	GMP status of the Finished product manufacturer	DML # 000030 ;Renewal on 24.04.2022 Tablet (General) section approved. GMP routine inspection conducted on 09/02/2022 GMP Certificate issued on 25/01/2021 on basis of inspection conducted on 29/10/2020 ;valid upto 28/10/2022
	Name and address of API manufacturer.	M/s CHIFENG ARKER PHARMACEUTICAL CO.LTD CHINA ; Address: No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng , Inner Mongolia, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	In-house monograph of Empagliflozin. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for

		impurity A,B & C & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months Batches: (**EGF20151201**, **EGF20151202**, **EGF20151203**)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Diampa Tablets 25mg ; Batch # **019FB6** manufactured by Getz Pharma Pakistan by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Diampa Tablets 25mg manufactured by Getz Pharma Pakistan in Acid media (pH 1.2 HCl & pH 4.5 Acetic Acid) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity etc.

STABILITY STUDY DATA	
Manufacturer of API	M/s CHIFENG ARKER PHARMACEUTICAL CO.LTD CHINA ; Address: No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng , Inner Mongolia, China
API Lot No.	D89-200401
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2 x7's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 06 months Accelerated: 06 months
Frequency	Accelerated: 0, 1,2,3,6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	TR-001	TR-002	TR-003
Batch Size	2000 Tablets	2000 Tablets	2000 Tablets
Manufacturing Date	09-2020	09-2020	09-2020
Date of Initiation	02.11.2020	02.11.2020	02.11.2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred the DRB 312th meeting Minutes for approval of new molecule "ZALPO (VONOPRAZAN) TABLETS 10mg & 20mg which were approved on basis of onsite inspection for another product of same dosage form. The said DRB Meeting minutes has mentioned that: □ The HPLC is 21CFR Compliant. □ Audit trail on the testing reports of "ZALPO Tablet 10mg & 20mg" were available. □ Adequate monitoring & control are available for stability chamber. The firm has installed software for recording temperature/Humidity of the chamber (for real time stability software V5.7T Thermo, India & Accelerated Stability studies, software is Logit Chrt; Technoman; Pakistan) & the data can been verified for 01 year.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. NM20150062 issued by CFDA
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm submitted the Form-6 & invoice dully attested by AD DRAP Karachi on 19/05/2020 , confirming the import of API "Empagliflozin" Qty: 560 gms ; Batch # D89-200401
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted complete compliance record of HPLC software 21CFR & audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	submitted

Remarks of Evaluator:

Sr. #	Section	Observation	Firms response vide dairy No.30445 dated 27-10-2022	

1.	1.1.5	GMP certificate of manufacturing site of API is required ,i-e M/s CHIFENG ARKER PHARMACEUTICAL CO.LTD CHINA ; Address: No. 8 Mysun Street, Hongshan Economic Development Zone, Chifeng , Inner Mongolia, China	Submitted.		
2.	3.2.S.4	Under the heading of "Control of Drug Substance", the manufacturer mentioned HPLC with UV detector assay of product at 225 nm wave length , however the assay of applied product is conducted at 230 nm whereas the innovator product Jardiance (USFDA) is conducted at 224 nm , clarification in this regard is required.	Please note that the selection of wavelength was carried out by preparing empagliflozin standard solution and all process impurities in diluent at the specification limit. The prepared solution injected into the HPLC system with PDA detector and spectra was recorded. The chromophoric structure of all the compounds almost similar and all compounds were found to have optimum UV absorption at 230 nm. Therefore, the 230 nm wavelength was chosen for the study and quantification of Empagliflozin and its impurities. We also conducted the test by using both wave lengths i.e : 225nm & 230nm & found no difference in retention time (Working sheet along with chromatograms are enclosed herewith for your ready reference)		
3.	3.2.P.5 .1	Dissolution specification of applied product does not mentioned the time of dissolution for Finished product for batch release specification.	Revised submitted, Internal control limit for dissolution as NLT 80 % within 30 minutes While for shelf life limit as NLT 80% within 15 minutes.		
4.	3.2.P.2 .2.1	Justification for setting of Dissolution time specification while conducting Comparative dissolution with reference product was set as 30 minutes whereas the innovator product has mentioned specification for dissolution time as 15 minutes.	Please note that we have conducted Comparative Dissolution Profile (CDP) up to 30minutes as per our internal control specification whereas the set product batch release dissolution specification is NLT 80% in 15minutes		
5.	3.2.P.8	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted		

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Firm shall submit revised COA after setting dissolution test specification as NLT 85 % within 15 minutes before issuance of registration letter.**

• **Registration letter shall be issued after submission of applicable fee for pre-registration variation ,i-e 7500/=as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction of finished product specifications.**		
328.	Name, address of Applicant / Marketing Authorization Holder	M/s Allmed (Pvt.) Ltd Plot# 590 Sunder Industrial Estate Raiwind Road- Lahore
	Name, address of Manufacturing site.	M/ s Allmed (Pvt.) Ltd Plot# 590 Sunder Industrial Estate Raiwind Road- Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27423-A dated 04/10/2021
	Details of fee submitted	PKR 20,000/-: Slip No.49001593033 dated 13/04/2021 PKR 10,000/- Slip No .93361876 dated 08/07/2021
	The proposed proprietary name / brand name	Sopra-Praz D 30mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Dual Delayed release pellets of Dexlansoprazole equivalent to Dexlansoprazole: ------- 30mg
	Pharmaceutical form of applied drug	Hard gelatin Capsule filled with white to off white dual delayed release pellets.
	Pharmacotherapeutic Group of (API)	PPIs (Proton Pump Inhibitors)
	Reference to Finished product specifications	Manufacturer Specifications
	Proposed Pack size	1×30’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Dexilant 30mg Capsule Takeda Pharmaceuticals USA Inc (Innovator)
	For generic drugs (me-too status)	Razodex 30mg Capsule by Getz Pharma Reg. # 086976
	GMP status of the Finished product manufacturer	GMP inspection was conducted on 11/06/2021 and report satisfactory. Capsule (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Vision Pharmaceuticals Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan Tel: (92-51) 4493587-88-89-90,

		Fax: (92-51) 4493591 Email: contact@visionpharmapk.com Web: www.visionpharmapk.com
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Monograph of Dexlansoprazole is not present in Pharmacopoeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities/related substances (Sulphone Impurity Sulphide Impurity Total Impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (SP-T40, SP-T41, SP-T42)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against Razodex 30mg Capsule (B # 039C47) by Getz Pharma by performing quality tests (Identification, Dissolution, Disintegration, Assay, Total Impurity, Microbial contamination). CDP has been performed against the same brand that is Razodex 30mg Capsule (B # 039C47) by Getz Pharma in Acid media (pH 1.0-1.2) & (pH 5.5 & 7). The values for f1 and f2 are in the acceptable range.

	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Vision Pharmaceuticals Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan		
API Lot No.	DLP569		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×30's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 6 (Months) Real Time: 0, 1, 2, 3, 4, 6 (Months)		
Batch No.	SP-T40	SP-T41	SP-T42
Batch Size	2500 Capsule	2500 Capsule	2500 Capsule
Manufacturing Date	09-2020	09-2020	09-2020
Date of Initiation	23/09/2020	23/09/2020	23/09/2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate F. 3-26/20 19-Addl. Dir. (QA & LT-I) issued by DRAP valid till 10/02/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Purchase order No PO-9-20-7 is submitted. Purchased from Vision Pharmaceuticals, Islamabad- Pakistan hence DRAP approval is not required.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. #	Section#	Observation
1.	**1.3.5.**	Evidence of approval of manufacturing facility / Approved Section from Licensing Authority
2.	**3.2.S.2.3**	Firm has not mentioned sucrose as part of their master formulation for manufacturing control of inactive material however firm has mentioned

		sucrose in section 2.3.S.2.5, i-e Manufacturing process development. which needs clarification.
3.	**3.2.S.2.6**	The specification of dual release pellets at enteric coating stage is mentioned as soluble at 6.7 PH , whereas QA release specification for IPQC is mentioned as dissolution at P.H.7, which needs clarification.
4.	**3.2.S.4.4**	• The submitted COA of source of API, (Dexlansoprazole) M/s Everest Organics Limited, India, has mentioned Identification /Assay through Chiral HPLC, however same is not depicted through COA of API by local pellets manufacturer. i-e M/s Vision pharmaceuticals, Islamabad. • Dexlansoprazole is a racemic enantiomer of Lansoprazole, Optical rotation test is performed by API manufacturer , however as per COA of Pellets , same is not performed by Pellet manufacturer , as well as finished product manufacturer which needs clarification.
5.	**3.2.S.7**	• API (Pellet) Manufacturer has not mentioned/conducted degradation product test while conducting stability study data of API(pellets) , which needs clarification.
6.	**3.2.P.2.2.1**	• Finished product manufacturer has submitted comparative dissolution Profile performance with Capsule Razodex ,Getz Pharma , However firm has not submitted non Model dependent Cohen's F2(Similarity factor) calculation to establish comparable dissolution with comparator .which needs clarification.

Decision: Registration Board has deferred the case for submission of the reply for abve cited shortcomings within six (6) months.

329.	Name, address of Applicant / Marketing Authorization Holder	M/s Allmed (Pvt.) Ltd Plot# 590 Sunder Industrial Estate Raiwind Road- Lahore
	Name, address of Manufacturing site.	M/ s Allmed (Pvt.) Ltd Plot# 590 Sunder Industrial Estate Raiwind Road- Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27423-B dated 04/10/2021
	Details of fee submitted	PKR 30,000/-: dated 20,000/- 13/04/2021 10,000/- 08/07/2021
	The proposed proprietary name / brand name	Sopra-Praz D 60mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Dual Delayed release pellets of Dexlansoprazole equivalent to Dexlansoprazole: ------- 60mg
	Pharmaceutical form of applied drug	Hard gelatin Capsule filled with white to off white dual delayed release pellets.

	Pharmacotherapeutic Group of (API)	PPIs (Proton Pump Inhibitors)
	Reference to Finished product specifications	Manufacturer Specifications
	Proposed Pack size	1×30's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Dexilant 60mg Capsule Takeda Pharmaceuticals USA Inc (Innovator)
	For generic drugs (me-too status)	Razodex 60mg Capsule by Getz Pharma Reg. # 086977
	GMP status of the Finished product manufacturer	GMP inspection was conducted on 11/06/2021 and report satisfactory. Capsule (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Vision Pharmaceuticals Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan Tel: (92-51) 4493587-88-89-90, Fax: (92-51) 4493591 Email: contact@visionpharmapk.com Web: www.visionpharmapk.com
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Monograph of Dexlansoprazole is not present in Pharmacopoeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities/related substances (Sulphone Impurity Sulphide Impurity Total Impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (SP-T37, SP-T38, SP-T39)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and

		controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the brand leader that is Razodex 60mg Capsule (B # 038C48) by Getz Pharma by performing quality tests (Identification, Dissolution, Disintegration, Assay, Total Impurity, Microbial contamination). CDP has been performed against the same brand that is Razodex 60mg Capsule (B # 038C48) by Getz Pharma in Acid media (pH 1.0-1.2) & (pH 5.5 & 7). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Vision Pharmaceuticals Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan		
API Lot No.	DLP569		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×30's)		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 6 (Months) Real Time: 0, 1, 2, 3, 4, 6 (Months)		
Batch No.	SP-T37	SP-T38	SP-T39
Batch Size	2500 Capsule	2500 Capsule	2500 Capsule
Manufacturing Date	09-2020	09-2020	09-2020
Date of Initiation	21/09/2020	21/09/2020	21/09/2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate F. 3-26/20 19-Addl. Dir. (QA & LT-I) issued by DRAP valid till 10/02/2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Purchase order No PO-9-20-7 is submitted.

		Purchased from Vision Pharmaceuticals, Islamabad- Pakistan hence DRAP approval is not required.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. #	Section#	Observation
1.	**1.3.5.**	Evidence of approval of manufacturing facility / Approved Section from Licensing Authority
2.	**3.2.S.2.3**	Firm has not mentioned sucrose as part of their master formulation for manufacturing control of inactive material however firm has mentioned sucrose in section 2.3.S.2.5, i-e Manufacturing process development. which needs clarification.
3.	**3.2.S.2.6**	The specification of dual release pellets at enteric coating stage is mentioned as soluble at 6.7 PH , whereas QA release specification for IPQC is mentioned as dissolution at P.H.7, which needs clarification.
4.	**3.2.S.4.4**	• The submitted COA of source of API, (Dexlansoprazole) M/s Everest Organics Limited, India, has mentioned Identification /Assay through Chiral HPLC, however same is not depicted through COA of API by local pellets manufacturer. i-e M/s Vision pharmaceuticals, Islamabad. • Dexlansoprazole is a racemic enantiomer of Lansoprazole, Optical rotation test is performed by API manufacturer , however as per COA of Pellets , same is not performed by Pellet manufacturer , as well as finished product manufacturer which needs clarification.
5.	**3.2.S.7**	• API (Pellet) Manufacturer has not mentioned/conducted degradation product test while conducting stability study data of API(pellets) , which needs clarification.
6.	**3.2.P.2.2.1**	• Finished product manufacturer has submitted comparative dissolution Profile performance with Capsule Razodex ,Getz Pharma , However firm has not submitted non Model dependent Cohen's F2(Similarity factor) calculation to establish comparable dissolution with comparator .which needs clarification.

Decision: Registration Board has deferred the case for submission of the reply for above cited shortcomings within six (6) months.

Human (Import) Form 5 F (New)

330.	**Name, address of Applicant / Importer**	**M/s. Novartis Pharma (Pakistan) Limited, 15 West Wharf, Karachi, Pakistan**
	Details of Drug Sale License of importer	**License No:** 007 **Address:** Novartis Pharma (Pakistan) Limited, 15 West Wharf, Dockyard Road, Karachi, Pakistan.

		Address of Godown: C-21, SITE, Karachi. **Validity:** 12-3-2023. **Status:** By way of wholesale **Renewal:** Not Applicable
	Name and address of marketing authorization holder (abroad)	Sandoz Pharmaceuticals AG, 6343 Risch, Schweiz.
	Name, address of manufacturer(s)	Sandoz GmbH, Biochemiestrasse 10, 6250 Kundl Austria
	Name of exporting country	Switzerland
	Detail of certificates attached (CoPP, Free-sale certificate, GMP certificate)	Firm has submitted original & legalized CoPP certificate (No. 20003187) dated 29-06-2020 issued by Swissmedic for Piperacillin/Tazobactam Sandoz 2.25g. The CoPP confirms that this product is on the market in exporting country as well as GMP compliant status of manufacturer. **The name of importing country on CoPP is mentioned as Pakistan.**
	Details of letter of authorization / sole agency agreement	Firm has submitted original & legalized letter of Authorization/ Sole Agency Agreement. This letter specifies that the manufacturer appoints M/s Novartis Pharma (Pakistan) Ltd., Karachi. to register and market the product as Sole Agent in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No31767 .Dated: 10-08-2021
	Details of fee submitted	PKR 150,000/-: slip No.373355053674 dated 10-08-2021
	The proposed proprietary name / brand name	Piperacillin/Tazobactam Sandoz 4.5g Powder for solution for Injection/Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Piperacillin sodium.....4.168g (Corresponding to 4000mg of Piperacillin) Tazobactam sodium ..... 0.53638g (Corresponding to 500mg of Tazobactam)

	Pharmaceutical form of applied drug	Powder for Solution for Injection/Infusion
	Pharmacotherapeutic Group of (API)	Antibacterial for systemic use
	Reference to Finished product specifications	Manufacturer's Specs
	Proposed Pack size	1 Vial powder for solution for injection/infusion
	Proposed unit price	Proposed MRP per pack shall be furnished later
	The status in reference regulatory authorities	Product has been approved in many stringent regulatory authorities such as Belgium, France, Spain, Switzerland, etc.
	For generic drugs (me-too status)	Tacip by M/S Macter International Limited (Reg # 073632), Tazomax by M/S Mediceena Pharma (Pvt.) Ltd. (Reg. # 052920), Mepnem by M/S English Pharmaceuticals Industries (Reg. # 064557), etc.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO-QOS-PD template. Firm has provided the summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	**Tazobactam** Shandong Anxin Pharmaceutical Co., Ltd. **Piperacillin:** Phase 1: North China Pharmaceutical Group Semisyntech Co., Ltd and Zhuhai United Laboratories Co.,Ltd. Phase 2: Shandong Anxin Pharmaceutical Co., Ltd.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Piperacillin:** Firm has submitted stability study data of Piperacillin under the 25 ± 2°C / 60%RH ± 5 % for Accelerated and 2°C to 8°C for accelerated condition. The stability study for long term data up to 24 months is provided.

		Tazobactam Sodium: The stability data of Tazobactam Sodium under Long-term stability condition: 25°C ± 2°C 60 % ± 5 % rel. humidity and Accelerated stability condition: 40°C ± 2°C 75 % ± 5 % rel. humidity was provided. The Stability Study for long term data up to 24 months is provided.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has provided data of comparative Studies. Comparative studies (physicochemical and impurities profiles) have been performed with originator products (i.e. Tazocin®, Tazocilline® 2.25g and 4.5 g, respectively) currently marketed in several European countries (BE, GB, NO, FR)and the Sandoz product. The results clearly indicate that all European originator products tested and the Sandoz product are essentially similar.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Injection Vial Glass Type III, Infusion bottle Glass Type II, infusion bottle stopper, injection vial stopper, flip-off boarded cap
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data for 24 months long-term stability conditions of 30°C/75% RH. Stability was also monitored at accelerated storage condition at 40 °C/75% RH for 6 months.

Evaluation by PEC:

Sr. #	Section #	Observation
1.	1.1.5	Provided GMP certificate of manufacturing site is expired on 25-11-2021, provide valid and embassy attested GMP certificate of manufacturer.
2.	2.3. S.4	Under the heading of "Control of Drug Substance", the manufacturer mentioned is M/s Qilu Tianhe whereas per 2.3.S.2 the manufacturer of drug substance i-e Piperacillin, /Tazobactam/Sterile Lyophilized mixture of Piperacillin Tazobactam (8:1)1 is mentioned as M/s Shandong Axin Co. ltd. Clarification is needed.
3.	3.2. S	The Substance part of CTD dossier is submitted for Piperacillin and tazobactam as separate powder substances whereas the actual substance to be shipped to manufacturer M/s Sandoz Austria, is Piperacillin: Tazobactam

		lyophilized bulk powder (8:1), therefore S Part with all its components of Piperacillin: Tazobactam Lyophilized bulk powder in fixed ration 8:1 is required.
4.	3.2.S.1.1	Active Substance Master File of Qilu Tianhe Pharmaceutical Co, Ltd is provided for Piperacillin and Tazobactum which needs clarification.
5.	3.2.P.3.4	Control of Intermediate Piperacillin: Tazobactam Intermediate 8:1 is provided by Qilu Tianhe whereas manufacturing site is mentioned as M/s Shandong Axin Pharmaceutical Co.Ltd.
6.	3.2.P.3.4	COA of Sodium bicarbonate is issued by Qilu Tianhe, which needs clarification.
7.	3.2.P.3.4	COA for water for Injection is issued by Qilu Tianhe, which needs clarification.
8.	3.2.P.4.3	Validation of Analytical procedure for Assay of Piperacillin and related substance is conducted by M/s Qilu Pharmaceutical Cot Ltd and transferred to Qilu Tianhe, however no such transfer document is provided in this regard.
9.	3.2.S.4.5	Firm is intended to testing specification of Piperacillin monohydrate as per Ph.Eur however the chromatographic conditions submitted for assay is varied form Pharmacopoeia specifications.
10.	3.2.P.3.4	COA of Piperacillin Tazobactam Sterile bulk Powder is issued by Qilu Tianhe, which needs clarification
11.	3.2.P.2.1 .1	Justification for not conducting complete Pharmacopoeial tests as required to establish pharmaceutical equivalence. (Dissolving time, Particulate matter, Clarity of reconstituted solution etc.)
12.	3.2. P.8.2	The stability data provided for accelerated study for batch NoAK1646 depicts significant change of 5 % from zero to 1st time point, which needs clarification.

Decision: Registration Board has deferred the case for submission of the reply for above cited shortcomings within six (6) months.

331.	**Name, address of Applicant / Importer**	**M/s. Novartis Pharma (Pakistan) Limited, 15 West Wharf, Karachi, Pakistan**
	Details of Drug Sale License of importer	**License No:** 007 **Address:** Novartis Pharma (Pakistan) Limited, 15 West Wharf, Dockyard Road, Karachi, Pakistan. **Address of Godown:** C-21, SITE, Karachi. **Validity:** 12-3-2023. **Status:** By way of wholesale **Renewal:** NA
	Name and address of marketing authorization holder (abroad)	Sandoz Pharmaceuticals AG, 6343 Risch, Schweiz.
	Name, address of manufacturer(s)	Sandoz GmbH, Biochemiestrasse 10, 6250 Kundl Austria
	Name of exporting country	Switzerland

	Detail of certificates attached (CoPP, Free-sale certificate, GMP certificate)	Firm has submitted original & legalized CoPP certificate (No. 20003187) dated 29-06-2020 issued by Swissmedic for Piperacillin/Tazobactam Sandoz 2.25g. The CoPP confirms that this product is on the market in exporting country as well as GMP compliant status of manufacturer. The name of importing country on CoPP is mentioned as Pakistan.
	Details of letter of authorization / sole agency agreement	Firm has submitted original & legalized letter of Authorization/ Sole Agency Agreement. This letter specifies that the manufacturer appoints M/s Novartis Pharma (Pakistan) Ltd., Karachi. to register and market the product as Sole Agent in Pakistan.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No.31766 Dated: 10-08-2021
	Details of fee submitted	PKR 150,000/-slip No. 72231786648 10-08-2021
	The proposed proprietary name / brand name	Piperacillin/Tazobactam Sandoz 2.25g Powder for solution for Injection/Infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Piperacillin sodium.....2.12655g (corresponding to 2000mg of Piperacillin) Tazobactam sodium ..... 0.27366g (Corresponding to 250mg of Tazobactam)
	Pharmaceutical form of applied drug	Powder for Solution for Injection/Infusion
	Pharmacotherapeutic Group of (API)	Antibacterial for systemic use
	Reference to Finished product specifications	Manufacturer's Specs
	Proposed Pack size	1 Vial powder for solution for injection/infusion
	Proposed unit price	Proposed MRP per pack shall be furnished later

	The status in reference regulatory authorities	Product has been approved in many stringent regulatory authorities such as Belgium, France, Spain, Switzerland, etc.
	For generic drugs (me-too status)	Tacip by M/S Macter International Limited (Reg # 081175), Tazomax by M/S Mediceena Pharma (Pvt.) Ltd. (Reg. # 059514), Mepnem by M/S English Pharmaceuticals Industries (Reg. # 064556), etc.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO-QOS-PD template. Firm has provided the summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	**Tazobactam** Shandong Anxin Pharmaceutical Co., Ltd. **Piperacillin:** Phase 1: North China Pharmaceutical Group Semisyntech Co., Ltd and Zhuhai United Laboratories Co.,Ltd. Phase 2: Shandong Anxin Pharmaceutical Co., Ltd.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	**Piperacillin:** Firm has submitted stability study data of Piperacillin under the 25 ± 2°C / 60%RH ± 5 % for Accelerated and 2°C to 8°C for accelerated condition. The stability study for long term data up to 24 months is provided. **Tazobactam Sodium:** The stability data of Tazobactam Sodium under Long-term stability condition: 25°C ± 2°C 60 % ± 5 % rel. humidity and Accelerated stability condition: 40°C ± 2°C 75 % ± 5 % rel. humidity was provided. The Stability Study for long term data up to 24 months is provided.

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has provided data of comparative Studies. Comparative studies (physicochemical and impurities profiles) have been performed with originator products (i.e. Tazocin®, Tazocilline® 2.25g and 4.5 g, respectively) currently marketed in several European countries (BE, GB, NO, FR)and the Sandoz product. The results clearly indicate that all European originator products tested and the Sandoz product are essentially similar.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Injection Vial Glass Type III, injection vial stopper, flip-off boarded cap
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data for 24 months' long-term stability conditions of 30°C/75% RH. Stability was also monitored at accelerated storage condition at 40 °C/75% RH for 6 months.

Evaluation by PEC:

Sr. #	Section #	Observation
1.	1.1.5	• Provided GMP certificate of manufacturing site M/s Sandoz Austria, is expired on 25-11-2021, provide valid and embassy attested GMP certificate of manufacturer. • Provided CoPP is issued by Switzerland Authorities(swismedic), country of export is mentioned as Switzerland however authority Letter is issued by Sandoz, Austria which needs clarification. • Marketing Authorization holder abroad is not clarified in form 5-F application.
2.	2.3. S.4	Under the heading of "Control of Drug Substance", the manufacturer mentioned is M/s Qilu Tianhe whereas per 2.3.S.2 the manufacturer of drug substance i-e Piperacillin, /Tazobactam/Sterile Lyophilized mixture of Piperacillin Tazobactam (8:1)1 is mentioned as M/s Shandong Axin Co. ltd. Clarification is needed.
3.	3.2. S	The Substance part of CTD dossier is submitted for Piperacillin and tazobactam as separate powder substances whereas the actual substance to be shipped to manufacturer M/s Sandoz Austria, is Piperacillin: Tazobactam lyophilized bulk powder (8:1), therefore S Part with all its components of

		Piperacillin: Tazobactam Lyophilized bulk powder in fixed ration 8:1 is required.
4.	3.2.S.1.1	Active Substance Master File of Qilu Tianhe Pharmaceutical Co, Ltd is provided for Piperacillin and Tazobactum which needs clarification.
5.	3.2.P.3.4	Control of Intermediate Piperacillin: Tazobactam Intermediate 8:1 is provided by Qilu Tianhe, whereas manufacturing site is mentioned as M/s Shandong Axin Pharmaceutical Co.Ltd.
6.	3.2.P.3.4	COA of Sodium bicarbonate is issued by Qilu Tianhe, which needs clarification.
7.	3.2. P.3.4	COA for water for Injection is issued by Qilu Tianhe, which needs clarification.
8.	3.2. P.4.3	Validation of Analytical procedure for Assay of Piperacillin and related substance is conducted by M/s Qilu Pharmaceutical Cot Ltd and transferred to Qilu Tianhe however no such transfer document is provided in this regard.
9.	3.2. S.4.5	Firm is intended to testing specification of Piperacillin monohydrate as per Ph.Eur however the chromatographic conditions submitted for assay is varied form Pharmacopoeial specifications.
10.	3.2. P.3.4	COA of Piperacillin Tazobactam Sterile bulk Powder is issued by Qilu Tianhe which needs clarification.
11.	3.2.P.2.1 .1	Justification for not conducting complete Pharmacopoeial tests as required to establish pharmaceutical equivalence. (Dissolving time, Particulate matter, Clarity of reconstituted solution etc.)
12.	3.2. P.8.2	The stability data provided for accelerated study for batch NoAK1642 depicts significant change of 5 %, from zero to 6 month, which needs clarification.

Decision: Registration Board has deferred for submission of the reply for above cited shortcomings within six (6) months.

332	Name, address of Applicant / Marketing Authorization Holder	M/S Welmark pharmaceuticals Industrial estate Hattar, Kpk Pakistan
	Name, address of Manufacturing site.	M/S Welmark pharmaceuticals Plot No 122 Block-B phase-5 Industrial estate Hattar Kpk Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	GMP status of the firm	The firm is granted GMP certificate based on inspection conducted on 11-11-2021 and it is valid till 23-11-2023.
	Evidence of approval of manufacturing facility	The firm has provided Tablet general section as confirmed from GMP certificate.
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy No. 34234 dated 31-12-2021
	Details of fee submitted	PKR 30000/= dated
	The proposed proprietary name / brand	Empazin 25mg Tablet

	name	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin……25mg
	Pharmaceutical form of applied drug	Chocolate brown color 8mm round shaped both sides plain film coated tablets.
	Pharmacotherapeutic Group of (API)	Anti diabatic
	Reference to Finished product specifications	Innovator's Specs
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	Status in reference regulatory authorities	Empaa 25mg tablet by M/S Weather Folds pharmaceuticals Hattar, Drap Approved
	For generic drugs (me-too status)	Empaa 25mg tablet by M/S Weather Folds pharmaceuticals Hattar, Drap Approved
	Name and address of API manufacturer	Fuxin Long Rui Pharmaceutical Co Ltd
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure

		system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	24 months real time stability data at 30°C ± 2°C / 65% ± 5%RH of 03 batches. 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 03 batches.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product against Empaa 25mg Tablets (Batch No. 755, Mfg date 09-2020) by Weather Folds Pharmaceuticals Industrial Estate Hattar. Firm has submitted results of CDP for their product against Empaa 25mg Tablets (Batch No. 755, Mfg date 09-2020). Firm has tested CDP in three dissolutions medium ie. (0.1N Hcl pH 1.2, Acetate Buffer pH 4.5, Phosphate Buffer pH 6.8 and the results of f1, f2 factor are within the acceptable limit.
	Analytical method validation/verification of product	Firm has submitted protocols and reports of validation studies of analytical method.

STABILITY STUDY DATA

Manufacturer of API	Fuxin Long Rui Pharmaceutical Co Ltd		
API Lot No.	E-20181027-D02-E06-01		
Description of Pack (container closure system)	14's Tablets Empazin 25mg Tablets will be packed in blister and Secondary Packing in Unit Carton.		
Stability Storage Condition	Real Time stability 30°C ± 2°C / 65% ± 5%RH Accelerated stability 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real Time 09 Months Accelerated 06		
Frequency	Real Time 0,3,6,9 (Months) Accelerated 0,3,6 (Months)		
Batch No.	EG01	EG02	EG03
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	11-2020	11-2020	11-2020

Date of Initiation		09-11-2020	10-11-2020	11-11-2020
No of Batches		03		
1.	Reference of previous approval of applications with stability study data of the firm (If any)	The firm has referred to onsite inspection report of their product Sofosbuvir 400mg Tab, Registration Board decided to approve registration of Sofosbuvir 400mg tab in minutes of 291 meeting by M/S Welmark Pharmaceuticals Hattar. The firm has referred to onsite inspection report of their product Dapagliflozin 10mg Tab, Registration Board decided to approve registration of Dapagliflozin 10mg tab in minutes of 307 meeting by M/S Welmark Pharmaceuticals Hattar.		
2.	Approval of API/ DML/ GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted GMP certificate Manufacturer issued by China food and drug administration valid until 27-09-2020		
3. .	Documents for the procurement of API with approval from DRAP (in case of import)	Firm has submitted copy of ADC attested commercial invoice specifying purchase of 410g. Copy of License to import drugs letter No 0031/2019-DRAPCPS/135 dated 09-01-2019 is submitted.		
4.	Data of stability batches will be supported by attested respective documents like chromatogram, Raw data sheet, COA, summary data sheet etc.	Submitted		
5. .	Compliance record of HPLC software 21CFR & audit trail reports on product testing.	Submitted		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers(real time and accelerated)	Submitted		

S.No	Section	Observation	Justifications
1)	1.4.1	Applicant has checked for New Drug Product (NDP) Whereas the applied molecule Empagliflozin has already been registered, revised submission as Generic Drug Product is required.	Revised submission of Generic Drug Product is submitted.
2)	2.3.S.1.3	Data/ information against this section as mentioned in CTD guidance document is missing, which is required.	Submitted

	3)	2.3.S.3.1	Summary of studies performed to identify the particle size distribution of the API, including identification of and data on the drug substance lot used in stability studies is required as the article size is mentioned in Specification of Empagliflozin for Innovator product Jardiance (USFDA).	Submitted
	4)	2.3.S.4.4	COA of the Empagliflozin Batch No E-20181027-D02-E06-01conducted by API manufacturer does not reflect Identification through IR method more over test for residual solvent is not conducted, which needs clarification / revised COA as per submitted specification of API under section 2.3.S.4.1.	The manufacturer identification of Empagliflozin by HPLC. Test for Residual solvent is mentioned, Revised COA as per submitted specification is Submitted.
	5)	2.3.S.4.5	Justification of Specification of API including exclusion of IR identification, water content, residual solvents, sulphated ash and particle size is required.	The manufacturer identification of Empagliflozin by HPLC. Water content, residual solvents, sulphated ash and particle size is submitted.
	6)	2.3.P.3.2	The proposed commercial batch size(s) (e.g. number of dosage units) mentioning list f all components of the drug product to be used in the manufacturing process and their amounts on per batch basis (including individual components of mixtures prepared in house(e.g coating) and overages, if any) is missing which is required.	Submitted.
	7)	2.3.P.3.3	The flow chart diagram of tableting process shows wet granulation as well as direct compression method. The descriptive part of section 2.3.P.3.3 does not mention wet granulation method and literature provided in dossier depicts mixing and direct compression method. However section 2.3.P.2.3 mentions only wet granulation method, Clarification and harmonization of manufacturing method is required.	Firm has submitted revised manufacturing process as direct compression are following Direct Compression.
	8)	2.3.P.3.4	The specifications/ limits mention for weight variation is ± 5% whereas in 2.3.5.1 it is mentioned as ± 7.5% which needs clarification.	The weight variation limit is ± 7.5%. Documents submitted.
	9)	2.3.P.4.5	For excipients of human or animal origin, a certificate shall be provided, confirming that the excipient(s) are	We are not using excipients of Human or animal origin.

			free from BSE and TSE. Which is missing and is required?	
	10)	2.3.P.5.1 & 2.3.P.5.4	• Content uniformity is not conducted which is required to be conducted as applied API is 25mg and also the total content of API is 12% w/w of proposed finished Drug product/tablet? • Specifications shall include the degradation products and related substances which are missing.	Firm have performed Content uniformity. (limit 85-115 %) Specification of Related substance submitted.
	11)	3.2.S.3	Discussion on the potential for isomerism and identification of stereochemistry, studies performed to identify potential polymorphic forms and particle size distribution of the Drug substance shall be submitted, which are missing.	Submitted.
	12)	3.2.S.7	Stability data of API for batch No 20161017 under accelerated condition is out of specifications at 6-month point (97.19). Moreover the stability data of the same batch under real time conditions is also out of specifications at 12th, 18th and 24 months. (91.85%, 91.83%, and 91.80% respectively which needs clarifications? Provide API stability data for 3 batches on accelerated and real time study as conducted by API manufacturer.	• M/s WELMARK has submitted revised COA of API of Batch No.20161017 at 6th month stability mentioning assay as 99.19 under accelerated conditions. Firm has also submitted revised COA of API batch No.20161017 at 12th ,18th, and 24 months (98.85 %,99.39% and 98.95 %) at real time. • API stability study data conducted by API manufacturer is not submitted.
	13)	3.2.P.2.3	Description of manufacturing process mention wet granulation, whereas in section 3.2.P.3.3 depicts direct compression, clarification is needed.	Description of manufacturing process is direct compression. Documents submitted.
	14)	3.2.P.3.4	The specification limit mention for weight variation is ±5% whereas in 3.2.P.5.1 it is mention as ±7.5% which is needed clarification.	The specification limit for weight variation is ±7.5. Documents submitted.
	15)	3.2.P.5.1	• Content uniformity test is not conducted which is required to be conducted as applied API is 25mg and also the total content of API is 12% w/w of proposed finished Drug product/ tablet? • Specification shall include the degradation products and	Content uniformity test is conducted. Documents submitted. Specification of Related substances are included. Documents submitted.

		related substances which are missing.	

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued upon submission of stability studies data of the drug substances as per the conditions of zone IV-A or otherwise provision of degradation studies of the finished product for 6 months as per the decision of Registration Board**

333.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29541 dated 29-10-2021
	Details of fee submitted	PKR 20,000/-: manual slip No1907516 dated 01-02-2021 & differential fee of PKR 10000/- slip No.720791777477 dated 18-06-2021
	The proposed proprietary name / brand name	Dexil 30mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Dual Delayed Release Dexlansoprazole (Enteric coated pellets) …… 30mg
	Pharmaceutical form of applied drug	Capsule Oral
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	Manufacturer's Specs
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved
	For generic drugs (me-too status)	Rasodex Capsule 30mg M/s Gets Pharma Reg. No. 086976

	GMP status of the Finished product manufacturer	cGMP No. FID-797667-1346 issued by DRAP valid till 25/10/2022. Section Renewal granted on 12-03-2021 section approval Copy Submitted by the firm.
	Name and address of API manufacturer.	Vision Pharmaceutical (Pvt)Ltd Plot No 22-23 Industrial Triangle Khuta Road Islamabad
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Dexlansoprazole DDR pellets are preparing under manufacturer's Specs. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DXL 01, DXL 02, DXL 03)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence established vis-à-vis the brand leader, Rasodex Capsule 30mg by M/s Gets Pharma by performing quality tests. The results of all the tests of both products fall within the specifications and are comparable. The firm has performed

		comparative analyses with innovator's product. The studies demonstrate comparable results with the innovator product. Jaskan pharma has been performed against the same brand that is Rasodex Capsule 30mg by Getz Pharma in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted reports of verification studies of analytical method for the drug substance. Firm has also submitted reports of validation of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	Vision Pharmaceutical (Pvt)Ltd Plot No 22-23 Industrial Triangle Khuta Road Islamabad		
API Lot No.	DLP562		
Description of Pack (Container closure system)	Sealed In Alu-Alu Poly bag in Plastic Drum		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	DXL 01	DXL 02	DXL 03
Batch Size	1000 Capsules	1000 Capsules	1000 Capsules
Manufacturing Date	21-02-2020	21-02-2020	21-02-2020
Date of Initiation	02-04-2020	02-04-2020	02-04-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Jaxikan 100mg/5ml Susp Arixkan 1gm IV Injection Aquakan 5ml Injection
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML certificate No. 000806 and GMP Certificate No. F. 3-26/2019-Addl.Dir(QA & LT-1) both issued by DRAP Pakistan has been submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Local procurement

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Ezchrome Software with HPLC is being used. Data submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section#	Observation
1.	**3.2.S.4.1**	The Drug substance specification of Dexlansoprazole pellets as per innovator product does not mention optical rotation ,enantiomer ratio , and Chiral HPLC assay , which needs submission.
2.	**3.2.S.4.3**	• The submitted COA of Dexlansoprazole, conducted by M/s Vision Pharma does not mention identification/Assay of Dexlansoprazole through Chiral HPLC as Dexlansoprazole is R-isomer of Lansoprazole, nor optical rotation test is conducted. As the innovator product Cap Dexilent is USFDA approved, the review of innovator product specifically mention that drug substance should be assay by such method which ensures its enantiomeric form. • Justification of existing analytical method by HPLC and UV spectroscopy for conducting identification, assay and dissolution assay of Dexlansoprazole is required.
3.	**3.2.S.5**	The submitted COA of source of API working standard, (Dexlansoprazole) M/s Everest Organics Limited, India, has mentioned Identification /Assay through Chiral HPLC, however same is not depicted through COA of API by local pellets manufacturer. i-e M/s Vision pharmaceuticals, Islamabad. Dexlansoprazole is a racemic enantiomer of Lansoprazole, Optical rotation test is performed by API manufacturer, however as per COA of Pellets , same is not performed by Pellet manufacturer , as well as finished product manufacturer which needs clarification
4.	**3.2.P.2.2.1**	The comparative dissolution study and F2 calculation is not conducted at PH. 5.5 as required to establish similarity of initial release at ph 5.5.
5.	**3.2.P.5**	• Complete drug product specification(s) including tests, acceptance criteria and reference to analytical procedure along with impurities testing is required. • Complete analytical method validation study 0f assay on HPLC including specificity, Method precision, Accuracy, linearity, reproducibility, robustness and ruggedness is needed.
6.	**3.2.P.8**	• Frim has used UV spectroscopy method instead of HPLC method for conducting Assay for stability study data.which needs justification. • Invoice of procurement of pellets from source is missing which is also required.

Decision: Registration Board has deferred the case for submission of the reply for above cited shortcomings within six (6) months.

334.	Name, address of Applicant / Marketing Authorization Holder	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore

	Name, address of Manufacturing site.	M/s Jaskan Pharmaceutical Private Limited Plot No 50 Sunder Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28226 dated 13-09-2021
	Details of fee submitted	PKR 20,000/-: manual slip No1907515 dated 01-02-2021 & differential fee of PKR 10000/- slip No.30406862 dated 18-06-2021
	The proposed proprietary name / brand name	Dexil 60mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: DDR Dexlansoprazole (Enteric coated pellets) …. 60mg
	Pharmaceutical form of applied drug	Capsule Oral
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	Manufacturer's Specs
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved
	For generic drugs (me-too status)	Rasodex Capsule 60mg M/s Gets Pharma Reg. No. 086977
	GMP status of the Finished product manufacturer	cGMP No. FID-797667-1346 issued by DRAP valid till 25/10/2022. Section Renewal granted on 12-03-2021 section approval Copy Submitted by the firm.
	Name and address of API manufacturer.	Vision Pharmaceutical (Pvt)Ltd Plot No 22-23 Industrial Triangle Khuta Road Islamabad
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is

		submitted.
	Module III (Drug Substance)	Dexlansoprazole DDR pellets are prepare under manufacturer's Specs The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DXT 01, DXT 02, DXT 03)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence established vis-à-vis the brand leader, Rasodex Capsule 60mg by M/s Gets Pharma by performing quality tests the results of all the tests of both products fall within the specifications and are comparable. The firm has performed comparative analyses with innovator's product. The studies demonstrate comparable results with the innovator product. Jaskan pharma has been performed against the same brand that is Rasodex Capsule 60mg by Getz Pharma in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted reports of verification studies of analytical method for the drug substance. Firm has also submitted reports of validation of analytical method for the drug product.

STABILITY STUDY DATA			
Manufacturer of API	Vision Pharmaceutical (Pvt)Ltd Plot No 22-23 Industrial Triangle Khuta Road Islamabad		
API Lot No.	DLP562		
Description of Pack (Container closure system)	Sealed In Alu-Alu Poly bag in Plastic Drum		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months) Real Time: 0, 3, 6, (Months)		
Batch No.	DXT 01	DXT 02	DXT 03
Batch Size	1000 Capsules	1000 Capsules	1000 Capsules
Manufacturing Date	21-02-2020	21-02-2020	21-02-2020
Date of Initiation	02-04-2020	02-04-2020	02-04-2020
No. of Batches	03		

Administrative Portion

7.	Reference of previous approval of applications with stability study data of the firm (if any)	Jaxikan 100mg/5ml Susp Arixkan 1gm IV Injection Aquakan 5ml Injection
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of DML certificate No. 000806 and GMP Certificate No. F. 3-26/2019-Addl.Dir(QA & LT-1) both issued by DRAP Pakistan has been submitted
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Local procurement
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Ezchrome Software with HPLC is being used. Data submitted.
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section#	Observation
1.	**3.2.S.4.1**	The Drug substance specification of Dexlansoprazole pellets as per innovator product does not mention optical rotation ,enantiomer ratio , and Chiral HPLC assay , which needs submission.
2.	**3.2.S.4.3**	• The submitted COA of Dexlansoprazole, conducted by M/s Vision Pharma does not mention identification/Assay of Dexlansoprazole through Chiral HPLC as Dexlansoprazole is R-isomer of Lansoprazole,

		nor optical rotation test is conducted. As the innovator product Cap Dexilent is USFDA approved, the review of innovator product specifically mention that drug substance should be assay by such method which ensures its enantiomeric form. • Justification of existing analytical method by HPLC and UV spectroscopy for conducting identification, assay and dissolution assay of Dexlansoprazole is required.
3.	**3.2.S.5**	The submitted COA of source of API working standard, (Dexlansoprazole) M/s Everest Organics Limited, India, has mentioned Identification /Assay through Chiral HPLC, however same is not depicted through COA of API by local pellets manufacturer. i-e M/s Vision pharmaceuticals, Islamabad. Dexlansoprazole is a racemic enantiomer of Lansoprazole, Optical rotation test is performed by API manufacturer, however as per COA of Pellets , same is not performed by Pellet manufacturer , as well as finished product manufacturer which needs clarification
4.	**3.2.P.2.2.1**	The comparative dissolution study and F2 calculation is not conducted at PH. 5.5 as required to establish similarity of initial release at ph 5.5.
5.	**3.2.P.5**	• Complete drug product specification(s) including tests, acceptance criteria and reference to analytical procedure along with impurities testing is required. • Complete analytical method validation study 0f assay on HPLC including specificity, Method precision, Accuracy, linearity, reproducibility, robustness and ruggedness is needed.
6.	**3.2.P.8**	• Frim has used UV spectroscopy method instead of HPLC method for conducting Assay for stability study data.which needs justification. • Invoice of procurement of pellets from source is missing which is also required.

Decision: Registration Board has deferred the case for submission of the reply for above cited shortcomings within six (6) months.

C: Human (Local) (Deferred) Form- 5 F (CTD)

335.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s May & Baker Pharmaceuticals (Pvt.) Ltd. 45 Km, Thokar Multan road, Lahore**
	Name, address of Manufacturing site.	M/s May & Baker Pharmaceuticals (Pvt.) Ltd. 45 Km, Thokar Multan road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP)

		☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Evidence of Manufacturing facility	Issuance of DML vide letter no. F.1-10/2019-Lic. Dated 29-04-2022 for sections of Injectable ampoule (General), Capsule section (general), Dry powder suspension section (general), Dry powder vial section (general)
	Dy. No. and date of submission	Dy. No 26359 dated 19-09-2022
	Details of fee submitted	Rs.30,000/- dated 12-09-2022
	The proposed proprietary name / brand name	**WFI 5 ml Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5 ml ampoule contains: Water for Injection …….5 ml
	Pharmaceutical form of applied drug	Liquid injection
	Pharmacotherapeutic Group of (API)	Solvent/ Diluent
	Reference to Finished product specifications	USP/BP
	Proposed Pack size	1ml(1x1,s) (10's,14's,100's)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by USFDA, MHRA, Sterile water for Injection
	For generic drugs (me-too status)	WFI 5ml by Global Pharma
	GMP status of the Finished product manufacturer	Issuance of DML vide letter no. F.1-10/2019-Lic. Dated 29-04-2022 for sections of Injectable ampoule (General), Capsule section (general), Dry powder suspension section (general), Dry powder vial section (general)
	Name and address of API manufacturer.	N/A
	Module-II (Quality Overall Summary)	Firm has submitted summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, batch analysis and justification of specification, and stability studies of drug product is submitted.
	Module III (Drug Substance)	Official monograph of sterile Water for injection is present in BP and USP. The firm as submitted detail of nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, tests for, specifications, analytical procedures, batch analysis and justification of specification.
	Stability studies	N/A

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical and batch analysis and justification of specification, container closure system and stability studies of drug product
	Pharmaceutical equivalence and comparative dissolution profile	Water for Injection Mfg By : Amros Phamrceuticals .
	Analytical method validation/verification of product	N/A

STABILITY STUDY DATA

Manufacturer of API	N/A		
API Lot No.	N/A		
Description of Pack (Container closure system)	BP type 1 ,Glass ampoules		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 01	Trial 02	Trial 03
Batch Size	1000 ampoules	1000 ampoules	1000 ampoules
Manufacturing Date	02-2022	02-2022	02-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	N/A
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Submitted

Remarks of Evaluator:

1. Firm has mentioned drug substance specification with acceptance criteria mentioning white or off-white, FTIR absorption, impurities and assay that does not corresponds to Claimed B.P & USP specifications., clarify.

2. Declared Pharmacopoeia specification in 1.5.6 are mentioned USP specification where in COA of Bulk water for injection mention BP. Clarify
3. Test for Total Organic Carbon is not mentioned in COA, same is required.
4. Container Closure mentioned as inner Packaging material: LDPE for medical packing, justification for this container closure is required.
5. The description of primary container is required along with justification.
6. Specification of bulk water testing does not mention Total Organic Carbon (TOC) and microbial testing.
7. Firm has mentioned sieving process through mechanical sifter under description of manufacturing process, which needs clarification and resubmission.
8. Under filling process, firm has mentioned "Dark green color vol. yellow color body injection containing off whit colour "Justification is required
9. The finished product specification is mentioned as BP whereas under 1.5.6 it is mentioned as USP, Clarification of applied specification of product is required
10. Complete testing specification of finished product is required including test for sub visible particle.
11. The declared B.P monograph is "sterilized water for injection" for finished drug product, whereas firm has adopted nomenclature 4for finish drug product as 'water for injection', therefore correction throughout module 2 & 3, (P part) is required
12. Firm has mentioned Inactive martial as Shell No.03, Which needs clarification.
13. Required complete testing results conducted for stability studies data including PH/Alkalinity testing, Chloride, Ammonium, Calcium, Nitrate, sulphate, sub visible particles. TOC, conductivity test and, residue on evaporation for both real time and accelerated stability data for 6 months of trial batches.

Previous Decision of 320th meeting: The Board deferred the case for the above mentioned points.

Reply of firm vide dairy No 3002 dated 24-10-2022

SR #	Observation	Response of firm
1	Firm has mentioned drug substance specification with acceptance criteria mentioning white or off-white, FTIR absorption, impurities and assay that does not corresponds to Claimed B.P & USP specifications., clarify	It is typo error
2	Declared Pharmacopoeia specification in 1.5.6 are mentioned USP specification where in COA of Bulk water for injection mention BP. Clarify	It's a typo error B.P monograph has been adopted by the firm for the analysis of water and its specifications.
3	Test for Total Organic Carbon is not mentioned in COA, same is required.	Revised COA is submitted by firm .mentioning TOC test.
4	Container Closure mentioned as inner Packaging material: LDPE for medical packing, justification for this container closure is required	It's a typo error whereas the WFI is packed in 10 ml or 5 ml
5	The description of primary container is required along with justification	It is packed in glass ampoule of 5 ml or 10 ml .
6	Specification of bulk water testing does not mention Total Organic Carbon (TOC) and microbial testing	Firm has submitted revised COA mentioning TOC and microbial testing specifications.
7	Firm has mentioned sieving process through mechanical sifter under description of manufacturing process,	Revised manufacturing process is submitted by firm.

	which needs clarification and resubmission.	
8.	Under filling process, firm has mentioned "Dark green color vol. yellow color body injection containing off whit colour "Justification is required.	It's a typo error .The firm has submitted revised manufacturing process
9	The finished product specification is mentioned as BP whereas under 1.5.6 it is mentioned as USP, Clarification of applied specification of product is required	It's a typo error .The firm has adopted BP monograph for its testing specifications.
10	Complete testing specification of finished product is required including test for sub visible particle	Revised testing specification of finished product is submitted mentioning sub visible particle test.
11	Firm has mentioned Inactive martial as Shell No.03, Which needs clarification.	It's a typo error.
12	Required complete testing results conducted for stability studies data including PH/Alkalinity testing, Chloride, Ammonium, Calcium, Nitrate, sulphate, sub visible particles. TOC, conductivity test and, residue on evaporation for both real time and accelerated stability data for 6 months of trial batches	Firm has submitted revised stability study data for 6 months a per adopted BP specification for real time and accelerated data.

Decision: Approved with B.P specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Registration Board further decided that registration letter shall be issued after submission of applicable fee for pre-registration variation ,i-e 30000/= as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.**

336.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s May & Baker Pharmaceuticals (Pvt.) Ltd. 45 Km, Thokar Multan road, Lahore**
	Name, address of Manufacturing site.	M/s May & Baker Pharmaceuticals (Pvt.) Ltd. 45 Km, Thokar Multan road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Evidence of Manufacturing facility	Issuance of DML vide letter no. F.1-10/2019-Lic. Dated 29-04-2022 for sections of Injectable

		ampoule (General), Capsule section (general), Dry powder suspension section (general), Dry powder vial section (general)
	Dy. No. and date of submission	Dy. No 26360 dated 19-09-2022
	Details of fee submitted	Rs.30,000/- dated 12-09-2022
	The proposed proprietary name / brand name	**WFI 10 ml Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 10 ml ampoule contains: Water for Injection …….10 ml
	Pharmaceutical form of applied drug	Liquid injection
	Pharmacotherapeutic Group of (API)	Solvent/ Diluent
	Reference to Finished product specifications	USP/BP
	Proposed Pack size	1ml(1x1,s) (10's,14's,100's)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by USFDA, MHRA, Sterile water for Injection
	For generic drugs (me-too status)	Water for Injection of M/s Visison Pharma (Reg.# 032340)
	GMP status of the Finished product manufacturer	Issuance of DML vide letter no. F.1-10/2019-Lic. Dated 29-04-2022 for sections of Injectable ampoule (General), Capsule section (general), Dry powder suspension section (general), Dry powder vial section (general)
	Name and address of API manufacturer.	N/A
	Module-II (Quality Overall Summary)	Firm has submitted QOS information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, batch analysis and justification of specification, and stability.studies of drug product is submitted.
	Module III (Drug Substance)	Official monograph of sterile Water for injection is present in BP and USP. The firm as submitted detail of nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, tests for, specifications, analytical procedures, batch analysis and justification of specification.
	Stability studies	N/A
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical and batch analysis and justification of specification, container closure system and stability studies of drug product

	Pharmaceutical equivalence and comparative dissolution profile	Water for Injection Mfg. By : Amros Pharmaceuticals .
	Analytical method validation/verification of product	N/A

STABILITY STUDY DATA			
Manufacturer of API	N/A		
API Lot No.	N/A		
Description of Pack (Container closure system)	BP type 1 ,Glass ampoules		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 01	Trial 02	Trial 03
Batch Size	1000 ampoules	1000 ampoules	1000 ampoules
Manufacturing Date	02-2022	02-2022	02-2022
No. of Batches	03		

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	N/A
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	N/A
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Submitted

Remarks of Evaluator:

1. Firm has mentioned drug substance specification with acceptance criteria mentioning white or off-white, FTIR absorption, impurities and assay that does not corresponds to Claimed B.P & USP specifications., clarify.
2. Declared Pharmacopoeia specification in 1.5.6 are mentioned USP specification where in COA of Bulk water for injection mention BP. Clarify
3. Test for Total Organic Carbon is not mentioned in COA, same is required.
4. Container Closure mentioned as inner Packaging material: LDPE for medical packing, justification for this container closure is required.
5. The description of primary container is required along with justification.

6. Specification of bulk water testing does not mention Total Organic Carbon (TOC) and microbial testing.
7. The finished product specification is mentioned as BP whereas under 1.5.6 it is mentioned as USP, Clarification of applied specification of product is required
8. Complete testing specification of finished product is required including test for sub visible particle.
9. The declared B.P monograph is "sterilized water for injection" for finished drug product, whereas firm has adopted nomenclature for finish drug product as 'water for injection' , therefore correction throughout module 2 & 3, (P part) is required
10. Required complete testing results conducted for stability studies data including PH/Alkalinity testing, Chloride, Ammonium, Calcium, Nitrate, sulphate, sub visible particles. TOC, conductivity test and, residue on evaporation for both real time and accelerated stability data for 6 months of trial batches.

Previous Decision of 320th meeting: The Board deferred the case for the above mentioned points.

Reply of firm vide dairy No 3002 dated 24-10-2022

SR #	Observation	Response of firm
1	Firm has mentioned drug substance specification with acceptance criteria mentioning white or off-white, FTIR absorption, impurities and assay that does not corresponds to Claimed B.P & USP specifications., clarify	It is typo error
2	Declared Pharmacopoeia specification in 1.5.6 are mentioned USP specification where in COA of Bulk water for injection mention BP. Clarify	It's a typo error B.P monograph has been adopted by the firm for the analysis of water and its specifications.
3	Test for Total Organic Carbon is not mentioned in COA, same is required.	Revised COA is submitted by firm .mentioning TOC test.
4	Container Closure mentioned as inner Packaging material: LDPE for medical packing, justification for this container closure is required	It's a typo error whereas the WFI is packed in 10 ml or 5 ml
5	The description of primary container is required along with justification	It is packed in glass ampoule of 5 ml or 10 ml .
6	Specification of bulk water testing does not mention Total Organic Carbon (TOC) and microbial testing	Firm has submitted revised COA mentioning TOC and microbial testing specifications.
7	Firm has mentioned sieving process through mechanical sifter under description of manufacturing process, which needs clarification and resubmission.	Revised manufacturing process is submitted by firm.
8.	Under filling process, firm has mentioned "Dark green color vol. yellow color body injection containing off whit colour "Justification is required.	It's a typo error .The firm has submitted revised manufacturing process
9	The finished product specification is mentioned as BP whereas under 1.5.6 it is mentioned as USP, Clarification of applied specification of product is required	It's a typo error .The firm has adopted BP monograph for its testing specifications.

10	Complete testing specification of finished product is required including test for sub visible particle	Revised testing specification of finished product is submitted mentioning sub visible particle test.
11	Firm has mentioned Inactive martial as Shell No.03, Which needs clarification.	It's a typo error.
12	Required complete testing results conducted for stability studies data including PH/Alkalinity testing, Chloride, Ammonium, Calcium, Nitrate, sulphate, sub visible particles. TOC, conductivity test and, residue on evaporation for both real time and accelerated stability data for 6 months of trial batches	Firm has submitted revised stability study data for 6 months a per adopted BP specification for real time and accelerated data.

Decision: Approved with B.P specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**
- **Registration Board further decided that registration letter shall be issued after submission of applicable fee for pre-registration variation ,i-e 30000/= as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.**

D- Human (Import) (Deferred) Form-5-A

337.	Name and address of Applicant	Name: Revive Healthcare Address: 503, 5th floor, Eden Hieghts,6 Main Gulberg, Jail road, Lahore
	Detail of Drug Sale License	Name: Revive Healthcare Address: 503, 5th floor, Eden Hieghts,6 Main Gulberg, Jail road, Lahore Go-down address: N/A License No: 05-352-0065-031159D Validity: 21st May 2020 Status: Distributor license in Form No. 11
	Name and address of manufacturer	United Biotech (p) Limited, Bagbania, Baddi-Nalagarh Road, District Solan(HP)-174 101,India
	Name and address of marketing authorization holder	United Biotech (p) Limited, Bagbania, Baddi-Nalagarh Road, District Solan(HP)-India
	Name of exporting country	India
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No. 13066 dated 06-03-2019
	Fee including differential fee	Rs.100000/- dated 06-03-2019 Challan No.1902056 dated: 06.03.2019
	Brand Name +Dosage Form + Strength	UNIFOLIN 100 Injection
	Composition	Each Vail Contains; Leucovorin Calcium ……100 mg/10 ml
	Finished Product Specification	USP

	Pharmacological Group	Detoxifying agent for antineoplastic treatment
	Shelf life	24 Month (2-8 C)
	Demanded Price	As per DPC
	Pack size	1's
	International availability	Not traceable
	Me-too status	Not varified
	Stability studies	Firm has submitted real-time stability data sheets conducted at 5^0C ± 3ºC three industrial batches for 24 months (Shelf life 24 months) and accelerated stability data sheets conducted at 25^0C ± 2 ºC and 65%RH ± 5%RH of three industrial batches for six months. Mfg. Date: 06-2013
	Detail of certificates attached	**legalized GMP certificate:** Certificate No: HFW-H(Drugs)427/05 Certifying Authority: State Drugs Controller, Controlling Cum Licensing Authority Nagar panchayat Bhawan, Sai road baddl dist,Solan. **Scan copy of legalized DML.** Serial: Not Provided **Original legalized CoPP (Embassy attested).** Certificate No: **HFW-H9(DRUGS) 461/05/241 18-09-2019** Certificate date:22-01-2018 Certifying Authority: Office of State Drugs Controller, Licensing Authority Cum Controlling Authority Health & family welfare Department, Himachal Pradesh, India Validity: 18-09-2019 **legalized Free sale Certificate.** Certificate No: HFW-H(DRUGS)/427/09 Certifying Authority: State Drugs Controller, Licensing Authority Cum Controlling Authority, Baddi, District -Solan (HP) Issuing Date: 21-11-2017 **Agency Agreement (Copy)** Between Revive Healthcare, 503, 5th floor, Eden Hieghts,6 Main Gulberg, Jail road, Lahore. (Distributor) and United BioTech (P) Limited, E-142, aket, New Dehli 110017. India. **Date of Agreement:** 01-03-2012 **Validity:** Complete agreement mentioning validity is not provided.
	Remark of the Evaluator [XVI]	1. DML (copy) is not provided. 2. Firm has conducted Accelerated stability study for 3 batch at 65 % RH, whereas recommended Relative Humidity is 60 % for accelerated stability study.

		3. Original legalized (Embassy attested) CoPP is missing. Copy is provided which is also expired. 4. Legalized copy of GMP certificate is missing, Photocopy is provided valid up to 18-09-2019. 5. Complete Agency /Exclusive distribution agreement mentioning validity is not provided. 6. DSL expired. 7. Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting. 8. Form 5-A mentioning "UNIFOLIN(Leucovorin) Injection 50 mg, where in attached annexures the composition as label claim is Each Vial Contains Leucovorin calcium Injection 100 mg/10 ml. 9. evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. 10. Product label does not have" URDU "Inscription as required under drug labeling and packaging rule 1978.

Decision of 321st meeting: Deferred for following shortcomings:

1. DSL (copy) is not provided.
2. Firm has conducted Accelerated stability study for 3 batch at 65 % RH, whereas recommended Relative Humidity is 60 % for accelerated stability study.
3. Original legalized (Embassy attested) CoPP is missing. Copy is provided which is also expired.
4. Legalized copy of GMP certificate is missing, Photocopy is provided valid up to 18-09-2019.
5. Complete Agency /Exclusive distribution agreement mentioning validity is not provided.
6. DSL expired.
7. Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.
8. Form 5-A mentioning "UNIFOLIN(Leucovorin) Injection 50 mg, where in attached annexures the composition as label claim is Each Vial Contains Leucovorin calcium Injection 100 mg/10 ml.
9. evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
10. Product label does not have" URDU "Inscription as required under drug labeling and packaging rule 1978.

Reply/response of Firm vide dairy No.23549 dated 19-08-2022

Sr#	Shortcomings	Reply
1	DML (copy) is not provided	DML copy attached
2	Firm has submitted Accelerated stability study data for 3 batches at 65 % RH, whereas recommended Relative Humidity is 60 % for	We have already provided Accelerated stability at Humidity of 60%, Nevertheless we have again attached stability study data for your reference of 60% RH.

	accelerated stability study which needs clarification.	
3	Original legalized (Embassy attested) CoPP is missing. Copy is provided which is also expired	Original legalized Valid (Embassy attested) CoPP is attached
4	Legalized copy of GMP certificate is missing, Photocopy is provided valid up to 18-09-2019.	Legalized Valid copy of GMP attached
5	Complete Agency /Exclusive distribution agreement mentioning validity is not provided.	Valid Complete Agency /Exclusive distribution agreement attached
6	DSL expired	Valid DSL copy attached
7	Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting	Evidence of applied product in RRA attached **Product:** Leucovorin Calcium Injection 100mg/10ml **Company:** Bedford Laboratories (**USFDA Approved)**
8	Form 5-A mentioning UNIFOLIN(Leucovorin) Injection 50 mg, where in attached annexures the composition as label claim is ''Each Vial Contains Leucovorin calcium Injection 100 mg/10 ml''.	It was typographic mistake 50mg, Updated form 5-A attached with corrected amount of API in vial (100 mg/10ml) and **Label Claim:** Each mL contains: Leucovorin calcium eq. to Leucovorin …….10 mg
9	Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.	**Evidence of generic-me too approval by DRAP:** CALFONATE INJECTION 100MG by M/s GHAZALI BROTHERS, Reg. No. 70936
10	Proposed Product label does not have" URDU "Inscription as required under drug labeling and packaging rule 1978	Updated artworks with URDU "Inscription" attached

Remarks of Evaluator:

- Firm has provided RRA reference of Injection Lecuvorin Calcium 100mg/10 ml manufactured by M/s Bedford laboratories, (USFDA approved), The said RRA reference is not verifiable.
- Firm has submitted scan copy of COPP with original embassy attestation
- Applied finished product Injection Leucovorin calcium 100 mg/10ml is approved in MHRA under the generic drug as Injection Calcium Folinate (as Folinic Acid) 100 mg/ 10 ml.

Decision: Approved with USP specification as under.

"Each 10 ml Vial contain;

Leucovorin Calcium eq to Leucovorin……100 mg (10mg/ml)".

- **Registration Board further decided that registration letter shall be issued after submission of applicable full fee for pre-registration variation ,i-e 100000/= as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction of label claim.**

338.	Name and address of Applicant	Name: Revive Healthcare Address: 503, 5th floor, Eden Hieghts,6 Main Gulberg, Jail road, Lahore
	Detail of Drug Sale License	Name: Revive Healthcare

		Address: 503, 5th floor, Eden Hieghts,6 Main Gulberg, Jail road, Lahore Go-down address: N/A License No: 05-352-0065-031159D Validity: 21st May 2020 Status: Distributor license in Form No. 11
	Name and address of manufacturer	United Biotech (p) Limited, Bagbania, Baddi-Nalagarh Road, District Solan(HP)-174 101,India
	Name and address of marketing authorization holder	United Biotech (p) Limited , Bagbania, Baddi-Nalagarh Road, District Solan(HP)-India
	Name of exporting country	India
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No. 13065 dated 06-03-2019
	Fee including differential fee	Rs.100000/- dated 06-03-2019 Challan No.1902057 dated: 06.03.2019
	Brand Name +Dosage Form + Strength	UNIPLATIN Injection 50 mg
	Composition	Each Vail Contains; Cisplatin …….50 mg/50ml
	Finished Product Specification	BP
	Pharmacological Group	Other antineoplastic agents (Platinum compounds)
	Shelf life	24 Month
	Demanded Price	As per DPC
	Pack size	1's * 50 ml
	International availability	Cisplatin 1 mg/ml Concentrate for solution for infusion (50ml vial) by M/s EBEWE Pharma (MHRA approved)
	Me-too status	UNISTIN 50mg vial by M/s Al- Habib Pharma (Reg#020661)
	Stability studies	Firm has submitted long term stability data sheets conducted at 25 ºC ± 2ºC and 60% RH for three industrial batches for 24 months (Shelf life 24 months) and accelerated stability data sheets conducted at 40^0C ± 2 ºC and 75%RH ± 5%RH of three industrial batches for six months. Mfg. Date: 07-2015
	Detail of certificates attached	**legalized GMP certificate:** Certificate No: HFW-H(Drugs)427/05 Certifying Authority: State Drugs Controller, Controlling Cum Licensing Authority Nagar panchayat Bhawan, Sai road baddl dist, Solan. Validity: 18-09-2019 **Scan copy of legalized DML.** Serial: Not Provided **Original legalized CoPP (Embassy attested).** Certificate No: **HFW-H(DRUGS) 461/05/231** Certificate date:22-01-2018 Certifying Authority: Office of State Drugs Controller, Licensing Authority Cum

		Controlling Authority Health & family welfare Department, Himachal Pradesh, India. Validity: 18-09-2019 **legalized Free sale Certificate.** Certificate No: HFW-H(DRUGS)/427/09 Certifying Authority: State Drugs Controller, Licensing Authority Cum Controlling Authority, Baddi, District -Solan (HP) Issuing Date: 21-11-2017 **Agency Agreement (Copy)** Between Revive Healthcare, 503, 5th floor, Eden Hieghts,6 Main Gulberg, Jail road, Lahore. (Distributor) and United BioTech (P) Limited, E-142, aket, New Dehli 110017. India. **Date of Agreement:** 01-03-2012 **Validity:** Complete agreement mentioning validity is not provided.
	Remark of the Evaluator [XVI]	1. DML (copy) is not provided. 2. The temperature and humidity conditions (25 ºC ± 2ºC and 60% RH) of the submitted stability study data for long term stability of 3 batches is not according to zone IV a, which needs clarification. 3. Original legalized (Embassy attested) CoPP is missing. Copy is provided which is also expired. 4. Legalized copy of GMP certificate is missing, Photocopy is provided valid up to 18-09-2019. 5. Complete Agency /Exclusive distribution agreement mentioning validity is not provided. 6. DSL expired. 7. Label claim in firm 5A mentions 50 mg/5ml, where in attached annexure master formulation is mentioned as 50 mg/20 ml, which needs clarification.
	Decision of 321st meeting: Deferred for following shortcomings: 1. DSL (copy) is not provided. 2. The temperature and humidity conditions (25 ºC ± 2ºC and 60% RH) of the submitted stability study data for long term stability of 3 batches is not according to zone IV a, which needs clarification. 3. Original legalized (Embassy attested) CoPP is missing. Copy is provided which is also expired. 4. Legalized copy of GMP certificate is missing, Photocopy is provided valid up to 18-09-2019. 5. Complete Agency /Exclusive distribution agreement mentioning validity is not provided. 6. DSL expired. 7. Label claim in firm 5A mentions 50 mg/5ml, where in attached annexure master formulation is mentioned as 50 mg/20 ml, which needs clarification.	
	Reply of firm vide dairy No.23548 dated 19-08-2022	

Sr#	Shortcomings	Reply
1	DML (copy) is not provided	DML copy attached
2	The temperature and humidity conditions (25 ^{o}C ±2^{o}C and 60% RH) of the submitted stability study data for long term stability of 3 batches is not according to zone IVa, which needs clarification	Product manufacturer (United Biotech India), performed stability studies both on Zone IVa & Zone IVb. Zone IVa stability study data (30 ^{o}C ±2^{o}C and 65% ± 5% RH) is attached for your reference
3	Original legalized (Embassy attested) CoPP is missing. Copy is provided which is also expired	Original legalized Valid (Embassy attested) CoPP is attached
4	Legalized copy of GMP certificate is missing, Photocopy is provided valid up to 18-09-2019.	Legalized Valid copy of GMP attached
5	Complete Agency /Exclusive distribution agreement mentioning validity is not provided.	Valid Complete Agency /Exclusive distribution agreement attached
6	DSL expired	Valid DSL copy attached
7	Label claim in firm 5A mentions 50 mg/5ml, where in attached annexure master formulation is mentioned as 50 mg/20 ml, which needs clarification	It was typographic mistake in Form 5-A & Master formula. Updated form 5-A & Master formula attached with corrected label claim of **50 mg/50ml** (as per COPP)
8	Proposed Product label does not have" URDU "Inscription as required under drug labeling and packaging rule 1978	Updated artworks with URDU "Inscription" attached

Remarks of Evaluator:
Firm has submitted scan copy of COPP with original embassy attestation

Decision: Approved with B.P specifications with following label claim,
"Each 5ml Vial Contains:
Cisplatin ……50 mg (10mg/ml)"
Registration Board further decided that registration letter shall be issued after submission of applicable full fee for pre-registration variation, i-e 100000/= as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021 for correction of master formulation as 50mg/5 ml .

E :- Human (Local) (Deffered) Form-5

339.	Name and address of manufacturer/ Applicant	Genix Pharma (Pvt) Ltd.44,45-B, Korangi Chowk Road, Karachi.
	Brand Name + Dosage Form + Strength	TEGLIP Tablet 20 mg
	Composition	Each Film Coated Tablet Contains: Teneligliptin Hydrobromide Hydrate eq. to Teneligliptin……20 mg
	Diary No. Date of R & I & fee	Dy. No 11977 dated 06-03-2019; Rs.50,000/- dated 06-03-2019.
	Pharmacological Group	Antidiabetic
	Type of Form	Form – 5D
	Finished product Specification	Innovator Specification
	Pack size & Demanded Price	7's,14's,28's,10's,20's &30's, As per SRO.
	Approval status of product in Reference Regulatory Authorities	Tablet Tenelia, Mitsubishi Tanabe Pharma, PMDA Japan.

	Me-too status	Not provided.	
	GMP status	GMP inspection was conducted on 12-02-2020 and concluded as, "*Based on the area inspected, the people met and the document reviewed and considering the findings of the inspection including the observation listed above M/s Genix Pharma Private Limited Located at Plot No.44-45-B Korangi, Creek Road Karachi, Pakistan was considered to be operating at a good level of compliance with cGMP guideline as of today."*	
	Remarks of the Evaluator	• Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. • Stability study data as per guidelines provided in 293rd meeting of Registration Board is required. • Form-5 Annexure as per prescribed format of Drug (L, R&A) rules 1976.	• Form submitted reply and submitted me-too reference as tablet Tenliptin,Reg # 105239,Indus Pharma , the same is not verifiable from available record. • Firm has submitted scan copy of Form-5 annexure on prescribed format.
	Previous decision of 321st meeting: Deferred for following • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. • Stability study data as per guidelines provided in 293rd meeting of Registration Board is required.		
	Reply of the firm : Firm has attached mee too reference of Tablet Tenliptin ,Reg No 105239 of Indus Pharma khi.		
	Remarks of evaluator : Stability study data as per guidelines provided in 293rd meeting of Registration Board is required		
	Decision: Registration Board deferred for submission of stability study data as per guidelines in 293rd meeting of Registration board and evaluation /consideration on its own turn.		
340.	Name and address of manufacturer/ Applicant	Reliance Pharma, Plot No.08, street No. S-8, RCCI Industrial Estate, Rawat, Islamabad.	
	Brand Name + Dosage Form + Strength	RELISONE Tablet 50 mg	
	Composition	Each Film Coated Tablet Contains: Eperisone HCl Eq to Eprisoone …….50 mg	
	Diary No. Date of R & I & fee	Dy. No 12508 dated 06-03-2019; Rs.50,000/- dated 06-03-2019.	
	Pharmacological Group	SSRI	
	Type of Form	Form-5	
	Finished product Specification	Innovator's Specification	

	Pack size & Demanded Price	3*10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities	Expose 50mg film coated tablet, AIFA approved.
	Me-too status	Perispa 50mg tablets, Platinum pharma, Reg. No. 039302.
	GMP status	GMP status/report within last 3 years not provided
	Remarks of the Evaluator	Deficiency letter was issued to firm and asked to provide: • Finished Product specification not provided or undertaking to follow innovator's specification. • Firm has mentioned Methylene chloride in their master formulation which is prohibited. • All the submitted Form-5 Annexures are without any signature/stamp on plain paper. • GMP inspection report conducted within last 3 years is not provided. • Preregistration variation fee challan.
	Previous decision of 317th meeting: Deferred for following shortcomings; 1. Finished Product specification not provided or undertaking to follow innovator's specification. 2. Firm has mentioned Methylene chloride in their master formulation which is prohibited. 3. All the submitted Form-5 Annexures are without any signature/stamp on plain paper. 4. GMP inspection report conducted within last 3 years is not provided. 5. Preregistration variation fee challan.	
	Reply of the Firm vide dairy No 24112 dated 26-08-2022 • Firm has submitted revised / signed Form -5 annexure along with finished good specification as "Innovators specification " • Firm has submitted copy of GMP certificate dated 11-08-2022 issued on the basis of inspection conducted on 19-01-2022 (Capsule Section) • Firm has submitted revised master formulation without methylene chloride.	
	Remarks :	
	Decision: Approved with innovators specification. Registration Board further decided that registration letter shall be issued after submission of applicable fee of Rs. 30,000/=for pre-registration variation/correction of master formulation, as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.	
341.	Name and address of manufacturer/ Applicant	Reliance Pharma, Plot No.08, street No. S-8, RCCI Industrial Estate, Rawat, Islamabad.

	Brand Name + Dosage Form + Strength	RELIFOXINE CAPSULE 50 mg
	Composition	Each Capsule Contains: Etifoxine Hcl …….5o mg
	Diary No. Date of R & I & fee	Dy. No 12507 dated 06-03-2019; Rs.50,000/- dated 06-03-2019.
	Pharmacological Group	SSRI
	Type of Form	Form-5
	Finished product Specification	Manufacturer's Specification
	Pack size & Demanded Price	3*10's, As per SRO.
	Approval status of product in Reference Regulatory Authorities	STRESAM, capsule". ANSM, France approved
	Me-too status	Stresam capsule 50mg of M/s CCL Pharma (Reg# 024595)
	GMP status	GMP status/report within last 3 years not provided
	Remarks of the Evaluator	Deficiency letter was issued to firm and asked to provide: • Finished Product specification not provided or undertaking to follow innovator's specification. • All the submitted Form-5 Annexures are without any signature/stamp on plain paper. • `GMP inspection report conducted within last 3 years is not provided. • Preregistration variation fee challan.
	Previous decision of 317th meeting: Deferred for following Shortcomings; 1. Finished Product specification not provided. 2. All the submitted Form-5 Annexures are without any signature/stamp on plain paper. 3. GMP inspection report conducted within last 3 years is not provided. 4. Preregistration variation fee challan.	
	Reply of the Firm vide dairy No. 24111 dated 26-08-2022 • Firm has submitted revised / signed Form -5 annexure along with finished good specification as "Innovators specification " • Firm has submitted copy of GMP certificate dated 11-08-2022 issued on the basis of inspection conducted on 19-01-2022 (Capsule Section **)**	
	Evaluators remarks :	
	Decision: Approved with innovators specification. Registration Board further decided that registration letter shall be issued after submission of applicable fee of Rs. 30,000/=for pre-registration variation/correction of master formulation, as per notification No.F.7-11/2012-B&A/DRAP dated 07- 05-2021.	
342.	Name and address of manufacturer / Applicant	Pharmasol (Pvt) Ltd. Plot No. 549, Sundar Industrial Estate, Raiwind Road, Lahore

	Brand Name +Dosage Form + Strength	Soquin Cream 4% w/w
	Composition	Each Gram of Cream Contains: Hydroquinone ……4gm
	Diary No. Date of R& I & fee	Dy. No. 12742 dated 06.03.2019 Rs. 20,000/- dated 06.03.2019
	Pharmacological Group	
	Type of Form	Form 5
	Finished Product Specification	The firm has claimed USP specs.
	Pack size & Demanded Price	10g, 15g, 20g; As per SRO
	Approval status of product in Reference Regulatory Authorities.	Corrector 4% Cream by M/s VIVIER CANADA INCORPORATED (Health Canada approved) Status of the product on the website of Health Canada is "***Cancelled Post Market***"
	Me-too status	Hydrofair Cream 4% by M/s Scotmann (Reg#028278)
	GMP status	Firm has submitted copy of GMP certificate No. 140/2022-DRAP (AD-084433115014) dated 26-08-2022 on the basis of inspection conducted on 22-08-2022.
	Remarks of the Evaluator.	• The drug product specifications have not been evaluated.
		• Revise the label claim from Hydroquinone…4gm to Hydroquinone…40mg. • You have not mentioned any emulsifying agent. Clarify. • Add packing process to the manufacturing outlines. • Revise the pharmacological group. • For above revisions, submit the applicable fee as per notification 7-11/2012-B&A/DRAP dated 07.05.2021 and 13.07.2021.
	Previous decision of 321st meeting: Deferred for followings; • Revision of the label claim from Hydroquinone 4gm to Hydroquinone 40mg with applicable fee as per notification 7-11/2012-B&A/DRAP dated 07.05.2021 and 13.07.2021. • Justification for not mentioning any emulsifying agent. • Revision of the manufacturing outlines with adding packing process. • Revise the pharmacological group. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.	
	Reply of the Firm vide dairy No.30795 dated 31-10-2022: • Firm has submitted revised formulation as under, with preregistration variation fee challan of PKR 30000/= vide slip No; 025524845 dated 28-10-2022 Soquin Cream 4 % "**Each Gram Contains:** **Hydroquinone ……40 mg"** • **Firm has submitted revised Form-5 mentioning Pharmacological group as Depigmentation agent and finished product specifications as USP specifications.** • **Firm has submitted revised masterformulation mentioning Cetomacrogol 100 as emulsifying agent.**	

	• **Firm has submitted revised manufacturing outline and incorporated packaging process.**
	Evaluator remarks : Status of the product on the website of Health Canada is "***Cancelled Post Market***"
	Decision: Registration Board deferred the case for submission of RRA reference as submitted reference of product stands canceled post market.

Item No. VIII: Agenda of Evaluator-XVIII (Mr. Muneeb Ahmed)

Case No. 1 Priority Consideration based on Export.

Below mentioned products have been referred by PR section vide letter No. 1-6/2019-PR (EFD) dated 06.10.2022 for consideration on priority as per direction of Authority in its 133rd meeting for the firms who have achieved benchmark f export of more than 100000USD. Accordingly, the details are as under

343.	**Name and address of manufacture / Applicant**	**M/s Sante (Pvt) Ltd., A-97 S.I.T.E. Super Highway Karachi**
	Brand Name + Dosage Form and Strength	Xebrom Ophthalmic Solution
	Composition	Each ml contains: Bromfenac Sodium Hydrate eq. to Bromfenac…….0.9
	Dairy No. date of R &I fee	Dy. No. 88 dated 31.01.2013 Rs. 20000/- and Rs. 30000/- dated 23.04.2014
	Pharmacological Group	Anti-inflammatory agents, non-steroids
	Type of form	Form 5D
	Finished product specifications	Manufacturer Specifications
	Pack size and Demand Price	Rs. 575 1.7ml bottle
	Approval status of product in Reference Regulatory Authorities	Yellox 0.9 mg/ml eye drops solution (EMA Approved)
	Me-too-status	Not provided
	GMP Status	
	Remark of the Evaluator	
	Decision:	

STABILITY STUDY DATA	
Manufacturer of API	M/s Farmak A.S. Na Vlcinci 16/3 Klasterni Hradisko 77900 Olomouc Czech Republic
API Lot No.	01010917
Description of Pack (Container closure system)	LDPE bottle of 5ml with LDPE Nozzle and HDPE Cap
Stability Storage Condition	Accelerated: 40°C ± 25°C% RH Real Time: 30°C ± 2°C / 35% ± 5%RH
Time Period	Accelerated: 6 Months Real Time: 6 Months
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0,1, 2, 3, 4 & 6 (months)
XEBROM OPHTHALMIC SOLUTION	

Batch No.		007-SO7	007-SO8	007-SO9
Batch Size		5L	5L	5L
Manufacturing Date		09.2020	09.2020	09.2020
Date of Initiation		27.10.2020	27.10.2020	27.10.2020
DOCUMENTS / DATA PROVIDED BY THE APPLICANT			
1.	Reference of previous approval of applications with stability study data of the firm	The firm has submitted reference of previous approval of applications with stability study data of the firm	
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA of the drug substance from API Manufacturer and COA by them	
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	The firm has submitted method used for analysis of API from both API Manufacturer and Finished Product manufacturer	
4.	Stability study data of API from API manufacturer	The firm has submitted stability study data of API from API manufacturer	
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate of API manufacturer issued by concerned regulatory authority.	
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted the Airway bill and invoice but not DRAP attested.	
7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study	
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of FPP	
9.	Drug-excipients compatibility studies (where applicable)	The firm has submitted that formulation is qualitatively same with the Innovator brand hence the compatibility studies are not required.	
10.	Complete batch manufacturing record of three stability batches.	Submitted	
11.	Record of comparative dissolution data (where applicable)	Submitted	
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies	
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and audit trail reports for HPLC analysis for all the three batches.	
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted.	
Remarks:			

The firm has addressed all the observations as reflected in the agenda vide response submitted dated 03.11.2022 Dy. No. 31576. Hence the keeping in view the response of the firm Board decided as under:

Decision: Approved as per Innovator's Specifications with following conditions before issuance of registration:

i. **Firm shall submit new brand name as applied name has resemblance with Innovator brand name.**

ii. **As the firm has added specifications for antimicrobial preservative assay in Finished product specifications, hence the aforesaid assay results shall be submitted for the next time point along with method of analysis & chromatograms for confirmation.**

344.	**Name and address of manufacture / Applicant**	**M/s Sante (Pvt) Ltd., A-97 S.I.T.E. Super Highway Karachi**
	Brand Name + Dosage Form and Strength	Nepac Forte 0.3% Ophthalmic suspension
	Composition	Each ml contains: Nepafenac (Sterile, Micronized)……..3mg
	Dairy No. date of R &I fee	Dy. No. 1128: 2-6-2016PKR 20,000/- 1-6-2016
	Pharmacological Group	Non-steroidal anti-inflammatory (Prodrug)
	Type of form	Form 5
	Finished product specifications	
	Pack size and Demand Price	5ml: Rs. 1000/-
	Approval status of product in Reference Regulatory Authorities	Nevanac ophthalmic suspension by Novartis (MHRA Approved)
	Me-too-status	ILevro Eye Drops of M/s Novartis Pharma Karachi
	GMP Status	
	Remark of the Evaluator [II]	
	Decision:	

STABILITY STUDY DATA			
Manufacturer of API	M/s ArkGen Pharma Pvt Limited Plot No. 53-B Kohlar KIADB Industrial Area Bidar-585 401		
API Lot No.	NEPFA00819		
Description of Pack (Container closure system)	Plastic bottle of 5ml		
Stability Storage Condition	Accelerated: 40°C ± 25°C% RH Real Time: 30°C ± 2°C / 35% ± 5%RH		
Time Period	Accelerated: 6 Months Real Time: 6 Months		
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0,1, 2, 3, 4 & 6 (months)		
NEPAC FORTE 0.3% OPHTHALMIC SUSPENSION			
Batch No.	007-SO7	007-SO8	007-SO9
Batch Size	5L	5L	5L
Manufacturing Date	09.2020	09.2020	09.2020
Date of Initiation	27.10.2020	27.10.2020	27.10.2020
DOCUMENTS / DATA PROVIDED BY THE APPLICANT			

1.	Reference of previous approval of applications with stability study data of the firm	
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA of the drug substance from API Manufacturer and Finished Product manufacturer.
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	
4.	Stability study data of API from API manufacturer	
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate vide No. DCD/SPL-1/CR-148/2021-22 dated 16.06.2021 which is valid till one year issued by drug Control Department Govt. of Karnataka.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted the Airway bill and invoice but not DRAP attested.
7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of FPP
9.	Drug-excipients compatibility studies (where applicable)	Not submitted
10.	Complete batch manufacturing record of three stability batches.	
11.	Record of comparative dissolution data (where applicable)	
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and audit trail reports for HPLC analysis for all the three batches.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	

Evaluation by PEC:

Queries	**Reply**
Invoice submitted for the import of API i.e. Nepafenac manufactured by M/s ArkGen Pharma Pvt Limited Bidar India is not attested by the DRAP. Further another DRAP attested invoice for import of API manufactured/ exported by Hangzhou Zhongbao Imp & Exp. China is submitted. This needs clarification.	Firm has submitted the copy of DRAP Karachi attested invoice vide Dy. Bo. 12251 dated 060.11.2019.

Invoice submitted for the import of API i.e. Nepafenac manufactured by M/s ArkGen Pharma Pvt Limited Bidar India is not attested by the DRAP. Further another DRAP attested invoice for import of API manufactured/ exported by Hangzhou Zhongbao Imp & Exp. China is submitted. This needs clarification.	Don't consider these documents, it's our alternate approved source for Nepac 0.1% ophthalmic suspension (075809)
Justification for using 3% overage.	3% overage is used to avoid transfer losses and production loses in small scale stability batches, we will review the overage percentage at the time of commercial scale production.
The stability data provided for API does not reflect that it has been provided by the API manufacturer. Hence following needs to be submitted: i. Letter of authorization for provision of API from manufacturer i.e. M/s ArkGen Pharma Pvt Limited India. ii. Stability data accelerated and long term indicating the batch size, batch number and container closure systems. iii. Clarification for not performing sterility testing during stability testing. iv. Clarification required as 24 months of long term data is provided, however the retest period as per Certificate of analysis is 48 months (four years). v. Justification for proposing retest period rather shelf life as the API is known to be (heat) labile.	Firm has submitted commercial invoioce attested by AD I&E DRAP & stability data accelerated (6 months) and long term (60months) indicating the batch size, batch number and container closure systems along with performance of sterility testing.
API specifications proposed by you includes identification, particle size determination and sterility but procedure is not submitted.	Identification and sterility method has been incorporated in API test method, however particle size determination complies as per manufacturer.
In stability batches you are proposing 1.7ml filled volume in 5ml bottle but the innovator product contains 3ml filed volume in 5ml bottle. This needs justification.	In stability batches we have used, we have used 1.7ml pack size as per Innovator Ilevro by Alcon having pack size of 1.7ml. However the proposed pack size will be 3ml as per other brands registered by DRAP
Justification with suitable references of proposing pH 4.0 to 8 in finished product specifications.	Firm has submitted that they followed general Chapter of USP <771>.
Justification for not performing identity and assay of benzalkonium chloride and sodium edetate, particle size, osmolality, redispersibility, viscosity, uniformity of dosage unit and filled volume being critical quality attributes of the applied product. This needs to clarify with references	Firm informed that they have used benzalkonium chloride only as preservative and they are not using disodium edetate, however the formulation details submitted indicates that 0.1mg/ml of disodium edetate.

	Particle size test is justified with particulate matter in ophthalmic solutions <789> benzalkonium chloride assay, particle size, osmolality, redispersibility, viscosity, uniformity of dosage unit and filled volume were performed at the initial stage. Justification of specifications for aforesaid parameters is required.
Certificate of analysis (COA) submitted in respect of all three stability batches indicates storage conditions at 2-25^{o}C. This needs to justified with literature references/ Innovator product.	Firm informed that Innovator Ilevro by Alcon has storage conditions of 2-25C
Batch size is mentioned as 2L on stability data sheets, however master formula of 5L is provided.	This typo error, batch size is %5L
Justification for not performing assay of preservatives in stability testing	Firm submitted that they have performed assay at initial and final stage. Results have been submitted but method of analysis along with chromatograms are required for further confirmations.
Drug-excipients compatibility studies are not submitted, needs justification.	Firm informed that their formulation is same as Ilvero of Alcon i.e. Innovator.
Description & details regarding material of construction of container closure systems for applied product needs to be submitted.	Firm has submitted the CoA of 10ml bottle of year 2015 however applied product is 5ml.
Under manufacturing process at 4.4 (addition of API) requires detailed elaboration regarding dispensing of 15.525gm of API from API container for each batch of 5L.	Firm informed that they have precise balance for dispensing of small quantities having readability 0. 001g. Pictures have been provided.
Justification of milling in manufacturing process is required as you have already used micronized API having particle size of 5um. Further after grinding purportedly for seven days at step 4 (as per submitted manufacturing method) particle size evaluation studies are not performed. This needs to be responded with justification.	Grinding of API has been performed for equal distribution of particles in product. This procedure has been adopted for homogenization of suspension and to improve the sustainability (not for particle size reduction). As the API is sterile and aseptically added into the grinding jar for milling, it becomes difficult to sample the portion from the jar due to sterility aspect as well as quantitation also disturbed.
Validation studies are required that sterilization through moist heat/ autoclave at manufacturing step 4.3 and 4.5 and sanitization of mixing tank at 4.8 ensures sterility.	Firm has referred to provisions of general chapter of sterility testing of USP for compliance to sterility parameters.
Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted the Record of Digital data logger for temperature and humidity monitoring of stability chambers
Pharmaceutical equivalence studies with the reference/ innovator product are required which are not provided.	Firm submitted pharmaceutical equivalence studies against “Ilevro” of Novartis

Decision: Approved with Innovator's specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
345.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s. Pharmatec Pakistan (Private) Limited D-86/A, S.I.T.E., Karachi-75700 Tel: 021-32561155-8, Fax: 32561330**
	Name, address of Manufacturing site.	M/s. Pharmatec Pakistan (Private) Limited D-86/A, S.I.T.E., Karachi-75700 Tel: 021-32561155-8, Fax: 32561330
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13246 dated 31/05/2022
	Details of fee submitted	PKR 30,000/-: dated 05/04/2022
	The proposed proprietary name / brand name	Diaflo-Met 5/850mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Dapagliflozin ……..5mg (as Dapagliflozin Propanediol Monohydrate) Metformin Hydrochloride……..850mg
	Pharmaceutical form of applied drug	Beige colored oval biconvex film coated tablets plain from both sides.
	Pharmacotherapeutic Group of (API)	Combination of Oral Blood Glucose Lowering drugs
	Reference to Finished product specifications	In-house specifications
	Proposed Pack size	14's, 28's, 56's & 60's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	XIGDUO 5mg/850mg film coated tablet by ASTRAZENECA UK Limited, MHRA Approved.
	For generic drugs (me-too status)	DAPLOZMET 5/850mg Tablet by M/s. CCL Pharmaceutical (Pvt.) Limited, Reg. No. 106270
	GMP status of the Finished product manufacturer	GMP certificate No. 32/2022-DRAP(K) Tablet (General) section is approved.

	Name and address of API manufacturer.	**For Dapagliflozin:** M/s. Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd .China Daixi Street, Luoyang Town, Wujin District, Changzhou City, Jiangsu Province 213105, China **For Metformin HCl:** M/s. Ipca Laboratories Limited International House 48, Kandivli Industrial Estate, Kandivli (West), Mumbai 400 067, India India-400 067 Mumbai, Maharashtra
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Dapagliflozin Propanediol Monohydrate is USP and Metformin Hydrochloride is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **For Dapagliflozin Propanediol Monohydrate:** Batches:(20PD256DMHT02, 20PD267DMHT03, 21PD042DMHT04) **For Metformin HCl:** Batches:(9002ML2RMI,9003ML2RMI, 9004ML2RMI
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is DAPA-MET

		5/850mg Tablets by Hilton Pharma (Pvt.) Ltd, Karachi, Pakistan by performing quality tests(Identification, Assay, Dissolution, Hardness, Disintegration Time, Friability, Content uniformity). CDP has been performed against the same brand that is DAPA-MET 5/850mg Tablets by Hilton Pharma (Pvt.) Ltd, Karachi, Pakistan in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including System Suitability, Linearity, Accuracy, precision, Specificity, Limit of Quantification, Limit of Detection, Robustness.

STABILITY STUDY DATA

Manufacturer of API	M/s. Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd .China		
API Lot No.	For Metformin HCl: 2048ML2ARMI Dapagliflozin Propanediol Monohydrate: DGF20180501		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20PD255DMHT02	21PD043DMHT03	21PD044DMHT04
Batch Size	1500 tablets	1500 tablets	1500 tablets
Manufacturing Date	02-2021	03-2021	03-2021
Date of Initiation	09-04-2021	09-04-2021	09-04-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Extract of DRB 289 Meeting reference is attached.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**For Dapagliflozin Propanediol Monohydrate:** Copy of GMP certificate No. JS20180935 valid till 26/11/2023. **For Metformin HCl:** Copy of GMP certificate No: NEW-WHO-GMP/CERT/AD/104179/2021/11/37725 Valid till 27/08/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**For Dapagliflozin Propanediol Monohydrate:** • Form 6 of Licence No. 1850/18 DRAP(K) dated 21/06/18 is submitted wherein the permission to import API DAPAGLIFLOZIN

		PROPANEDIOL MONOHYDRATE for the purpose of test/analysis and stability studies is granted. • Commercial Invoice No. WIS180048 dated 05/06/2018 **For Metformin HCl:** • Commercial Invoice No. MEG2021/1631969 dated 28/09/2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms,Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Certificate of compliance and Audit trial Reports are attached.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Stability chamber data (real time and accelerated) having monitoring of temperature and humidity are attached.
Remarks: The firm has submitted the response to the observations as reflected in agenda vide reply submitted on 04.11.2022 vide Dy. No. 31758. The firm has submitted long term stability data of sixty months of three commercial scale batches for Zone IV-A conditions with retest period of two years.		
Decision: Approved with Innovator's specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
346.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s. Pharmatec Pakistan (Private) Limited D-86/A, S.I.T.E., Karachi-75700 Tel: 021-32561155-8, Fax: 32561330**
	Name, address of Manufacturing site.	M/s. Pharmatec Pakistan (Private) Limited D-86/A, S.I.T.E.,Karachi-75700 Tel: 021-32561155-8, Fax: 32561330
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13247 dated 31/05/2022
	Details of fee submitted	PKR 30,000/-: dated 05/04/2022

	The proposed proprietary name / brand name	Diaflo-Met 5/1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Dapagliflozin……..5mg (as Dapagliflozin Propanediol Monohydrate) Metformin Hydrochloride……1000mg
	Pharmaceutical form of applied drug	Yellow color, oval shaped, Biconvex, Film coated, and Plain from both sides.
	Pharmacotherapeutic Group of (API)	Combinations of Oral Blood Glucose Lowering Drugs
	Reference to Finished product specifications	In-house Specifications
	Proposed Pack size	14's, 28's, 56's & 60's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	XIGDUO 5mg/1000mg Film coated Tablets by ASTRAZENECA UK LIMITED, MHRA Approved.
	For generic drugs (me-too status)	DAPLOZMET 5/1000 mg Tablet by M/s. CCL Pharmaceutical (Pvt.) Limited, Reg. No. 106271
	GMP status of the Finished product manufacturer	GMP certificate No. 32/2022-DRAP(K) Tablet (General) section is approved.
	Name and address of API manufacturer.	**For Dapagliflozin:** M/s. Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd .China. Daixi Street, Luoyang Town, Wujin District, Changzhou City, Jiangsu Province 213105, China **For Metformin HCl:** Ipca laboratories Limited, International House 48, Kandivli Industrial Estate, Kandivli (West), Mumbai 400 067, India India-400 067 Mumbai, Maharashtra
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Dapagliflozin Propanediol Monohydrate is present in USP and Metformin HCL is in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 25°C ± 2°C / 60% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months **For Dapagliflozin Propanediol Monohydrate:** Batches:(D20161001, D20161001 20PD267DMHT03, 21PD042DMHT04) **For Metformin HCl:** Batches:(9002ML2RMI,9003ML2RMI, 9004ML2RMI
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is DAPA-MET 5/1000mg Tablets by Hilton Pharma (Pvt.) Ltd, Karachi, Pakistan by performing quality tests(Identification, Assay, Dissolution, Hardness, Disintegration Time, Friability, Content uniformity). CDP has been performed against the same brand that is DAPA-MET 5/1000mg Tablets by Hilton Pharma (Pvt.) Ltd, Karachi, Pakistan in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including System Suitability, Linearity, Accuracy, precision, Specificity, Limit of Quantification, Limit of Detection, Robustness.

STABILITY STUDY DATA	
Manufacturer of API	M/s. Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd .China
API Lot No.	**For Metformin HCl:** 2048ML2ARMI **Dapagliflozin Propanediol Monohydrate:** DGF20180501
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (14's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.		20PD256DMHT02	20PD267DMHT03	21PD042DMHT04
Batch Size		1200 Tablets	1200 Tablets	1200 Tablets
Manufacturing Date		02-2021	03-2021	03-2021
Date of Initiation		09-04-2021	09-04-2021	09-04-2021
No. of Batches		03		
Administrative Portion				
7.	Reference of previous approval of applications with stability study data of the firm (if any)	Extract of DRB 289 Meeting reference is attached.		
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**For Dapagliflozin Propanediol Monohydrate:** Copy of GMP certificate No. JS20180935 valid till 26/11/2023. **For Metformin HCl:** Copy of GMP certificate No: NEW-WHO-GMP/CERT/AD/104179/2021/11/37725 valid till 27/08/2024.		
9.	Documents for the procurement of API with approval from DRAP (in case of import).	**For Dapagliflozin Propanediol Monohydrate:** • Form 6 of Licence No. 1850/18 DRAP(K) dated 21/06/18 is submitted wherein the permission to import API DAPAGLIFLOZIN PROPANEDIOL MONOHYDRATE for the purpose of test/analysis and stability studies is granted. • Commercial Invoice No. WIS180048 dated 05/06/2018 **For Metformin HCl:** • Commercial Invoice No. MEG2021/1631969 dated 28/09/2020		
10.	Data of stability batches will be supported by attested respective documents like chromatograms,Raw data sheets, COA, summary data sheets etc.	Submitted		
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Certificate of compliance and Audit trial Reports are attached.		
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Stability chamber data (real time and accelerated) having monitoring of temperature and humidity are attached.		
Remarks of Evaluator: Stability data sheets of different batches submitted by the firm than those indicated in 3.2. S.7.1. for Dapagliflozin. Certificate of analysis of Dapagliflozin issued by API manufacturer is required as same is nit submitted in the dossier. Clarification is required regarding the copy of DRAP attested invoice submitted by you for import of Dapagliflozin imported from M/s. Shanghai Pharma Group Changzhou Kony Pharmaceutical Co., Ltd. China, DRAP vide invoice No. WIS180048 dated 05/06/2018 does not reflect the batch No, mfg. and expiry date.				

Justification is required as the Certificate of analysis issued by FPP manufacturer i.e. by you in respect of Dapagliflozin for batch No. DGF20180501 indicates mfg. of May 2018 and retest date of 17.11.2021, however as per submitted stability data the API retest period is two years.

Remarks:
The firm has submitted the response to the observations as reflected in agenda vide reply submitted on 04.11.2022 vide Dy. No. 31758. The firm has submitted long term stability data of sixty months of three commercial scale batches for Zone IV-A conditions with retest period of two years.

Decision: Approved with Innovator's specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

347.	**Name and address of manufacture / Applicant**	**M/s Seraph Pharmaceutical, Plot No. 210, Industrial triangle Kahuta road, Islamabad.**
	Brand Name + Dosage Form and Strength	Flozin 10mg Tablet
	Composition	Each film coated tablet contains: Empagliflozin IH …….10mg
	Dairy No. date of R &I fee	Form-5D Dy. No.11249 dated 01.03.2019 & Dy. No. 14273 dated 13.06.2022
	Pharmacological Group	Oral blood glucose lowering drugs
	Type of form	Form 5D
	Finished product specifications	Innovator's specifications
	Pack size and Demand Price	14's, 28's, 56's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Jardiance 10mg film coated tablet Manufactured by Boehringer Ingelheim Pharma GmbH & Co. KG. Germany
	Me-too-status	EMSYN Tablets 10mg Manufactured by SEARLE (Karachi)
	GMP Status	
	Remark of the Evaluator	
	Decision:	

STABILITY STUDY DATA	
Manufacturer of API	**Empagliflozin:** HuaiNan Shunglong Pharmaceutical Co. Ltd. Address: No. 9th YongXing Road, Huaninan economic and Technological Development zone, Huaninan City, China
API Lot No.	**Empagliflozin:** 20201201 & 20201204
Description of Pack (Container closure system)	Alu-Alu blister foil with unit carton
Stability Storage Condition	Accelerated: 40°C ± 2°C / 75% ± 5%RH Real Time: 30°C ± 2°C / 65% ± 5%RH
Time Period	Accelerated: 6 Months

		Real Time: 6 Months		
Frequency		Real Time: 0,3 & 6 (months) Accelerated: 0,1, 2, 3, 4 & 6 (months)		
FLOZIN TABLET 10MG				
Batch No.		T 001	T 002	T 003
Batch Size		730 Tablets	730 Tablets	730 Tablets
Manufacturing Date		05-2021	05-2021	05-2021
Date of Initiation		18 – 05 -2021	18 – 05 -2021	18 – 05 -2021
DOCUMENTS / DATA PROVIDED BY THE APPLICANT				
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product Dexpro 30mg DDR Capsule which was conducted on 11th June, 2018 and was presented in 285st meeting of Registration Board held on 03-04th October, 2018. According to the report following points were confirmed. • The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. • The firm possesses stability chambers with digital data loggers.		
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA of the drug substance from both API Manufacturer and Finished Product manufacturer.		
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Firm has submitted copy of method used for analysis of API from both API Manufacturer and Finished Product manufacturer		
4.	Stability study data of API from API manufacturer	**Empagliflozin:** The submitted stability data as per zone IV-A conditions. The real time stability data is till 24 months. Firm has submitted both accelerated (40°C ± 2°C & 75±5%RH) stability studies & long term (30°C ± 2°C & 65±5%RH) stability studies reports of three batches till 24 months.		
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Firm has submitted copy of DML certificate (No. Wan 20160342) issued by Anhui Food and Drug Administration, China. The certificate is valid till 30-04-2021. Copy of GMP certificate (AH20180451) issued by CFDA, Valid up to 07.04.2023.		
6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of commercial invoice cleared dated 08-02-2021 specifying import of 100g Empagliflozin. The invoice is signed by AD (I&E) DRAP Islamabad office dated 02-04-2021. Second lot of Empagliflozin (lot no. 20201204) 100g, The invoice is signed by AD (I&E) DRAP Islamabad, on 27-05-2021.		

7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of FPP
9.	Drug-excipients compatibility studies (where applicable)	Firm has used same excipients as that of the innovator's product therefore compatibility studies are not required
10.	Complete batch manufacturing record of three stability batches.	Firm has provided Batch Manufacturing Record for all the batches
11.	Record of comparative dissolution data (where applicable)	Firm has submitted CDP for 10mg with EMSYN 10mg tablet.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and audit trail reports for HPLC analysis for all the three batches.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for both stability chambers for accelerated as well as real time stability studies.

Evaluation by PEC:

Decision: Approved with Innovator's specifications.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

348.	**Name and address of manufacture / Applicant**	**M/s Seraph Pharmaceutical, Plot No. 210, Industrial triangle Kahuta road, Islamabad.**
	Brand Name + Dosage Form and Strength	Flozin 25mg Tablet
	Composition	Each film coated tablet contains: Empagliflozin IH …….25mg
	Dairy No. date of R &I fee	Form-5D Dy. No. 11249 dated: 05.03.2019 20000/- Dy. No. 14274 dated 19.06.2022
	Pharmacological Group	Oral blood glucose lowering drugs
	Type of form	Form 5D
	Finished product specifications	Innovator's specifications
	Pack size and Demand Price	14's, 28's, 56's; As per SRO
	Approval status of product in Reference Regulatory Authorities	Jardiance 25mg film coated tablet manufactured by Boehringer Ingelheim Pharma GmbH & Co. KG. Germany
	Me-too-status	Diampa Tablets 25mg Manufactured by Getz Pharma
	GMP Status	
	Remark of the Evaluator	
	Decision:	

STABILITY STUDY DATA	
Manufacturer of API	**Empagliflozin:** HuaiNan Shunglong Pharmaceutical co. Ltd. Address: No. 9th YongXing Road, Huaninan economic and Technological Development zone, Huaninan City, China
API Lot No.	**Empagliflozin:** 20201201 & 20201204

Description of Pack (Container closure system)	Alu-Alu blister foil with unit carton		
Stability Storage Condition	Accelerated: 40°C ± 2°C / 75% ± 5%RH Real Time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Accelerated: 6 Months Real Time: 6 Months		
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0,1, 2, 3, 4 & 6 (months)		
FLOZIN TABLET 25MG			
Batch No.	T 001	T 002	T 003
Batch Size	730 Tablets	730 Tablets	730 Tablets
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	18 – 05 -2021	18 – 05 -2021	18 – 05 -2021

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product Dexpro 30mg DDR Capsule which was conducted on 11th June, 2018 and was presented in 285st meeting of Registration Board held on 03-04th October, 2018. According to the report following points were confirmed. • The firm has 21 CFR compliant HPLC software • The firm has audit trail reports available. • The firm possesses stability chambers with digital data loggers.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA of the drug substance from both API Manufacturer and Finished Product manufacturer.
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Firm has submitted copy of method used for analysis of API from both API Manufacturer and Finished Product manufacturer
4.	Stability study data of API from API manufacturer	**Empagliflozin:** The submitted stability data as per zone IV-A conditions. The real time stability data is till 24 months. Firm has submitted both accelerated (40°C ± 2°C & 75±5%RH) stability studies & long term (30°C ± 2°C & 65±5%RH) stability studies reports of three batches till 24 months.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Empagliflozin:** Firm has submitted copy of DML certificate (No. Wan 20160342) issued by Anhui Food and Drug Administration, China. The certificate is valid till 30-04-2021. Copy of GMP certificate (No. s1[2018]79) issued by Anhui Food and Drug Administration, China, Valid up to 28-09-2023.

6.	Documents for the procurement of API with approval from DRAP (in case of import).	**Empagliflozin:** Firm has submitted copy of commercial invoice cleared dated 08-02-2021 specifying import of 100g Empagliflozin. The invoice is signed by AD (I&E) DRAP Islamabad office dated 02-04-2021. Second lot of Empagliflozin (lot no. 20201204) 100g, The invoice is signed by AD (I&E) DRAP Islamabad, on 27-05-2021.
7.	Protocols followed for conduction of stability study	Firm has submitted protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Firm has provided detailed method for analysis of FPP
9.	Drug-excipients compatibility studies (where applicable)	Firm has used same excipients as that of the innovator's product therefore compatibility studies are not required
10.	Complete batch manufacturing record of three stability batches.	Firm has provided Batch Manufacturing Record for all the batches
11.	Record of comparative dissolution data (where applicable)	Firm has submitted CDP for 25mg with Diampa 25mg tablet.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted documents like chromatograms, raw data sheets, COA, summary data sheets for the stability studies
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Firm has submitted certificate of compliance and audit trail reports for HPLC analysis for all the three batches.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for both stability chambers for accelerated as well as real time stability studies.

Evaluation by PEC:

Decision: Approved with Innovator's specifications.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

349.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Seraph Pharmaceutical, Plot no. 210, Industrial Triangle Kahuta road. Islamabad.**
	Name, address of Manufacturing site.	M/s Seraph Pharmaceutical, Plot no. 210, Industrial Triangle Kahuta road. Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10714 dated 28/04/2022
	Details of fee submitted	PKR 75,000/-: dated 28/04/2022
	The proposed proprietary name / brand	SERROX 250mg tablet

	name	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dispersible tablet contains: Deferasirox …….250mg
	Pharmaceutical form of applied drug	Dispersible Tablets
	Pharmacotherapeutic Group of (API)	Iron Chelating agent
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Exjade Tablets 250mg M/s Novartis, USFDA Approved.
	For generic drugs (me-too status)	Dasirox Dispersible Tablets 250mg, CCL Pharmaceutical, Lahore.
	GMP status of the Finished product manufacturer	GMP certificate granted on 11/07/2019 Tablet (General) section approved.
	Name and address of API manufacturer.	M/s BDR Lifesciences Private Limited, R.S. No. 578, near Effluent channel road, Village-Luna Ta-Padra, Dist.-Vadodara, Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	In house product analytical method was developed. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (001, 002 & 003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing, batch analysis and

		justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Dasirox 250mg tablet by CCL Pharmaceutical, Lahore. performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Dasirox 250mg tablet. Tablet by CCL Pharmaceutical in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s BDR Lifesciences Private Limited, R.S. No. 578, near Effluent channel road, Village-Luna Ta-Padra, Dist.-Vadodara, Gujarat, India.		
API Lot No.	DFZP200013		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	04-08-2020	04-08-2020	04-08-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted previous approval of document with stability data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted the copy of Eudra GMP certificate of the API manufacturer.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted the copy of import invoice vide No.EX/BDR/196/20-21 dated 27.07.2020

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	HPLC is not CFR compliant as per statement of the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator:

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

350.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Seraph Pharmaceutical, Plot no. 210, Industrial Triangle Kahuta road. Islamabad.**
	Name, address of Manufacturing site.	M/s Seraph Pharmaceutical, Plot no. 210, Industrial Triangle Kahuta road. Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.10715 dated 28/04/2022
	Details of fee submitted	PKR 75,000/- dated 28/04/2022
	The proposed proprietary name / brand name	SERROX 500mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each dispersible tablet contains: Deferasirox …….500mg
	Pharmaceutical form of applied drug	Dispersible Tablets
	Pharmacotherapeutic Group of (API)	Iron Chelating agent
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Exjade Tablets 250mg M/s Novartis, USFDA Approved.
	For generic drugs (me-too status)	Dasirox Dispersible Tablets 500mg, CCL Pharmaceutical, Lahore.
	GMP status of the Finished product manufacturer	GMP certificate granted on 11/07/2019 Tablet (General) section approved.
	Name and address of API manufacturer.	M/s BDR Lifesciences Private Limited, R.S. No. 578, near Effluent channel road, Village-Luna Ta-Padra, Dist.-Vadodara, Gujarat, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	In house product analytical method was developed. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (004, 005 & 006)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Dasirox 500mg tablet by CCL Pharmaceutical, Lahore. performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Dasirox 500mg tablet. Tablet by CCL Pharmaceutical in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		

Manufacturer of API	M/s BDR Lifesciences Private Limited, R.S. No. 578, near Effluent channel road, Village-Luna Ta-Padra, Dist.-Vadodara, Gujarat, India.		
API Lot No.	DFZP200013		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	004	005	006
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	08-2020	08-2020	08-2020
Date of Initiation	04-08-2020	04-08-2020	04-08-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted previous approval of document with stability data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted the copy of Eudra GMP certificate of the API manufacturer.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted the import documents of API.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	HPLC is not CFR compliant as per statement of the firm.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted by the firm.

Remarks of Evaluator:

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

350.	Name, address of Applicant / Marketing Authorization Holder	M/s Seraph Pharmaceutical, Plot no. 210, Industrial Triangle Kahuta road. Islamabad.
	Name, address of Manufacturing site.	M/s Seraph Pharmaceutical, Plot no. 210, Industrial Triangle Kahuta road. Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10716 dated 28/04/2022
	Details of fee submitted	PKR 75,000/-: dated 28/04/2022
	The proposed proprietary name / brand name	KALSEPH 10mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan fumarate eq. to Vonoprazan ……10mg
	Pharmaceutical form of applied drug	Tablets
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab Tablet 10mg, Takeda Pharmaceutical, Japan (PMDA)
	For generic drugs (me-too status)	Vonozan Tablet 10mg, by M/s Getz Pharma (Pvt.) Ltd
	GMP status of the Finished product manufacturer	GMP certificate granted on 11/07/2019 Tablet (General) section approved.
	Name and address of API manufacturer.	Jiangxi Synergy Pharmaceutical Co., Ltd. Jiangxi Fengxin Industrial Park, Fengxin, 330700, Jiangxi Province, P.R. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	In house product analytical method was developed.

		The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T001,T002 & T003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Vonozan 10mg tablet by Getz Pharma. Performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Vonozan 10mg tablet. Tablet by Getz Pharmaceutical in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Jiangxi Synergy Pharmaceutical Co., Ltd. Jiangxi Fengxin Industrial Park, Fengxin, 330700, Jiangxi Province, P.R. China		
API Lot No.	20210801BD		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	836 tab	836 tab	836 tab
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	28-10-2021	28-10-2021	28-10-2021

No. of Batches		03
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted previous approval of document with stability data. Dexpro 30 & 60mg Capsules approved in 285th meeting of Registration Board. Novel 800mg Tablet approved in 288th meeting of Registration Board.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of Pharmaceutical Production License vide No. GAN 20160125 dated 27.11.2020 issued by Jiangxi Provincial Medical Products Administration China valid till 26.11.2025
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted DRAP attested invoice vide No. JXSG210904 dated 13.10.2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	The firm has submitted the stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	As per statement of the firm the HPLC system used in the analysis is not CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)
Remarks of Evaluator:		
Decision: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
351.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Seraph Pharmaceutical, Plot no. 210, Industrial Triangle Kahuta road. Islamabad.**
	Name, address of Manufacturing site.	M/s Seraph Pharmaceutical, Plot no. 210, Industrial Triangle Kahuta road. Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10717 dated 28/04/2022

	Details of fee submitted	PKR 75,000/-: dated 28/04/2022
	The proposed proprietary name / brand name	KALSEPH 20mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan fumarate eq. to Vonoprazan ……20mg
	Pharmaceutical form of applied drug	Tablets
	Pharmacotherapeutic Group of (API)	PPI
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab Tablet 20mg, Takeda Pharmaceutical, Japan (PMDA)
	For generic drugs (me-too status)	Vonozan Tablet 20mg, by M/s Getz Pharma (Pvt.) Ltd
	GMP status of the Finished product manufacturer	GMP certificate granted on 11/07/2019 Tablet (General) section approved.
	Name and address of API manufacturer.	Jiangxi Synergy Pharmaceutical Co., Ltd. Jiangxi Fengxin Industrial Park, Fengxin, 330700, Jiangxi Province, P.R. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	In house product analytical method was developed. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (001, 002 & 003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure

		(including dissolution testing, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand that is Vonozan 20mg tablet by Getz Pharma. Performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Vonozan 20mg tablet. Tablet by Getz Pharmaceutical in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Jiangxi Synergy Pharmaceutical Co., Ltd. Jiangxi Fengxin Industrial Park, Fengxin, 330700, Jiangxi Province, P.R. China		
API Lot No.	20210801BD		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T001	T002	T003
Batch Size	836 tab	836 tab	836 tab
Manufacturing Date	10-2021	10-2021	10-2021
Date of Initiation	28-10-2021	28-10-2021	28-10-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted previous approval of document with stability data. Dexpro 30 & 60mg Capsules approved in 285th meeting of Registration Board. Novel 800mg Tablet approved in 288th meeting of Registration Board.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of Pharmaceutical Production License vide No. GAN 20160125 dated 27.11.2020 issued by Jiangxi Provincial Medical Products Administration China valid till 26.11.2025

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted DRAP attested invoice vide No. JXSG210904 dated 13.10.2021 for batch No. 20210801BD.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	The firm has submitted the stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	As per statement of the firm the HPLC system used in the analysis is not CFR compliant
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)

Remarks of Evaluator:

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

352.	**Name and address of manufacture / Applicant**	**M/s English Pharmaceutical Industries, Link Kattar Band Road, Thokar Niaz Baig Lahore.**
	Brand Name + Dosage Form and Strength	Zarox 5mg Tablet
	Composition	Each tablet contains: Metolazone…….5mg
	Dairy No. date of R &I fee	Dy.No.20434; 08-11-2017; Rs.20,000/- (08-11-2017)
	Pharmacological Group	(Diuretic/saluretic/antihypertensive drug of the quinazoline class)
	Type of form	Form 5D
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Zaroxolyn Tablet 5mg of (USFDA approved)
	Me-too-status	
	GMP Status	Firm has submitted copy of GMP certificate dated 17-08-2022
	Remark of the Evaluator	
	Decision:	

STABILITY STUDY DATA

Manufacturer of API	M/s Centaur Pharmaceuticals Pvt Limited. Plot No. 75,76 & 76/1 Chikhloli MIDC Ambernath (W) Dist. Thane 421 501 Maharashtra India.
API Lot No.	1803604P
Description of Pack (Container closure system)	Alu-Alu blister of 1x10's
Stability Storage Condition	Accelerated: 40°C ± 75°C% RH Real Time: 30°C ± 2°C / 65% ± 5%RH

Time Period	Accelerated: 6 Months Real Time: 6 Months		
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0,1, 2, 3, 4 & 6 (months)		
ZAROX 5MG TABLET			
Batch No.	MLT 001	MLT 003	MLT 005
Batch Size	2000	2000	2000
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	08-10-2019	15.10.2019	22.10.2019

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
1.	Reference of previous approval of applications with stability study data of the firm	Not provided.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA of the drug substance from API Manufacturer dated 04.07.2018 and COA by FPP manufacturer dated: 24.10.2018
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	The API manufacturer has provided the BP specs and firm will use USP specifications.
4.	Stability study data of API from API manufacturer	The firm has submitted stability study data of API from API manufacturer.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted the Eudra GMP certificate of the manufacturer issued on 14.08.2018
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted the copy of DRAP attested invoice vide No. CP/EXP/C?297/18-19 dated 21.08.2018.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	The firm will follow USP monograph.
9.	Drug-excipients compatibility studies (where applicable)	Same qualitative composition as Innovator.
10.	Complete batch manufacturing record of three stability batches.	Submitted.
11.	Record of comparative dissolution data (where applicable)	Submitted.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The has submitted audit trail reports.

14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted.

Remarks:

Decision: Approved with USP Specifications.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

353.	**Name and address of manufacture / Applicant**	**M/s English Pharmaceutical Industries, Link Kattar Band Road, Thokar Niaz Baig Lahore.**
	Brand Name + Dosage Form and Strength	Zarox 10mg Tablet
	Composition	Each tablet contains: Metolazone…….10mg
	Dairy No. date of R &I fee	Dy.No.20435; 08-11-2017; Rs.20,000/- (08-11-2017)
	Pharmacological Group	(Diuretic/saluretic/antihypertensive drug of the quinazoline class)
	Type of form	Form 5D
	Finished product specifications	USP
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Zaroxolyn Tablet 10mg of (USFDA approved)
	Me-too-status	
	GMP Status	Firm has submitted copy of GMP certificate dated 17-08-2022
	Remark of the Evaluator	
	Decision:	

STABILITY STUDY DATA

Manufacturer of API	M/s Centaur Pharmaceuticals Pvt Limited. Plot No. 75,76 & 76/1 Chikhloli MIDC Ambernath (W) Dist. Thane 421 501 Maharashtra India.
API Lot No.	1803604P
Description of Pack (Container closure system)	Alu-Alu blister of 1x10's
Stability Storage Condition	Accelerated: 40°C ± 75°C% RH Real Time: 30°C ± 2°C / 65% ± 5%RH
Time Period	Accelerated: 6 Months Real Time: 6 Months
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0,1, 2, 3, 4 & 6 (months)

ZAROX 5MG TABLET

Batch No.	MLT 002	MLT 004	MLT 006
Batch Size	2000	2000	2000
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	05-10-2019	11.10.2019	19.10.2019

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

1.	Reference of previous approval of applications with stability study data of the firm	Not provided.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA of the drug substance from API Manufacturer dated 04.07.2018 and COA by FPP manufacturer dated: 24.10.2018
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	The API manufacturer has provided the BP specs and firm will use USP specifications.
4.	Stability study data of API from API manufacturer	The firm has submitted stability study data of API from API manufacturer.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted the Eudra GMP certificate of the manufacturer issued on 14.08.2018
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted the copy of DRAP attested invoice vide No. CP/EXP/C?297/18-19 dated 21.08.2018.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	The firm will follow USP monograph.
9.	Drug-excipients compatibility studies (where applicable)	Same qualitative composition as Innovator.
10.	Complete batch manufacturing record of three stability batches.	Submitted.
11.	Record of comparative dissolution data (where applicable)	Submitted.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The has submitted audit trail reports.
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted.
Remarks:		
Decision: Approved with USP Specifications. Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.		

354.	**Name and address of manufacture / Applicant**	**M/s English Pharmaceutical Industries, Link Kattar Band Road, Thokar Niaz Baig Lahore.**
	Brand Name + Dosage Form and Strength	Renvel 800mg Tablet
	Composition	Each film coated tablet contains: Sevelamer Carbonate…….800mg
	Dairy No. date of R &I fee	Dy.No.20433; 08-11-2017;

		Rs.20,000/- (08-11-2017)
	Pharmacological Group	(Diuretic/saluretic/antihypertensive drug of the quinazoline class)
	Type of form	Form 5D
	Finished product specifications	Manufacturer Specifications
	Pack size and Demand Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Renvela (USFDA Approved)
	Me-too-status	Genovel Tablets 800mg M/s Genome Pharmaceuticals Hattar.
	GMP Status	Firm has submitted copy of GMP certificate dated 17-08-2022
	Remark of the Evaluator	
	Decision:	

STABILITY STUDY DATA			
Manufacturer of API	Apothecon Pharmaceuticals Pvt Limited, Plot No. 1134 to 1137, 1143B, 1144A, 1144B and 1138A & 1138B Padra Jambusar Highway Tal Padra Dabhasa Vadodara Gujarat State India		
API Lot No.	DS185/008/05/21		
Description of Pack (Container closure system)	Alu-Alu blister of 3x10's		
Stability Storage Condition	Accelerated: 40°C ± 75°C% RH Real Time: 30°C ± 2°C / 65% ± 5%RH		
Time Period	Accelerated: 6 Months Real Time: 6 Months		
Frequency	Real Time: 0,3 & 6 (months) Accelerated: 0,1, 2, 3, 4 & 6 (months)		
RENVEL 800MG TABLET			
Batch No.	EP22-011-S1	EP22-011-S2	EP22-011-S3
Batch Size	2500	2500	2500
Manufacturing Date	02.2022	02.2022	02.2022
Date of Initiation	09-02-2022	11.02.2022	15.02.2022

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
1.	Reference of previous approval of applications with stability study data of the firm	Not provided.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA of the drug substance from API Manufacturer vide lot No. DS185/008/05/21
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Firm has submitted the method used for analysis of API from both API Manufacturer and Finished Product manufacturer
4.	Stability study data of API from API manufacturer	Long term data is submitted for three batches.

5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of API manufacturer issued by the concerned regulatory authority is submitted.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted the copy of DRAP attested invoice vide No. APO/21-22 dated 09.12.2021.
7.	Protocols followed for conduction of stability study	Firm has submitted the protocols followed for conduction of stability study
8.	Method used for analysis of FPP	Method used for analysis of FPP
9.	Drug-excipients compatibility studies (where applicable)	Not applicable
10.	Complete batch manufacturing record of three stability batches.	The firm has submitted complete batch manufacturing record of three stability batches
11.	Record of comparative dissolution data (where applicable)	Not applicable
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	IR spectra for submitted, the assay for titratable amine by potentiometric titration.
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not applicable
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)
Evaluation by PEC:		
Decision: Approved with Innovator's specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.**		

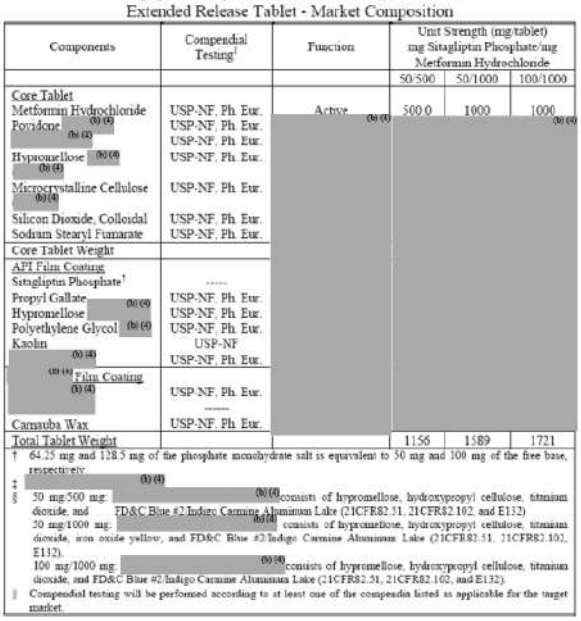
Case No. 2 Routine Cases of Form 5F

355.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Global Pharmaceuticals Pvt Limited, Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals Pvt Limited, Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28734 dated 20.10.2021

	Details of fee submitted	PKR 30000/- dated 13.07.2021
	The proposed proprietary name / brand name	INCRIT-M XR 50/500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…50mg Metformin HCl (Extended Release)….500mg
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Anti-Diabetic
	Reference to Finished product specifications	As per Innovators Specifications
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Janumet XR of Merck Sharp & Dhome USA
	For generic drugs (me-too status)	Tagipmet XR of Highnoon Labs Lahore
	GMP status of the Finished product manufacturer	GMP certificate was issued to the firm by DRAP Islamabad dated 28.12.2018 based on inspection dated 24.10.2018
	Name and address of API manufacturer.	**Sitagliptin Phosphate Monohydrate** M/s Anhui Haikang Pharmaceutical Co., No.21 Huancheng West Road Daguan District Anqing Anhui China **Metformin HCl** M/s Aarti Drugs Limited Plot No. 211-2013 Road No. 2 GIDC Sarigam District Valsad Gujarat India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 3 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 3 months

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Janumet XR Tablets CDP has been performed against the aforesaid brand in three media. The f2 value are in the acceptable range.		
	Analytical method validation/verification of product	Method validation studies have been submitted.		
STABILITY STUDY DATA				
Manufacturer of API		**<u>Sitagliptin Phosphate Monohydrate</u>** M/s Anhui Haikang Pharmaceutical Co., No.21 Huancheng West Road Daguan District Anqing Anhui China **<u>Metformin HCl</u>** M/s Aarti Drugs Limited Plot No. 211-2013 Road No. 2 GIDC Sarigam District Valsad Gujarat India.		
API Lot No.		**<u>Sitagliptin Phosphate Monohydrate</u>** 20050203 Mfg date: 02.05.2020 retest date date: 01.05.2022 **<u>Metformin HCl</u>** MEF/10030953 Mfg. date: 03.2020 Exp. Date: 02.2025		
Description of Pack (Container closure system)		Alu- Alu blister packed in unit carton (14's)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 24 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.		ST21D001	ST21D002	ST21D003
Batch Size		3000 tab	3000 tab	3000 tab
Manufacturing Date		04.2021	04.2021	04.2021
Date of Initiation		03.2023	03.2023	03.2023
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm submitted reference of Promig Plus Tablets 375/ 20mg approved in 289th meeting of Registration Board		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**<u>Sitagliptin Phosphate Monohydrate</u>** Copy of DML issued by Anhui Provincial drug Administration. **<u>Metformin HCl</u>**		

		Copy of GMP certificate issued by Food and Drug Control Administration Gujarat State India
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of DRAP attested invoice vide No. CI No: WD20200427-1 cleared on dated 18.06.2020 of Sitagliptin Phosphate Monohydrate and DRAP attested invoice vide No. EXP/302/20321 for Metformin HCl cleared on 05.08. 2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Provided
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided
Remarks of Evaluator:		
Boxed warning regarding Lactic Acidosis		
Shortcomings:		
Query		**Reply**
Propyl Gallate is added in formulation in metformin core as antioxidant, justification needs to be submitted with literature/ innovator product references.		The firm informed that Propyl Gallate antioxidant will used in both solid and liquid phase to prevent oxidation/free radical reaction. The use of propyl gallate in core hinder the Metformin hydrochloride acidic activity to produce free radical chain reaction in provided condition of tablet drug layering via coating. Structural study of metformin and propyl Gallate shows, propyl gallate as an antioxidant reduces and prevents oxidation of Metformin HCl, as shown below. Nothing the dimethylamine moiety of metformin, this is convenient sire for activity of metformin. This N-C bond can be made by nucleophilic attack of dimethylamine at the electrophilic nitrile carbon of cyanoguanidine. In fact, this is how metformin's act. There are various patented procedures which differ in reaction conditions and purification strategy, but almost all involve reacting the hydrochloride salt of dimethylamine with cyanoguanidine, so we use propyl Gallate with metformin in sold. Propyl Gallate quantum chemistry and computational kinetics study on the reactivity of propyl Gallate towards H, Ooh, OOCH3 and OCHCH2 radicals, in aqueous and lipid. As per literature study it was also found propyl Gallate as antioxidant optionally used in core and solution for coating.

	However, the market composition of the innovator as approved by USFDA is as detailed below, Sitagliptin Phosphate (†) / Metformin Hydrochloride Extended Release Tablet - Market Composition  Components / Compendial Testing‡ / Function / Unit Strength (mg/tablet) mg Sitagliptin Phosphate†/mg Metformin Hydrochloride: 50/500, 50/1000, 100/1000 Core Tablet Metformin Hydrochloride — USP-NF, Ph. Eur. — Active — 500.0 — 1000 — 1000 Povidone — USP-NF, Ph. Eur. Hypromellose — USP-NF, Ph. Eur. Microcrystalline Cellulose — USP-NF, Ph. Eur. Silicon Dioxide, Colloidal — USP-NF, Ph. Eur. Sodium Stearyl Fumarate — USP-NF, Ph. Eur. Core Tablet Weight API Film Coating Sitagliptin Phosphate† Propyl Gallate — USP-NF, Ph. Eur. Hypromellose — USP-NF, Ph. Eur. Polyethylene Glycol — USP-NF, Ph. Eur. Kaolin — USP-NF Film Coating — USP-NF, Ph. Eur. Carnauba Wax — USP-NF, Ph. Eur. Total Tablet Weight — 1156 — 1589 — 1721 † 64.25 mg and 128.5 mg of the phosphate monohydrate salt is equivalent to 50 mg and 100 mg of the free base, respectively. § 50 mg/500 mg: consists of hypromellose, hydroxypropyl cellulose, titanium dioxide, and FD&C Blue #2/Indigo Carmine Aluminum Lake (21CFR82.51, 21CFR82.102, and E132) 50 mg/1000 mg: consists of hypromellose, hydroxypropyl cellulose, titanium dioxide, iron oxide yellow, and FD&C Blue #2/Indigo Carmine Aluminum Lake (21CFR82.51, 21CFR82.102, E132). 100 mg/1000 mg: consists of hypromellose, hydroxypropyl cellulose, titanium dioxide, and FD&C Blue #2/Indigo Carmine Aluminum Lake (21CFR82.51, 21CFR82.102, and E132). ‖ Compendial testing will be performed according to at least one of the compendia listed as applicable for the target market.
Stability data of three months is provided, additional data needs to be submitted.	Firm has submitted the additional stability data.

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Regsitration Board further decided as under:

i. **The firm shall market the product as per Innovator product composition i.e. Janumet XR including propyl gallate in its formulation as antioxidant**

ii. **Propyl gallate assay shall be added in finished product specifications.**

Moreoever the Board advised PE&R Division to issue an advisory to the industry to follow the composition of Janumet XR and propyl gallate assay for already registered products.

356.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Global Pharmaceuticals Pvt Limited, Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals Pvt Limited, Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28735 dated 20.10.2021
	Details of fee submitted	PKR 30000/- dated 13.10.2021

	The proposed proprietary name / brand name	INCRIT-M XR 50/1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…50mg Metformin HCl (Extended Release)….1000mg
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Anti-Diabetic
	Reference to Finished product specifications	As per Innovators Specifications
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Janumet XR of Merck Sharp & Dhome USA
	For generic drugs (me-too status)	Tagipmet XR of Highnoon Labs Lahore
	GMP status of the Finished product manufacturer	GMP certificate was issued to the firm by DRAP Islamabad dated 28.12.2018 based on inspection dated 24.10.2018
	Name and address of API manufacturer.	**Sitagliptin Phosphate Monohydrate** M/s Anhui Haikang Pharmaceutical Co., No.21 Huancheng West Road Daguan District Anqing Anhui China **Metformin HCl** M/s Aarti Drugs Limited Plot No. 211-2013 Road No. 2 GIDC Sarigam District Valsad Gujarat India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 3 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 3 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers,

		description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Janumet XR Tablets CDP has been performed against the aforesaid brand in three media. The f2 value are in the acceptable range.		
	Analytical method validation/verification of product	Method validation studies have been submitted.		
STABILITY STUDY DATA				
Manufacturer of API		**<u>Sitagliptin Phosphate Monohydrate</u>** M/s Anhui Haikang Pharmaceutical Co., No.21 Huancheng West Road Daguan District Anqing Anhui China **<u>Metformin HCl</u>** M/s Aarti Drugs Limited Plot No. 211-2013 Road No. 2 GIDC Sarigam District Valsad Gujarat India.		
API Lot No.		**<u>Sitagliptin Phosphate Monohydrate</u>** 20050203 Mfg date: 02.05.2020 retest date date: 01.05.2022 **<u>Metformin HCl</u>** MEF/10030953 Mfg. date: 03.2020 Exp. Date: 02.2025		
Description of Pack (Container closure system)		Alu- Alu blister packed in unit carton (14's)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 24 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.		ST21D004	ST21D005	ST21D006
Batch Size		3000 tab	3000 tab	3000 tab
Manufacturing Date		04.2021	04.2021	04.2021
Date of Initiation		26.05.2021	26.05.2021	26.05.2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm submitted reference of Promig Plus Tablets 375/ 20mg approved in 289th meeting of Registration Board		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**<u>Sitagliptin Phosphate Monohydrate</u>** Copy of DML issued by Anhui Provincial drug Administration. **<u>Metformin HCl</u>**		

		Copy of GMP certificate issued by Food and Drug Control Administration Gujarat State India
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of DRAP attested invoice vide No. CI No: WD20200427-1 cleared on dated 18.06.2020 of Sitagliptin Phosphate Monohydrate and DRAP attested invoice vide No. EXP/302/20321 for Metformin HCl cleared on 05.08. 2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Provided
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided
Remarks of Evaluator:		
Boxed warning regarding Lactic Acidosis		
Shortcomings & reply of the firm:		
Same as INCRIT-M XR 50/500mg Tablet		
Decision: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** **Regsitration Board further decided as under:** **i. The firm shall market the product as per Innovator product composition i.e. Janumet XR and submit the data of 1st commercial batch.** **ii. Propyl gallate assay shall be added in finished product specifications.** **Moreoever the Board advised PE&R Division to issue an advisory to the industry to follow the composition of Janumet XR and propyl gallate assay for already registered products.**		
357.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Global Pharmaceuticals Pvt Limited, Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.**
	Name, address of Manufacturing site.	M/s Global Pharmaceuticals Pvt Limited, Plot No. 204-205, Industrial Triangle Kahuta Road Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale

		☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28736 dated 20.10.2021
	Details of fee submitted	PKR 30000/- dated 13.10.2021
	The proposed proprietary name / brand name	INCRIT-M XR 50/1000mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…100mg Metformin HCl (Extended Release)….1000mg
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Anti-Diabetic
	Reference to Finished product specifications	As per Innovators Specifications
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Janumet XR of Merck Sharp & Dhome USA
	For generic drugs (me-too status)	Tagipmet XR of Highnoon Labs Lahore
	GMP status of the Finished product manufacturer	GMP certificate was issued to the firm by DRAP Islamabad dated 28.12.2018 based on inspection dated 24.10.2018
	Name and address of API manufacturer.	**Sitagliptin Phosphate Monohydrate** M/s Anhui Haikang Pharmaceutical Co., No.21 Huancheng West Road Daguan District Anqing Anhui China **Metformin HCl** M/s Aarti Drugs Limited Plot No. 211-2013 Road No. 2 GIDC Sarigam District Valsad Gujarat India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance

	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 3 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 3 months		
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Janumet XR Tablets CDP has been performed against the aforesaid brand in three media. The f2 value are in the acceptable range.		
	Analytical method validation/verification of product	Method validation studies have been submitted.		
STABILITY STUDY DATA				
Manufacturer of API		**Sitagliptin Phosphate Monohydrate** M/s Anhui Haikang Pharmaceutical Co., No.21 Huancheng West Road Daguan District Anqing Anhui China **Metformin HCl** M/s Aarti Drugs Limited Plot No. 211-2013 Road No. 2 GIDC Sarigam District Valsad Gujarat India.		
API Lot No.		**Sitagliptin Phosphate Monohydrate** 20050203 Mfg date: 02.05.2020 retest date date: 01.05.2022 **Metformin HCl** MEF/10030953 Mfg. date: 03.2020 Exp. Date: 02.2025		
Description of Pack (Container closure system)		Alu- Alu blister packed in unit carton (14's)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 24 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.		ST21D004	ST21D005	ST21D006
Batch Size		3000 tab	3000 tab	3000 tab
Manufacturing Date		04.2021	04.2021	04.2021
Date of Initiation		28.05.2021	28.05.2021	28.05.2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm submitted reference of Promig Plus Tablets 375/ 20mg approved in 289th meeting of Registration Board		

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Sitagliptin Phosphate Monohydrate** Copy of DML issued by Anhui Provincial Drug Administration. **Metformin HCl** Copy of GMP certificate issued by Food and Drug Control Administration Gujarat State India
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of DRAP attested invoice vide No. CI No: WD20200427-1 cleared on dated 18.06.2020 of Sitagliptin Phosphate Monohydrate and DRAP attested invoice vide No. EXP/302/20321 for Metformin HCl cleared on 05.08. 2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Provided
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided
Remarks of Evaluator:		
Boxed warning regarding Lactic Acidosis		
Shortcomings & response of the firm:		
Same as INCRIT-M XR 50/500mg Tablet		
Decision: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** **Regsitration Board further decided as under:** **i. The firm shall market the product as per Innovator product composition i.e. Janumet XR and submit the data of 1st commercial batch.** **ii. Propyl gallate assay shall be added in finished product specifications.** **Moreoever the Board advised PE&R Division to issue an advisory to the industry to follow the composition of Janumet XR and propyl gallate assay for already registered products.**		
358.	**Name, address of Applicant / Importer**	**M/s Sohail Corporation Plot No. 474 Siraj Colony Moosa Lane Karachi.**
	Details of Drug Sale License of importer	Drug License by the way of wholesale vide No. DHODSK(Drug)/-433/- dated 01.012.2020 valid till 19-11-2022
	Name and address of marketing authorization holder (abroad)	M/s Anhui Chengsi Pharmaceuticals Co., Ltd, No. 5068 Huaishang Road Bengbu Anhui China.
	Name, address of manufacturer(s)	M/s Anhui Chengsi Pharmaceuticals Co., Ltd, No. 5068 Huaishang Road Bengbu Anhui China.
	Name of exporting country	China

	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**GMP:** Copy of GMP certificate issued by CFDA vide No. CN20160035 valid till 08.03.2021.
	Details of letter of authorization / sole agency agreement	Firm has submitted copy of agency agreement.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 30796 dated 10.11.2021
	Details of fee submitted	PKR 100000/- dated 07.04.2021 and 50000/- dated 07.06.2021.
	The proposed proprietary name / brand name	**LINCOMYCIN HYDROCHLORIDE INJECTION 600MG/2ML**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ampoule of 2ml contains: Lincomycin HCl USP equivalent to Lincomycin …..600mg
	Pharmaceutical form of applied drug	Injection
	Pharmacotherapeutic Group of (API)	Antibiotic (Lincosamide antibacterial)
	Reference to Finished product specifications	BP 2013
	Proposed Pack size	Not submitted
	Proposed unit price	Not submitted
	The status in reference regulatory authorities	Lincomycin SXP manufactured by Southern XP IP Pty Ltd Australia (TGA Approved)
	For generic drugs (me-too status)	
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of

		drug substance.
	Name, address of drug substance manufacturer	M/s Xinyu Pharmaceutical Co., Ltd No. 158 Jintai 5th Road Economic development Zone Suzhou Anhui Province China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API (17081041, 17081042, 17081043) conducted at accelerated conditions 40°C ±2°C / 75% ± 5% RH for 6 months as well as real time conditions. The real time stability data is conducted at 25°C ± 2°C / 60 ± 5% RH & 30°C ± 2°C / 75 ± 5% RH. The stability study data is for 9 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical Equivalence with 5 chines manufactured products is submitted.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Low Borosilicate glass
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches (W170513, W170422 & W170722). The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 75% ± 5% RH. The real time stability study data of 3 batches is for 34 months
Evaluation by PEC:		
Copy of valid DSL.		The firm has submitted the copy of DSL.
Copy of GMP certificate is submitted and aforesaid GMP was valid till 08.03.2021. Valid legalized GMP certificate needs to be submitted.		The firm has submitted copy of compliance certificate issued by fifth sub office of Anhui Drug Administration However valid GMP certificate needs to be submitted.

Legalized valid CoPP is required.	Copy of CoPP issued by the company is provided. Valid legalized CoPP issued by the concerned drug authorities need to be submitted.
Sole agency agreement needs to be submitted.	Copy of sole agency agreement is submitted.
Proposed Price & Pack Size needs to be submitted (1.5.4)	Not provided.
3.2.P. 1. Function of Benzyl alcohol is mentioned as anesthetic and disinfectant, this needs to be justified by relevant references. Further quality standards of the ingredients are not provided.	Firm clarified that its role is as preservative.
3.2. P.3.2 The quantity of API calculated/ batch does not correspond to the label claim and BP monograph. This requires clarification.	Firm informed that API is calculated as Lincomycin 600mg equivalent to Lincomycin HCl 680.44mg.

Decision: Deferred for submission of valid legalized CoPP issued by the regulatory authority of country of origin.

359.	**Name, address of Applicant / Marketing Authorization Holder**	M/s Shaigan Pharmaceuticals Pvt Limited, 14 Km Adyala Road Post Office Dahgal Rawalpindi.
	Name, address of Manufacturing site.	M/s Shaigan Pharmaceuticals Pvt Limited, 14 Km Adyala Road Post Office Dahgal Rawalpindi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28729 dated 20.10.2021
	Details of fee submitted	PKR 30000/- dated 16.10.201
	The proposed proprietary name / brand name	Admit XR 50/1000 Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Sitagliptin as phosphate monohydrate…50mg Metformin HCl (Extended Release)….1000mg
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Anti-Diabetic

	Reference to Finished product specifications	As per Innovators Specifications
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Janumet XR of Merck Sharp & Dhome USA
	For generic drugs (me-too status)	Tagipmet XR of Highnoon Labs Lahore
	GMP status of the Finished product manufacturer	GMP certificate was issued to the firm by DRAP Islamabad dated 28.08.2020 based on inspection dated 25.09.2019
	Name and address of API manufacturer.	**Sitagliptin Phosphate Monohydrate** M/s Changzhou Pharmaceutical Factory, Address No. 518 Laodong East Road Changzhou Jiangsu Province, China. **Metformin HCl** M/s Smruthi Organics Limited, Plot No. A-27, M.I.D.C Chincoli Tal-Mohol Solapur 413255 Maharashtra India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 3 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 3 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and batch analysis and justification of specification, reference standard,

		container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Janumet XR Tablets CDP has been performed against the aforesaid brand in three media. The f2 value are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have been submitted.

STABILITY STUDY DATA

Manufacturer of API	**<u>Sitagliptin Phosphate Monohydrate</u>** M/s Changzhou Pharmaceutical Factory, Address No. 518 Laodong East Road Changzhou Jiangsu Province, China. **<u>Metformin HCl</u>** M/s Smruthi Organics Limited, Plot No. A-27, M.I.D.C Chincoli Tal-Mohol Solapur 413255 Maharashtra India		
API Lot No.	**<u>Sitagliptin Phosphate Monohydrate</u>** 20200805 Mfg. date: 08.2020 Exp. Date: 07.2022 **<u>Metformin HCl</u>** MNET-009/20 Mfg. date: 01.2020 Exp. Date: 12.2024		
Description of Pack (Container closure system)	Alu- Alu blister packed in unit carton (2x7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	3000 tab	3000 tab	3000 tab
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	05-2023	05-2023	05-2023
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not provided by the firm
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**<u>Sitagliptin Phosphate Monohydrate</u>** Copy of GMP certificate issued by CFDA which is valid till 12.11.2023. **<u>Metformin HCl</u>** Copy of GMP certificate issued by FDA Mahaxsrashtra State India which is valid till 13.11.2022.

3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided by the firm
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not provided
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided

Remarks of Evaluator:

Boxed warning regarding Lactic Acidosis

Query	Reply
<u>Sitagliptin</u> Studies for elucidation of structure are not submitted Batch size is not provided in stability summary/ data	Firm has submitted the route of synthesis of Sitagliptin instead the characterization studies.
Evidence of import of API (Sitagliptin Phosphate Monohydrate & Metformin HCl) used for product development.	Firm has submitted the copy of DRAP attested import invoice of Sitagliptin and metformin.
Propyl Gallate is added in formulation in metformin core as antioxidant, justification needs to be submitted with literature/ innovator product references	Firm has submitted prescribing information of Innovator emphasizing on the description of products rather addressing the query.
You have mentioned in pharmaceutical development that metformin core tablet is coated with Sitagliptin layer and same is again coated with polymeric layer, but the formulation and manufacturing method does not reflect the polymeric layer. This requires justification keeping in view the reference product.	The firm submitted that Sitagliptin is coated with soluble polymeric layer carried by film coating with Opadry green .
You have mentioned that 20% (overage) additional Sitagliptin is added to the formulation to compensate loss of Sitagliptin during coating process. This needs to be justified with experimental data.	The firm informed that 64.25mg of Sitagliptin monohydrate is equal to 50mg of free base. To compensate process losses vial film coating process Sitagliptin is used in 20% of excess to achieve 100% assay results.
Stability data of three months is provided, additional data needs to be submitted.	Firm has submitted the six months of stability data.

Decision: Approved with Innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Regsitration Board decided to advise that firm shall manufacture the product as per Innovator product composition i.e. Janumet XR wherein propyl gallate has been used in API cotaing solution of sitagliptin and shall also include test of Propyl gallate assay in drug product specification for commercial manufacturing.**

• **Registration Board advised PEC, PE&R Division to present agenda regarding abovementioned point for further deliberation and issuance of advisory accordingly.**		
360.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Weather Fold Pharmaceuticals Plot No. 69/1, Phase-II Industrial Estate Hattar.**
	Name, address of Manufacturing site.	M/s Weather Fold Pharmaceuticals Plot No. 69/1, Phase-II Industrial Estate Hattar.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32358 dated 26.11.2021
	Details of fee submitted	PKR 75000/- dated 03.10.2021
	The proposed proprietary name / brand name	Pirfond 801mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Pirfenidone (EP)….801mg
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Antifibrotic (Idiopathic Pulmonary Fibrosis)
	Reference to Finished product specifications	As per Innovators Specifications
	Proposed Pack size	1As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Esbriet Tablets of USFDA
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	Issuance of GMP certificate was recommended by the panel vide inspection dated: 02.02.2019.
	Name and address of API manufacturer.	M/s Optimus Drugs Pvt Limited, Sy. No. 239 & 240 Dothigudem Village Pochampally Mandal Yadari Bhuvanagiri District 5080284 Telangana India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures

		and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 3 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 3 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Estbreit
	Analytical method validation/verification of product	Method validation studies have been submitted.

STABILITY STUDY DATA			
Manufacturer of API	M/s Optimus Drugs Pvt Limited, Sy. No. 239 & 240 Dothigudem Village Pochampally Mandal Yadari Bhuvanagiri District 5080284 Telangana India		
API Lot No.	OP-PIF-A1-001/20 Mfg. date 28.06.2020 Exp. Date: 26.06.2024		
Description of Pack (Container closure system)	Alu- Alu blister packed in unit carton (30's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	1200 tab	1200 tab	1200 tab
Manufacturing Date	12.2020	12.2020	12.2020
Date of Initiation	29.12.2020	29.12.2020	29.12.2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate issued by Drugs Control Administration Govt. of Telangana India dated 03.03.2020 valid for three years from date of issuance
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm submitted copy of DRAP attested invoice No. 2021OD208/EXP dated 17.10.2020 and attestation by DRAP Peshawar dated 05.11.2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Provided
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided
Remarks of Evaluator:		
Decision: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
361.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Weather Fold Pharmaceuticals Plot No. 69/1, Phase-II Industrial Estate Hattar.**
	Name, address of Manufacturing site.	M/s Weather Fold Pharmaceuticals Plot No. 69/1, Phase-II Industrial Estate Hattar.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32872 dated 19.11.2021
	Details of fee submitted	PKR 75000/- dated 07.10.2021
	The proposed proprietary name / brand name	Pirfond 534mg Tablet

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Pirfenidone (EP)….534mg
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Antifibrotic (Idiopathic Pulmonary Fibrosis)
	Reference to Finished product specifications	As per Innovators Specifications
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Esbriet Tablets of USFDA
	For generic drugs (me-too status)	NA
	GMP status of the Finished product manufacturer	Issuance of GMP certificate was recommended by the panel vide inspection dated: 02.02.2019.
	Name and address of API manufacturer.	M/s Optimus Drugs Pvt Limited, Sy. No. 239 & 240 Dothigudem Village Pochampally Mandal Yadari Bhuvanagiri District 5080284 Telangana India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 3 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 3 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and	Pharmaceutical Equivalence have been established

	comparative dissolution profile	against the reference product Estbreit	
	Analytical method validation/verification of product	Method validation studies have been submitted.	
STABILITY STUDY DATA			
Manufacturer of API	M/s Optimus Drugs Pvt Limited, Sy. No. 239 & 240 Dothigudem Village Pochampally Mandal Yadari Bhuvanagiri District 5080284 Telangana India		
API Lot No.	OP-PIF-A1-001/20 Mfg. date 28.06.2020 Exp. Date: 26.06.2024		
Description of Pack (Container closure system)	Alu- Alu blister packed in unit carton (30's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.	PD-04	PD-05	PD-06
Batch Size	500 Tablets	500 Tablets	500 Tablets
Manufacturing Date	12.2020	12.2020	12.2020
Date of Initiation	08.12.2020	08.12.2020	08.12.2020
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not provided	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate issued by Drugs Control Administration Govt. of Telangana India dated 03.03.2020 valid for three years from date of issuance	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm submitted copy of DRAP attested invoice No. 2021OD208/EXP dated 17.10.2020 and attestation by DRAP Peshawar dated 05.11.2020.	
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Provided	

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided
Remarks of Evaluator:		
Decision: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		
362.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Weather Fold Pharmaceuticals Plot No. 69/1, Phase-II Industrial Estate Hattar.**
	Name, address of Manufacturing site.	M/s Weather Fold Pharmaceuticals Plot No. 69/1, Phase-II Industrial Estate Hattar.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33997 dated 29.12.2021
	Details of fee submitted	PKR 75000/- dated 05.10.2021
	The proposed proprietary name / brand name	Pirfond 267mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Pirfenidone (EP)….267mg
	Pharmaceutical form of applied drug	Film Coated Tablet
	Pharmacotherapeutic Group of (API)	Antifibrotic (Idiopathic Pulmonary Fibrosis)
	Reference to Finished product specifications	As per Innovators Specifications
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Esbriet Tablets of USFDA
	For generic drugs (me-too status)	NA

	GMP status of the Finished product manufacturer	Issuance of GMP certificate was recommended by the panel vide inspection dated: 02.02.2019.
	Name and address of API manufacturer.	M/s Optimus Drugs Pvt Limited, Sy. No. 239 & 240 Dothigudem Village Pochampally Mandal Yadari Bhuvanagiri District 5080284 Telangana India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 3 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 3 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product Estbreit
	Analytical method validation/verification of product	Method validation studies have been submitted.

STABILITY STUDY DATA	
Manufacturer of API	M/s Optimus Drugs Pvt Limited, Sy. No. 239 & 240 Dothigudem Village Pochampally Mandal Yadari Bhuvanagiri District 5080284 Telangana India
API Lot No.	OP-PIF-A1-001/20 Mfg. date 28.06.2020 Exp. Date: 26.06.2024
Description of Pack (Container closure system)	Alu- Alu blister packed in unit carton (30's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.	PD-07	PD-08	PD-09
Batch Size	500 tablets	500 tablets	500 tablets
Manufacturing Date	12.2020	12.2020	12.2020
Date of Initiation	08.12.2020	08.12.2020	08.12.2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate issued by Drugs Control Administration Govt. of Telangana India dated 03.03.2020 valid for three years from date of issuance
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm submitted copy of DRAP attested invoice No. 2021OD208/EXP dated 17.10.2020 and attestation by DRAP Peshawar dated 05.11.2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Provided
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Provided
Remarks of Evaluator:		
Decision: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		

Case No. 3 Deferred cases in previous meetings

363.	**Name, address of Applicant / Importer**	**M/s AMB HK Enterprises (Pvt) Ltd., 2nd Floor Plaza 60 Commercial Block-K, Phase 1 DHA Lahore**

	Details of Drug Sale License of importer	**License No:** 05-352-0058-066904D **Address:** 2nd Floor Plaza 60 Commercial Block-K, Phase 1 DHA Lahore **Address of Godown:** NA **Validity:** 24.02.2023 **Status:** License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s Reyoung Pharmaceutical Co., Ltd., No. 1 Ruiyang Road Yiyuan County Shandong Province P.R. China
	Name, address of manufacturer(s)	M/s Reyoung Pharmaceutical Co., Ltd., No. 1 Ruiyang Road Yiyuan County Shandong Province P.R. China
	Name of exporting country	People's Republic of China
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	**CoPP:** Firm has submitted original legalized COPP No. 201910002 issued by Yiyuan Market Supervision Administration of P.R China. Validity: 23.10.2021
	Details of letter of authorization / sole agency agreement	Copy of sole agency agreement is submitted b/w M/s Reyoung Pharmaceutical Co., Ltd., China and M/s AMB HK Enterprises (Pvt) Ltd. Lahore
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 33107 dated 21.10.2021
	Details of fee submitted	PKR /-: 150000/- dated 02.11.2021
	The proposed proprietary name / brand name	**CEFITRIN 1GM INJECTION**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone as sodium……1gm
	Pharmaceutical form of applied drug	Powder for Injection
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP Specifications
	Proposed Pack size	Pack of 1 Vial and 1ampoule of 10ml
	Proposed unit price	Rs. 319.50/- per vail
	The status in reference regulatory	Rocephin 1gm injection

	authorities	
	For generic drugs (me-too status)	Rocephin 1gm Injection (Reg No.050585)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per Module II.
	Name, address of drug substance manufacturer	M/s Reyoung Pharmaceutical Co., Ltd., No. 1 Ruiyang Road Yiyuan County Shandong Province P.R. China
	Module-III Drug Substance:	Firm has submitted drug substance data for sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, flow diagram of manufacturing process and controls, impurities, specifications, analytical procedures, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted long term stability study data of 3 batches of drug substance at 30°C ± 2°C / 75 ± 5% RH for 24 months. The accelerated stability data is conducted at 40°C ± 2°C / 75 ± 5% RH for 6 months
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, method validation studies, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence data submitted with Rocephin 1gm injection.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type I Glass Vial 10ml Type I Glass Ampoule
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. Accelerated stability studies have been conducted at 40°C±2°C and 75%±5% RH for 6 months. Real time stability studies conducted at 30°C±2°C and 65% ± 5% for 36 months Firm requested 36months shelf life

The above product was considered in 321st meeting of Registration Board and the Board decided as under:

- Issuance of CoPP by relevant regulatory authority.
- Submission of legalized CoPP as present expired on 23.10.2021 (2 days after submission of application).

In response the firm vide Dy. No. 31427 dated 02.11.2022 has now submitted the valid legalized CoPP vide No. Shandong 20223118 issued by Shandong Provincial Medical Products Administration dated 13.09.2022 valid till 12.09.2024.		
Decision: Approved as per Policy for inspection of Manufacturer abroad.		
364.	**Name, address of Applicant / Importer**	**M/s AMB HK Enterprises (Pvt) Ltd., 2nd Floor Plaza 60 Commercial Block-K, Phase 1 DHA Lahore**
	Details of Drug Sale License of importer	**License No:** 05-352-0058-066904D **Address:** 2nd Floor Plaza 60 Commercial Block-K, Phase 1 DHA Lahore **Address of Godown:** NA **Validity:** 24.02.2023 **Status:** License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s Haikou Pharmaceutical Factory Co., Ltd., No. 192 Nanahai Road, Xiuying District Haikou Hainan, China
	Name, address of manufacturer(s)	M/s Haikou Pharmaceutical Factory Co., Ltd., No. 192 Nanahai Road, Xiuying District Haikou Hainan, China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original legalized COPP (No. Hainan 20200007) issued on 30.04.2020 by Hainan Medical Products Administration, People's Republic of China. **Validity**: 20.12.2020
	Details of letter of authorization / sole agency agreement	Copy of sole agency agreement is submitted, which indicates agreement of M/s Haikou Pharmaceutical Factory Co., Ltd., & M/s Jilin North Biotech Pharma Imp & Exp Co. Ltd China with M/s AMB HK Enterprises (Pvt) Ltd Lahore
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 27485: 05-10-2021
	Details of fee submitted	PKR 100000/- dated 26-04-2021 and 50000/- dated 07-06-2021

	The proposed proprietary name / brand name	**MEROGON INJECTION 1g**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as Meropenem trihydrate) …….1g
	Pharmaceutical form of applied drug	Powder for Injection
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	Pack of 1's Vial
	Proposed unit price	Rs 2463/- per vial
	The status in reference regulatory authorities	**USFDA** Approved.
	For generic drugs (me-too status)	MERONEM Injection of Pfizer (reg no. 096203)
	Module-II (Quality Overall Summary)	Firm has submitted QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Chongqing Tiandi Pharmaceutical Co., Ltd., No. 1 Shenyang Road, Zhongzhou Avenue Zhongxian County Chongquing China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 2-8^{0}C. The stability study data is till 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard

		or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been submitted by the manufacturer.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	USP type-I glass
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30°C ±2°C / 75% ± 5% RH. The real time stability study data of 3 batches is for 24 months Firm has also submitted in-use stability data after reconstitution with various diluents used for bolus injection and infusion
Remarks of Evaluator: The above product was deferred in 321st meeting of Registration board for submission of valid legalized CoPP as present expired before submission of registration application. In response to the above decision the firm has submitted Legalized valid CoPP vide No. Hainan 20220062 issued by Hainan Medical Products Administration China dated 28.07.2022 valid till 01.01.2024.		
Decision: Approved as per Policy for inspection of Manufacturer abroad.		
365.	**Name, address of Applicant / Importer**	M/s AMB HK Enterprises (Pvt) Ltd., 2nd Floor Plaza 60 Commercial Block-K, Phase 1 DHA Lahore
	Details of Drug Sale License of importer	**License No:** 05-352-0058-066904D **Address:** 2nd Floor Plaza 60 Commercial Block-K, Phase 1 DHA Lahore **Address of Godown:** NA **Validity:** 24.02.2023 **Status:** License to sell drugs as distributor
	Name and address of marketing authorization holder (abroad)	M/s Haikou Pharmaceutical Factory Co., Ltd., No. 192 Nanahai Road, Xiuying District Haikou Hainan, China
	Name, address of manufacturer(s)	M/s Haikou Pharmaceutical Factory Co., Ltd., No. 192 Nanahai Road, Xiuying District Haikou Hainan, China.
	Name of exporting country	China
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original legalized COPP (No. Hainan 20200006) issued on 30.04.2020 by Hainan Medical Products Administration, People's Republic of China. **Validity**: 20.12.2020
	Details of letter of authorization / sole agency agreement	Copy of sole agency agreement is submitted, which indicates agreement of M/s Haikou Pharmaceutical Factory Co., Ltd., & M/s Jilin

		North Biotech Pharma Imp & Exp Co. Ltd China with M/s AMB HK Enterprises (Pvt) Ltd Lahore
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 27485: 05-10-2021
	Details of fee submitted	PKR 100000/- dated 26-04-2021 and 50000/- dated 07-06-2021
	The proposed proprietary name / brand name	**MEROGON INJECTION 500mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Meropenem (as Meropenem trihydrate) …….500mg
	Pharmaceutical form of applied drug	Powder for Injection
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	Pack of 1's Vial
	Proposed unit price	Rs 1289/- per vial
	The status in reference regulatory authorities	**USFDA** Approved.
	For generic drugs (me-too status)	MERONEM Injection of Pfizer (reg no. 096203)
	Module-II (Quality Overall Summary)	Firm has submitted QOS. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Chongqing Tiandi Pharmaceutical Co., Ltd., No. 1 Shenyang Road, Zhongzhou Avenue Zhongxian County Chongquing China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature,

		structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 2-8^{0}C. The stability study data is till 24 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence is submitted by the firm
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	USP type-I glass
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches The accelerated stability study data is conducted at 40^{o}C ±2^{o}C / 75% ± 5% RH for 6 months. The real time stability study data is conducted at 30^{o}C ±2^{o}C / 75% ± 5% RH. The real time stability study data of 3 batches is for 24 months Firm has also submitted in-use stability data after reconstitution with various diluents used for bolus injection and infusion
Remarks of Evaluator: The above product was deferred in 321st meeting of Registration board for submission of valid legalized CoPP as present expired before submission of registration application. In response to the above decision the firm has submitted Legalized valid CoPP vide No. Hainan 20220061 issued by Hainan Medical Products Administration China dated 28.07.2022 valid till 01.01.2024.		
Decision: Approved as per Policy for inspection of Manufacturer abroad.		
366.	**Name, address of Applicant / Importer**	**M/s. Glisten Pharma,** **Plot No. 520 Sector 7/A Korangi Industrial Area Karachi.**
	Details of Drug Sale License of importer	**License No:** 10930 dated 15.04.2019

		Address: Plot No. 520 Sector 7/A Korangi Industrial Area Karachi. **Address of Godown:** NA **Validity:** 19.02.2021 **Status:** Drug License by way of Whole Sale
	Name and address of marketing authorization holder (abroad)	M/s Pierrel Pharma S.R.L., Strada Statale Appia 46/48-& Bis 46/48 81043Capua Italy
	Name, address of manufacturer(s)	M/s Pierrel S.p.A Strada Statale Appia 46/48-& Bis 46/48 81043Capua Italy
	Name of exporting country	Italy
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	Firm has submitted legalized CoPP Bo. No CPP /2019/1312 dated 18.06.2019
	Details of letter of authorization / sole agency agreement	The firm has submitted original sole agency agreement dated 11.09.2019 by marketing authorization holder i.e. M/s Pierrel Pharma S.R.L., Strada Statale Appia 46/48-& Bis 46/48 81043Capua Italy
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 27812 dated 07.10.2021
	Details of fee submitted	PKR 100,000/- dated 06.01.2021
	The proposed proprietary name / brand name	ORABLOC 1:100,000
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1ml solution for injection contains: Articaine HCl….40mg Adrenaline (Epinephrine) as tartrate….0.01mg
	Pharmaceutical form of applied drug	Solution for Injection for dental use
	Pharmacotherapeutic Group of (API)	Local Anesthetic
	Reference to Finished product specifications	Ph. Eur.
	Proposed Pack size	Rs. 7000/- for 50 Cartridges of 1.8ml
	Proposed unit price	Price will be communicated at time of pricing.
	The status in reference regulatory authorities	USFDA approved

	For generic drugs (me-too status)	Articaine 4% with Epinephrine 1:100000 of continental Chemical Company Islamabad. Reg. No: 052238
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	**ARTICAINE HCL:** **Name of Holder**: Moehs Iberica S.L Cesar MArtinell Brunet No., 12 A Poligono Industrial rubi Sur Apain 08191 Rubi Barcelona **Sites of Production**: Benechim S.P.R.L Rue Rene Magritte, 163 Belgium 7860 Lessines **Name of Holder:** SIEGFRIED EVIONNAZ SA, Route du Simplon 1, 36 Switzerlan-1902 Evuibbaz **Sites of Production**: SIEGFRIED ST. VULBAS SAS Parc Industrial de la plaine de I'Ain France-01150 Saint-Vulbas **Siegfried Evionnaz SA** Route du Simplon 1, 36 Switzerlan-1902 Evuibbaz **ADERNALINE TARTRATE:** **Name of Holder**: CAMBREX PROFARMACO MILANO S.R.L. Via Curiel, 34 Italy-20067 Paullo, Milano **Site of Production: -** CAMBREX PROFARMACO MILANO S.R.L. Via Curiel, 34 Italy-20067 Paullo, Milano
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at $25^{o}C \pm 2^{o}C$. The stability study data is provided till 60 months.

	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	The firm has submitted the Pharmaceutical equivalence with reference products.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	The Primary container consists of a 1.8ml glass cartridge made of neutral glass type closed with bromobutyl rubber plunger and bromobutyl rubber seal with an aluminium cap.
	Stability study data of drug product, shelf life and storage conditions	Stability testing results of 3 batches of formulation are reported at 25^{o}C RH 60% for 24 months, **30^{o}C / 65%RH for 12 months** and 40^{o}C RH 75% for 6 months. The only impurity detected whose concentration varies with time and temperature is Articaine acid (Hydrolysis products of Articaine) which although reaches maximum concentration of 0.35% after 6 months at 40^{o}C (stressed condition) still remains within the set specification of NMT 0.4% in area with respect to Articaine. Articaine Acid is the main metabolite of Articaine and the concentrations found in the drug product, even at the end of shelf life does not pose any potential heal concern. The formulation is quite stable and remains within specifications after 24 months at 25^{o}C, consequently a shelf life storage condition of 24 months at 25^{o}C is proposed for the drug product stored in its commercial packaging.

Query	**Reply**
i. Valid Drug Sale License because the submitted copy indicates validity till 19.02.2022.	i. The firm has submitted new drug sale license issued vide No. 0129 No. DHO (East) Drug-786 dated 18.06.2021 valid till 10.06.2023. having address Office No. 403 4th Floor Al Reef Tower, Plot No. 391/3 BYCHS Alamgir Road Karachi. The address mentioned on the aforesaid new DSL is different from the address of the DSL submitted initially with the application.
ii. Differential fee of 50,000/- is required w.r.t. revised fee SRO because registration application was submitted on 07.10.2021.	ii. The firm has now submitted the differential fee of 50000/- vide Slip No. 17375749 dated 03.08.2022.
iii. Proposed Price needs to be submitted being requirement of application i.e. Form-5F.	

iv. Reference of other similar approved medicines with information pertaining to Manufacturer name, brand name, strength, composition, registration number & dosage form, Pack size and Price as required under 1.5.8. v. Long term stability study data need to be submitted as per Zone IV-A i.e. (30°C/65%RH).	iii. The firm submitted price of Rs. 7000/- for 50 Cartridges of 1.8ml. iv. Articaine 4% with Epinephrine 1:100000 of continental Chemical Company Islamabad. v. Reg. No: 052238. vi. The firm has attached intermediate study of 30°C / 65%RH for 12 months of three batches which has already been provided.
Evaluation by PEC: Registration Board in 321st meeting deferred for following and accordingly the reply is tabulated against each:	
Clarification whether the sole agency agreement is with M/s. Glisten Pharma, Plot No. 520 Sector 7/A Korangi Industrial Area Karachi or with M/s Glisten Pharma Office No. 403 4th Floor Al Reef Tower, Plot No. 391/3 BYCHS Alamgir Road Karachi.	The firm has submitted the new agency agreement indicating DSL: M/s Glisten Pharma Office No. 403 4th Floor Al Reef Tower, Plot No. 391/3 BYCHS Alamgir Road Karachi as warehouse of the firm and head office as M/s. Glisten Pharma, Plot No. 520 Sector 7/A Korangi Industrial Area Karachi
Clarification of the address of DSL since two DSL with different address have been submitted	The firm informed that we have change wareghouse due to safety reasons, hence DSL M/s Glisten Pharma Office No. 403 4th Floor Al Reef Tower, Plot No. 391/3 BYCHS Alamgir Road Karachi will be the ware house of the firm.
Submission of long term stability studies data as per Zone IV a conditions till claimed shelf life.	The storage conditions of the product is below 25C therefore stability studies for the Zone IV A are not conducted. Intermediate studies at 30C/65% RH have been performed.
Decision: Approved with Innovators specifications as per policy of inspections of manufacturer abroad with shelf life as per available data of long term stability studies on Zone IV conditions. The firm shall also submit following before issuance of registration letter: **i. New agency agreement in name of address as mentioned on the DSL because the earlier letter indicates DSL address as warehouse.** **ii. Full fee as address of Importer is changed as per submitted new DSL.**	

Item No. IX: Agenda of Evaluator-XX (Mst. Sana Kanwal)

EVALUATION OF REGISTRATION DOSSIERS ON PRIORITY BASIS ON ACCOUNT OF EXPORT FACILITATION.

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the pharmaceutical i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year. In compliance to the aforementioned decision of the Board, the following firm have achieved the benchmark of more than 100,000 USD during the fiscal Year 2021-2022 and submitted their applications for priority consideration/ evaluation as communicated by Assistant Director (PR-I/EFD) vide letter No No.F.1-6/2019-PR-I (EFD dated 06th October 2022.

367.	Name, address of Applicant / Marketing Authorization Holder	M/s WnsFeild Pharmaceutical Industrial Estate Hattar Haripur Kpk Pakistan.
	Name, address of Manufacturing site.	M/s WnsFeild Pharmaceutical Plot No. 122 Phase 5, Industrial Estate Hattar Haripur Kpk Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23665 DRAP (R&I) dated 22/08/2022
	Details of fee submitted	PKR 30,000/-: dated 22/06/2022
	The proposed proprietary name / brand name	Esonyp 20/375mg DR Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each modified release tablet contains: Esomeprazole (as magnesium trihydrate) as IR…….20mg Naproxen as enteric coated core …….375mg
	Pharmaceutical form of applied drug	White to Off White color Naproxen oblong shape enteric coated tablet over film coated Esomeprazole tablets.
	Pharmacotherapeutic Group of (API)	Esomeprazole: Proton Pump Inhibitors Naproxen: Anti-inflammatory and antirheumatic products, non-steroids. Propionic acid derivatives.
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	3x10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Vimovo delayed release tablet 20/375mg USFDA
	For generic drugs (me-too status)	Glomov 20/375mg tablet by M/s Global Pharmaceutical (Pakistan) Reg No 109338
	GMP status of the Finished product manufacturer	GMP inspection conducted on 10/12/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Esomeprazole: Metrochem API Private Ltd. India flat No 302, Bhanu Enclave , Sunder Nagar, Erragada, Hyderabad , India. Naproxen: Divis laboratories Limited India

		1-72/23(P)/DIVIS/303, Divi towers, cyber hills, Gachibowli, Hyderabad-500 032, Telangana, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Esomeprazole The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, specifications, analytical procedures and justification of specification, reference standard, container closure system and stability studies of drug substance Analytical verification studies not provide by both DS and FPP manufacturer. CoA of relevant batch of DS to be provided by FPP manufacturer Naproxen The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, specifications. CoA from both DS and FPP manufacturer is not provided Analytical verification studies not provide by both DS and FPP manufacturer.
	Stability studies	Esomeprazole Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (ESM M-089, ESM M-092 and ESM-M-091.) Naproxen Not provided
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification,

		reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has not been performed CDP has been performed against the same brand that is Glomov 20/375mg tablet Batch No 21G111 by Global Pharmaceutical (Pakistan), Esomeprazole: In water, Acetate Buffer (pH 4.5) and Phosphate Buffer (pH 6.8). Naproxen: Phosphate Buffer (pH 6.8).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API (Esomeprazole)	Metrochem API Private Ltd. India		
API Lot No. (Esomeprazole)	Not provided		
Manufacturer of API (Naproxen)	Divis laboratories Limited India		
API Lot No. (Naproxen)	Not provided		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	Esonyp 20/375mg DR Tablet		
Batch No.	EN-01	EN-02	EN-03
Batch Size	1200 tab	1200 tab	1200 tab
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	06-08-2021	06-08-2021	06-08-2021
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	N/A

	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not provided
	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Summary data sheet to be provided
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not provided
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not provided

Remarks of Evaluator

Sr.#	Observation	Reply
	Approval of Drug Substance/Drug Manufacturing License (DML)/Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided (for both Esomeprazole and Naproxen)	Firm has submitted copy of GMP certificate of Metrochem API Private Ltd. India No L.Dis.No 4084/A3/2019 dated 20.05.2020 Valid till three years **GMP certificate of Divis laboratories Limited India No L.Dis.No 816/DCA/AP/2018 dated 24.07.2018 Valid till three years**
2.	Characterization, Elucidation of Structure and other Characteristics of Naproxen to be provided.	**As naproxen is officially recognized and available in USP hence this section is not required.** **Drug substance (APIs) that are described in an officially recognized pharmacopoeia it is generally sufficient to provide copies of the IR spectrum. Same to be provided by the firm.**
3.	Detailed analytical procedures for the testing of drug substance to be provided by both Drug Substance and Drug Product manufacturer	**Not complied** **Firm has submitted analytical procedure of testing finished product rather than drug substance moreover only brief assay methods for both drug substances are submitted from DS manufacturer.**
4.	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug	complied

	Product manufacturer for both compendial as well as non compendial drug substance(s) to be provided	
5.	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacture.	Not complied Later on firm has submitted CoA of relevant batch by Drug Product manufacturer and Drug Substance manufacturer, also documents regarding procurement of relevant batch of Drug Substances.
6.	COA of primary / secondary reference standard for Naproxen including source and lot number to be provided.	Not complied Later on firm has submitted CoA of primary / secondary reference standard for Naproxen including source and lot number.
7.	For testing of Pharmacopeial Drug Substance, the use of primary reference standard is recommended, justify use of working standard for Esomeprazole magnesium	We have used working standard from Drug substances manufacturer which is qualified against primary standard.
8.	Stability data of Naproxen to be provided.	Firm has submitted stability data of naproxen as follows: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (2-M5L003, 2-M5L004 and 2M5L005)
9.	Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters of developed formulation against reference product	**Not complied** **Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters while firm has submitted comparison of assay only.** **Furthermore selection of following mediums in CDP to be justified** **Esomeprazole:** **In water, Acetate Buffer (pH 4.5) and Phosphate Buffer (pH 6.8).** **Naproxen:** **Phosphate Buffer (pH 6.8).**
10.	The dissolution of naproxen was evaluated in two different pH media, pH 1.2 and 6.8 and dissolution of Esomeprazole has	Firm has selected dissolution parameters as per USFDA dissolution method database.

	been performed at pH medium 7.4. Justify dissolution parameters adopted by firm.	
11.	Uniformity of dose and microbial attributes are not provided in finished product specification	Firm has provided Uniformity of dose and microbial attributes for 3 batches EN-01, EN-02 and EN-03.
12.	Provide summary data sheets for all 3 batches. EN-01, EN-02. EN-03	Complied.
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product and Record of Digital data logger for temperature and humidity monitoring of stability chambers to be provided.	**We use water HPLC (USA made) with Empower2 software which is not 21CFR compliant**. Manual record of temp and humidity control maintained in log book will be presented at the time of inspection.
14.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Wnsodex 60mg and 30mg DDR capsule (dexlansoprazole) on 1st September, 2020. Further, the said panel inspection report was discussed in 297th Drug Registration Board meeting. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Related manufacturing area, equipment, personnel and Related manufacturing area, equipment, personnel and utilities are GMP compliant.

Decision: Deferred for following observations:

- **Valid GMP certificate of Drug Substance manufacturer i.e M/s Divis laboratories Limited India.**
- **Details of analytical procedures for the testing of drug substances by both Drug Substance and Drug Product manufacturer including characterisation for Naproxen.**
- **Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters. Furthermore, selection of mediums in CDP studies hall be justified**

368.	Name, address of Applicant / Marketing Authorization Holder	M/s WnsFeild Pharmaceutical Industrial Estate Hattar Haripur Kpk Pakistan.
	Name, address of Manufacturing site.	M/s WnsFeild Pharmaceutical Plot No. 122 Phase 5, Industrial Estate Hattar Haripur Kpk Pakistan.
	Status of the applicant	☒ Manufacturer

		☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24965 DRAP (R&I) dated 02/09/2022
	Details of fee submitted	PKR 30,000/-: dated 22/06/2022
	The proposed proprietary name / brand name	Esonyp 20/500mg DR Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each modified release tablet contains: Esomeprazole (as magnesium trihydrate) as IR…….20mg Naproxen as enteric coated core …….500mg
	Pharmaceutical form of applied drug	White to Off White color Naproxen oblong shape enteric coated tablet over film coated Esomeprazole tablets.
	Pharmacotherapeutic Group of (API)	Esomeprazole: Proton Pump Inhibitors Naproxen: Anti-inflammatory and antirheumatic products, non-steroids. Propionic acid derivatives.
	Reference to Finished product specifications	Innovator's
	Proposed Pack size	3x10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Vimovo delayed release tablet 20/500mg USFDA
	For generic drugs (me-too status)	Glomov 20/500mg tablet by M/s Global Pharmaceutical (Pakistan) Reg No 109338
	GMP status of the Finished product manufacturer	GMP inspection conducted on 10/12/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Esomeprazole: Metrochem API Private Ltd. India flat No 302, Bhanu Enclave , Sunder Nagar, Erragada, Hyderabad , India. Naproxen: Divis laboratories Limited India 1-72/23(P)/DIVIS/303, Divi towers, cyber hills, Gachibowli, Hyderabad-500 032, Telangana, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and

		controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Esomeprazole The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form,specifications, analytical procedures and justification of specification, reference standard, container closure system and stability studies of drug substance Analytical verification studies not provide by both DS and FPP manufacturer. CoA of relevant batch of DS to be provided by FPP manufacturer Naproxen The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, specifications. CoA from both DS and FPP manufacturer is not provided Analytical verification studies not provide by both DS and FPP manufacturer.
	Stability studies	Esomeprazole Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (ESM M-089, ESM M-092 and ESM-M-091.) Naproxen Not provided
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has not been performed CDP has been performed against the same brand that is Glomov 20/500mg tablet Batch No 21G115 by Global Pharmaceutical (Pakistan), Esomeprazole: In water, Acetate Buffer (pH 4.5) and Phosphate Buffer (pH 6.8). Naproxen: Phosphate Buffer (pH 6.8).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API (Esomeprazole)	Metrochem API Private Ltd. India		
API Lot No. (Esomeprazole)	Not provided		
Manufacturer of API (Naproxen)	Divis laboratories Limited India		
API Lot No. (Naproxen)	Not provided		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	Esonyp 20/500mg DR Tablet		
Batch No.	EN-04	EN-05	EN-06
Batch Size	1200 tab	1200 tab	1200 tab
Manufacturing Date	08-2021	08-2021	08-2021
Date of Initiation	11-08-2021	11-08-2021	11-08-2021
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not provided

	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Inadequate
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not provided
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not provided

Remarks of Evaluator:

Sr.#	Observations	Reply
1.	Approval of Drug Substance/Drug Manufacturing License (DML)/Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided (for both Esomeprazole and Naproxen)	Firm has submitted copy of GMP certificate of Metrochem API Private Ltd. India No L.Dis.No 4084/A3/2019 dated 20.05.2020 Valid till three years **GMP certificate of Divis laboratories Limited India No L.Dis.No 816/DCA/AP/2018 dated 24.07.2018** **Valid till three years**
2.	Characterization, Elucidation of Structure and other Characteristics of Naproxen to be provided.	**As naproxen is officially recognized and available in USP hence this section is not required.** **Drug substance (APIs) that are described in an officially recognized pharmacopoeia it is generally sufficient to provide copies of the IR spectrum. Same to be provided by the firm.**
3.	Detailed analytical procedures for the testing of drug substance to be provided by both Drug Substance and Drug Product manufacturer	**Not complied** **Firm has submitted analytical procedure of testing finished product rather than drug substance moreover only brief assay methods for both drug**

		substances are submitted from DS manufacturer.
4.	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non compendial drug substance(s) to be provided	complied
5.	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacture.	Not complied Later on firm has submitted CoA of relevant batch by Drug Product manufacturer and Drug Substance manufacturer, also documents regarding procurement of relevant batch of Drug Substances.
6.	COA of primary / secondary reference standard for Naproxen including source and lot number to be provided.	Not complied Later on firm has submitted CoA of primary / secondary reference standard for Naproxen including source and lot number
7.	For testing of Pharmacopeial Drug Substance, the use of primary reference standard is recommended, justify use of working standard for Esomeprazole magnesium	We have used working standard from Drug substances manufacturer which is qualified against primary standard.
8.	Stability data of Naproxen to be provided.	Firm has submitted stability data of naproxen as follows: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (2-M5L003, 2-M5L004 and 2M5L005)
9.	Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters of developed formulation against reference product	**Not complied** **Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters while firm has submitted comparison of assay only.**
10.	Similarity factor f2 has not been calculated and result has not been concluded accordingly	Not complied. Later on firm has submitted calculation of f2 (similarity factor). **Furthermore, selection of following mediums in CDP to be justified**

		Esomeprazole: **In water, Acetate Buffer (pH 4.5) and Phosphate Buffer (pH 6.8).** **Naproxen:** **Phosphate Buffer (pH 6.8).**
10.	The dissolution of naproxen was evaluated in two different pH media, pH 1.2 and 6.8 and dissolution of Esomeprazole has been performed at pH medium 7.4. Justify dissolution parameters adopted by firm.	Firm has selected dissolution parameters as per USFDA dissolution method database.
11.	Uniformity of dose and microbial attributes are not provided in finished product specification	Firm has provided Uniformity of dose and microbial attributes for 3 batches EN-04, EN-05 and EN-06.
12.	Stability data particularly chromatograms , CoA and raw data sheets (both accelerated and real time) for batch No EN-06 is not provided for each time point	complied.
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product and Record of Digital data logger for temperature and humidity monitoring of stability chambers to be provided.	**We use water HPLC (USA made) with Empower2 software which is not 21CFR compliant.** **Manual record of temp and humidity control maintained in log book will be presented at the time of inspection.**
14.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Wnsodex 60mg and 30mg DDR capsule (dexlansoprazole) on 1st September, 2020. Further, the said panel inspection report was discussed in 297th Drug Registration Board meeting. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Related manufacturing area, equipment, personnel and utilities are GMP compliant.

Decision: Deferred for following observations:

- **Valid GMP certificate of Drug Substance manufacturer i.e M/s Divis laboratories Limited India.**
- **Details of analytical procedures for the testing of drug substances by both Drug Substance and Drug Product manufacturer including characterisation for Naproxen.**
- **Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters. Furthermore, selection of mediums in CDP shall be justified**

369.	Name, address of Applicant / Marketing Authorization Holder	M/s WnsFeild Pharmaceutical Industrial Estate Hattar Haripur Kpk Pakistan.
	Name, address of Manufacturing site.	M/s WnsFeild Pharmaceutical Plot No. 122 Phase 5, Industrial Estate Hattar Haripur Kpk Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 4446 (R&I) DRAP, dated 16/02/2022
	Details of fee submitted	PKR 30,000/-: dated 12/10/2021
	The proposed proprietary name / brand name	Verozen 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan (as Fumarate)…….10mg
	Pharmaceutical form of applied drug	Light yellow color round, Biconvex Film coated tablet.
	Pharmacotherapeutic Group of (API)	Potassium-Competitive Acid Blokers (PCAB)
	Reference to Finished product specifications	Innovator's specification
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab 10mg tablet by M/s Takeda pharmaceutical company Ltd. PMDA Japan approved
	For generic drugs (me-too status)	Vonseca 20mg tablet by M/s Tabros, Karachi ,Reg No. 112584

	GMP status of the Finished product manufacturer	GMP inspection conducted on 10/12/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Xianqiang Pharmaceutical Pvt Ltd, No. 6, industrial Avenue, Conghua, Economical Development zone, Guangzhou city, Guangdong province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Vonoprazan is not present in BP and USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(TAK09R150701, TAK09R150702, TAK09R150703)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	CDP has been performed against the same brand that is Voniza 10mg tablet by Hilton Pharma (Batch No 138849) in Acid media

		(pH 1.0-1.2) in Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Xianqiang Pharmaceutical Pvt Ltd, China		
API Lot No.			
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	20mg/Tablet		
Batch No.	VP-01	VP-02	VP-03
Batch Size	1200 tab	1200 tab	1200 tab
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	12-05-2021	12-05-2021	12-05-2021
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. GD20150397 of M/s Xianqiang Pharmaceutical Pvt Ltd, China issued by China Food and Drug Administration. The certificate is valid till 06-09-2020.
	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted import License No. 00169/2021-DRAP CPS/650 dated 16-02-2021 confirming import of 200g Vonoprazan from M/s Xianqiang Pharmaceutical Pvt Ltd, China for Batch No. TAK09R210101
	Data of stability batches will be supported by attested respective documents like chromatograms,	Submitted

	Raw data sheets, COA, summary data sheets etc.	
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Remarks of Evaluator:

Sr. #	Observation	Reply (dated 30/10/2022)
	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided	Not complied Later on firm has submitted copies of Drug manufacturing certificate No Yue20160016 dated 24.12.2020 valid till 23.12.2025 issued by Guandong provincial Drug Administration and GMP certificate (No 20220616) dated 16.06.2022 valid till 15.06.2026
	Detailed analytical procedures for the testing of drug substance to be provided by both Drug Substance and Drug Product manufacturer	complied
	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non compendial drug substance(s) to be provided	complied
	COA of primary / secondary reference standard for Vonoprazan Fumarate including source and lot number to be provided.	Working standard for Vonoprazan Fumarate batch No A061-210101 from Xianqiang Pharmaceutical Pvt Ltd, China is provided
	Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters of developed formulation against reference product	**Not complied** **Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters while firm has submitted comparison of assay only.**
	Uniformity of dose and microbial attributes are not provided in finished product specification	complied
	Stability data particularly chromatograms , CoA and raw data sheets (both accelerated and real time) is not provided for each time point	complied

	Compliance Record of HPLC software 21CFR & audit trail reports on product and Record of Digital data logger for temperature and humidity monitoring of stability chambers to be	**We use water HPLC (USA made) with Empower2 software which is not 21CFR compliant.** **Manual record of temp and humidity control maintained in log book will be presented at the time of inspection.**
	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Wnsodex 60mg and 30mg DDR capsule (dexlansoprazole) on 1st September, 2020. Further, the said panel inspection report was discussed in 297th Drug Registration Board meeting. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Related manufacturing area, equipment, personnel and utilities are GMP compliant.
	Justification to be provided for selection of dissolution parameters i.e Acceptance criteria and volume of dissolution medium	Dissolution parameters are selected as per USFDA guidance document for immediate release solid dosage form
	Compatibility of the Drug Substance(s) with excipients is not provided (mainly IPA which has been used by the firm in film coating). Specifications of IPA also not provided.	Not complied Later on firm submitted that they are using purified water in coating, IPA was written mistakenly.

Decision: Approved with Innovator's specifications. Registration letter will b eissued upon submission of Pharmaceutical equivalence studies including all test of batch release against the innovator/reference comparator product.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

370.	Name, address of Applicant / Marketing Authorization Holder	M/s WnsFeild Pharmaceutical Industrial Estate Hattar Haripur Kpk Pakistan.
	Name, address of Manufacturing site.	M/s WnsFeild Pharmaceutical

		Plot No. 122 Phase 5, Industrial Estate Hattar Haripur Kpk Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 4445 (R&I) DRAP, dated 16/02/2022
	Details of fee submitted	PKR 30,000/-: dated 12/10/2021
	The proposed proprietary name / brand name	Verozen 20mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan (as Fumarate)…….20mg
	Pharmaceutical form of applied drug	Light yellow color round, Biconvex Film coated tablet.
	Pharmacotherapeutic Group of (API)	Potassium-Competitive Acid Blokers (PCAB)
	Reference to Finished product specifications	Innovator's specification
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Takecab 20mg tablet by M/s Takeda pharmaceutical company Ltd. PMDA Japan approved
	For generic drugs (me-too status)	Vonseca 20mg tablet by M/s Tabros, Karachi ,Reg No. 112585
	GMP status of the Finished product manufacturer	GMP inspection conducted on 10/12/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Xianqiang Pharmaceutical Pvt Ltd, No. 6, industrial Avenue, Conghua, Economical Development zone, Guangzhou city, Guangdong province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls,

		impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Vonoprazan is not present in BP and USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(TAK09R150701, TAK09R150702, TAK09R150703)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	CDP has been performed against the same brand that is Voniza 20mg tablet by Hilton Pharma (Batch No 138864) in Acid media (pH 1.0-1.2) in Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Xianqiang Pharmaceutical Pvt Ltd, China
API Lot No.	
Description of Pack	Alu-Alu blister packed in unit carton (2×10's)

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	20mg/Tablet		
Batch No.	VP-04	VP-05	VP-06
Batch Size	1200 tab	1200 tab	1200 tab
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	12-05-2021	12-05-2021	12-05-2021
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. GD20150397 of M/s Xianqiang Pharmaceutical Pvt Ltd, China issued by China Food and Drug Administration. The certificate is valid till 06-09-2020.
	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted import License No. 00169/2021-DRAP CPS/650 dated 16-02-2021 confirming import of 200g vonoprazan from M/s Xianqiang Pharmaceutical Pvt Ltd, China for Batch No. TAK09R210101
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Remarks of Evaluator:

Sr.#	Observation	Reply (dated 30/10/2022)
	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API	Not complied

	manufacturer issued by concerned regulatory authority of country of origin to be provided	Later on firm has submitted copies of Drug manufacturing certificate No Yue20160016 dated 24.12.2020 valid till 23.12.2025 issued by Guandong provincial Drug Administration and GMP certificate (No 20220616) dated 16.06.2022 valid till 15.06.2026
	Detailed analytical procedures for the testing of drug substance to be provided by both Drug Substance and Drug Product manufacturer	complied
	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non compendial drug substance(s) to be provided	complied
	COA of primary / secondary reference standard for Vonoprazan Fumarate including source and lot number to be provided.	Working standard for Vonoprazan Fumarate batch No A061-210101 from Xianqiang Pharmaceutical Pvt Ltd, China is provided
	Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters of developed formulation against reference product	**Not complied** **Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters while firm has submitted comparison of assay only**.
	Uniformity of dose and microbial attributes are not provided in finished product specification	complied
	Stability data particularly chromatograms , CoA and raw data sheets (both accelerated and real time) is not provided for each time point	complied
	Compliance Record of HPLC software 21CFR & audit trail reports on product and Record of Digital data logger for temperature and humidity monitoring of stability chambers to be	We use water HPLC (USA made) with Empower2 software which is not 21CFR compliant. Manual record of temp and humidity control maintained in log book will be presented at the time of inspection.
	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Wnsodex 60mg and 30mg DDR capsule (dexlansoprazole) on 1st September, 2020. Further, the said panel inspection report was discussed in 297th Drug

		Registration Board meeting. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Related manufacturing area, equipment, personnel and utilities are GMP compliant.
	Justification to be provided for selection of dissolution parameters i.e Acceptance criteria and volume of dissolution medium	Dissolution parameters are selected as per USFDA guidance document for immediate release solid dosage form
	Compatibility of the Drug Substance(s) with excipients is not provided (mainly IPA which has been used by the firm in film coating). Specifications of IPA also not provided.	Not complied

Decision: Approved with Innovator's specifications. Registration letter will b eissued upon submission of Pharmaceutical equivalence studies including all test of batch release against the innovator/reference comparator product.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

371.	Name, address of Applicant / Marketing Authorization Holder	M/s WnsFeild Pharmaceutical Industrial Estate Hattar Haripur Kpk Pakistan.
	Name, address of Manufacturing site.	M/s WnsFeild Pharmaceutical Plot No. 122 Phase 5, Industrial Estate Hattar Haripur Kpk Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22379 dated 05/08/2022
	Details of fee submitted	PKR 75,000/- dated 13/06/2022

	The proposed proprietary name / brand name	Venospa 10/100mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Vonoprazan as Fumarate (outer immediate release layer)……...…10mg Aspirin (as enteric coated inner core) ……..…..100mg
	Pharmaceutical form of applied drug	White to off-white color Aspirin round shape enteric coated tablet surrounded by film coated Vonoprazan tablets.
	Pharmacotherapeutic Group of (API)	Vonoprazan: Potassium-Competitive Acid Blocker Aspirin: Antithrombotic Agents
	Reference to Finished product specifications	Innovator's specification
	Proposed Pack size	3×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cabpirin 10/100mg tablet by M/s Takeda Pharmaceutical (Japan)
	For generic drugs (me-too status)	Not available
	GMP status of the Finished product manufacturer	GMP inspection conducted on 10/12/2020 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Vonoprazan: Guangdong Xianqiang Pharmaceutical Pvt Ltd, No. 6, industrial Avenue, Conghua, Economical Development zone, Guangzhou city, Guangdong province, China Aspirin JQC (HUAYIN) Pharmaceutical Co, Ltd/ Yuquan Road, Huayin city, Shanxi province, P.R of China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted
	Module III (Drug Substance)	Vonoprazan and Aspirin: The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications,

		batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Vonoprazan: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: TAK09R150701, TAK09R150702, TAK09R150703 Aspirin: Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: A201104081, A201104082 A201104083
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence not performed. CDP has been performed against Cabpirin 10/100mg tablet by Takeda Pharma (Japan), in Acid media (pH 1.0-1.2) acetate buffer (Ph 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range. Release profile of aspirin has not been compared.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Guangdong Xianqiang Pharmaceutical China (vonoprazan) JQC (HUAYIN) Pharmaceutical Co, Ltd China (aspirin)
API Lot No.	TAK09210101(vonoprazan) A2012041 (aspirin)
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (3×10's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	10/100mg Tablet		
Batch No.	VA-01	VA-02	VA-03
Batch Size	1200 tab	1200 tab	1200 tab
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	07-01-2022	07-01-2022	07-01-2022
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not provided
	Documents for the procurement of API with approval from DRAP (in case of import).	Vonoprazan: Firm has submitted import License No. 00169/2021-DRAP CPS/650 dated 16-02-2021 confirming import of 200g VONOPRAZAN from M/s Guangdong Xianqiang Pharmaceutical Pvt Ltd, China for Batch No. TAK09R210101 Aspirin: Firm has submitted import License No. 00138/2021-DRAP 1PS/650 dated 10-02-2021 confirming import of 2Kg ASPIRIN from M/s JQC (HUAYIN) Pharmaceutical Co, Ltd China for Batch No. A2012041
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Inadequate
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not submitted

Remarks OF Evaluator:

Sr.#	Observation	Reply (dated 30.10.2022)

	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided	Firm has submitted GMP certificate of M/s Guangdong Xianqiang Pharmaceutical Pvt Ltd, China (GD20150397) issued by China Food and Drug Administration valid till 06.09.2020 **GMP certificate of M/s JQC (HUAYIN) Pharmaceutical Co, Ltd is not submitted** Later on firm has submitted copies of Drug manufacturing certificate of **M/s Guangdong Xianqiang Pharmaceutical Pvt Ltd,** China No Yue20160016 dated 24.12.2020 valid till 23.12.2025 issued by Guandong provincial Drug Administration and GMP certificate (No 20220616) dated 16.06.2022 valid till 15.06.2026
	Detailed analytical procedures for the testing of drug substance Aspirin to be provided by both Drug Substance and Drug Product manufacturer	Complied
	Provide results of analysis of relevant batch(es) of Drug Substance Aspirin performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacture	Complied
	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non compendial drug substance(s) to be provided	**Not complied** **Analytical method verification studies submitted for vonoprazan fumarate only.**
	COA of primary / secondary reference standard for Vonoprazan Fumarate and Aspirin including source and lot number to be provided	Not complied Later on firm has provided Working standard for Vonoprazan Fumarate batch No A061-210101 from Xianqiang Pharmaceutical Pvt Ltd. However reference standard is not required for Aspirin since it is analyzed by titrimetric method.
	Dissolution medium used in USFDA approved formulation VOQUEZNA for evaluation of release profile of vonoprazan tablet was 0.05M acetate buffer (pH 4.5) with 50rpm while dissolution medium used by the	***To avoid dissolution of enteric coated core of aspirin 0.1NHCl is used to affect only vonoprazan in film coating and further to check the enteric coating. 75rpm is***

	firm is 0.1NHCl and 75 rpm. .Justification to be provided for selection of dissolution medium and rpm for USP type II apparatus.	***selected as per general guideline of dissolution given in BP 2022 and USP.*** **Not justified since release profile of aspirin has been monitored separately by using acid stage (0.1N HCl) and buffer stage (phosphate buffer) dissolution.**
	Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters of developed formulation against reference product	**Not complied** **Pharmaceutical equivalence to be established against innovator/reference product by comparing the results of all quality parameters while firm has submitted comparison of assay only.**
	CDP for Aspirin has not been performed. Moreover, batch no of innovator product has not been mentioned in CDP of Vonoprazan	CDP for Aspirin has been provided as per following details: Feature / Reference product (Takeda pharma) / Product of M/s Wnsfeild Brand name / Cabiprin 10/100mg tablet / Venospa 10/100mg tablet Batch No. / 521559 / 19PD-219 Comparative dissolution studies have been performed in following mediums: 1. pH 4.5 Acetate buffer 2. pH 6.8 Phosphate buffer The values for f1 and f2 are in the acceptable range. **CDP of aspirin has not been assessed in acid medium (Ph 1.2)**
	Hardness, LOD and microbial attributes are not provided in finished product specification.	Hardness, LOD and microbial attributes are missed from finished product specification due to typographic error, now the firm has submitted results of aforementioned quality parameters.
	Stability data particularly chromatograms , CoA and raw data sheets (both accelerated and real time) is not provided for each time point (particularly 6th month for all 3 batches)	Complied
	There is a tendency for loss on drying to increase and hardness to decrease under high temperature and high humidity hence LOD and hardness test results to be submitted, performed during stability studies	Not complied Later on firm has provided LOD and hardness test as per innovator product.

	Compliance Record of HPLC software 21CFR & audit trail reports on product and Record of Digital data logger for temperature and humidity monitoring of stability chambers to be	We use water HPLC (USA made) with Empower2 software which is not 21CFR compliant. Manual record of temp and humidity control maintained in log book will be presented at the time of inspection.
	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Wnsodex 60mg and 30mg DDR capsule (dexlansoprazole) on 1st September, 2020. Further, the said panel inspection report was discussed in 297th Drug Registration Board meeting. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Related manufacturing area, equipment, personnel and utilities are GMP compliant.

Decision: Deferred for submission of following:

- **Pharmaceutical equivalence studies against the innovator/reference product by comparing the results of all quality parameters.**
- **Justification for selection of dissolution mediums in CDP studies, since CDP of Aspirin has not been performd in acidic medium of pH 1.2**
- **Justification for selection of dissolution medium for batch release test since already submitted justification of applying 0.1N HCl dissolutuion medium is not satisfactory.**
- **Complete method of analysis for dissolution test.**
- **Clarification of the formulation of innovator product, whetehr it is bilayer by way of compression or by way of active coating of Vonoprazan.**
- **Justification of the variation in chromatographic conditions mentioned in drug product analytical method and those reflected in the submitted HPLC chromatograms.**
- **Compliance Record of HPLC software 21CFR & audit trail reports on product and Record of Digital data logger for temperature and humidity monitoring of stability chambers.**

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the pharmaceutical i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year.

In compliance to the aforementioned decision of the Board, the following firm have achieved the benchmark of more than 100,000 USD during the fiscal Year 2020-2021 and submitted their applications for priority consideration/ evaluation as communicated by Assistant Director (PR-I/EFD) vide letter No No.F.1-6/2019-PR-I (EFD dated 06th October 2022.

Registration applications of drugs for which stability study data is submitted for exemption from onsite verification of stability data

372.	Name and address of manufacturer / Applicant	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.
	Brand Name +Dosage Form + Strength	Jarlina Tablets 10mg+5mg
	Diary No. Date of R& I & fee	Dy No. 777 (PEC DRAP) Dated 11.01.19 Rs: 50,000/- 10-12-2018
	Composition	Each film coated tablet contains: Empagliflozin…….10mg Linagliptin….5mg
	Pharmacological Group	Antidiabetic
	Type of Form	Form 5-D
	Finished Product Specification	Manufacturer Specs.
	Pack size & Demanded Price	As per country requirement
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved Glyxambi
	Me-too status	Linjardy 25/5mg tablet (Reg No 112052) by M/s CCl Lab, Lahore
	GMP status	GMP inspection conduced on 07/07/2022 Tablet (General & General Antibiotic) section approved dated 29.10.2022

STABILITY STUDY DATA			
Drug	Jarlina Tablets 10mg+5mg		
Name of Manufacturer	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.		
Manufacturer of API	Empagliflozin Anhui Youcare kaiyue Pharmaceutical Co.Ltd, CHINA	Linagliptin Ruyuan HEC Pharm Co., Ltd, CHINA	
API Lot No.	Empagliflozin 20181001002	Linagliptin S204A-RD201712201	
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 18 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6,9,12,18(months)		
Batch No.	19PD-219	19PD-220	19PD-221
Batch Size	2500 Tablets	2500 Tablets	2500 Tablet
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	11-2019	11-2019	11-2019

No. of Batches	03	
Date of Submission	22-09-2021 (Dy No. 2604 PEC, DRAP)	
DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
S. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product for Tapendol (Tapentadol) Tablets 75mg & 100mg on 11th March, 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th – 16th May 2019. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software. Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Empagliflozin: Firm has submitted COA of Empagliflozin (Batch # 20181001002) from M/s Anhui Youcare Kaiyue Pharmaceutical Co. Ltd., China. COA (Batch # 20181001002) from M/s The Searle Company Limited is also submitted. Linagliptin: Firm has submitted COA of Linagliptin (Batch # S204A-RD201712201) from Ruyuan HEC Pharma Co. Ltd., China. Copy of COA (Batch # S204A-RD201712201) from M/s The Searle Company Limited is also submitted.
3.	Method used for analysis of API from both API Manufacturer & Finished Product manufacturer	Submitted
4.	Stability study data of API from API manufacturer	Empagliflozin: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 36 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches Linagliptin: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 36 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Empagliflozin: Firm has submitted copy of GMP certificate by M/s Anhui Youcare Kaiyue Pharmaceutical Co. Ltd., China issued by Anhui Food and Drug Administration of the People's Republic of China. The certificate is valid till 05-03-2023.

<table>
<tr><td></td><td></td><td>Linagliptin:
Firm has submitted copy of GMP certificate of Ruyuan HEC Pharma Co. Ltd., China issued by Shaoguan Food and Drug Administration, China. The certificate is valid till 06-01-2024..</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Firm has submitted import License No. 0010/19-DRAP dated 01-01-2019 confirming import of 1Kg Empagliflozin from M/s Anhui Youcare Kaiyue Pharmaceutical Co. Ltd., China for Batch # 20181001002.
Firm has submitted import License No. 0546/18-DRAP dated 14-02-2018 confirming import of 0.5Kg Linagliptin from M/s Ruyuan HEC Pharma Co. Ltd., China for Batch # S204A-RD201712201</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Submitted</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Firm has submitted that same excipients has been used as used by innovator ‘GLYXAMBI Tablets 25mg + 5mg’. However, there is only difference in film coating materials Therefore, Drug-excipients compatibility studies were not performed.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has manufactured three stability batches of Empagliflozin + Linagliptin Tablets 25mg + 5mg and has submitted copy of complete batch manufacturing. Details are as under:
<table>
<tr><td colspan="3">Jarlina Tablets 10mg+5mg</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Date</td></tr>
<tr><td>19PD-219</td><td>2500 Tablets</td><td>October 2019</td></tr>
<tr><td>19PD-220</td><td>2500 Tablets</td><td>October 2019</td></tr>
<tr><td>19PD-221</td><td>2500 Tablets</td><td>October 2019</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “GLYXAMBI”. The details are as follows:
<table>
<tr><td>Feature</td><td>Reference product</td><td>Product of M/s The Searle Company</td></tr>
<tr><td>Brand name</td><td>GLYXAMBI Tablets 10mg + 5mg</td><td>Jarlina Tablets 10mg+5mg</td></tr>
<tr><td>Batch No.</td><td>803783A</td><td>19PD-219</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer</td></tr>
</table>

		The Average % release of both Drug substances in all three mediums is more than 85% at 15 minutes hence there is no need to calculate f2 value. The CDP of Jarlina Tablets 10mg+5mg against GLYXAMBI Tablets 10mg + 5mg shows equivalence.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of stability chambers.

Remarks of Evaluator:

Sr No.	**Observations**	**Firm's response (dated 25th October, 2022)**
1	Analytical Method Validation studies to be submitted by the firm.	Detailed analytical testing method along with validation studies are submitted including validation parameters such as accuracy, precision, system suitability, range, robustness and specificity
2	Justification shall be provided for selection of acceptance criteria of dissolution i.e NLT 80% (75% Q value) after 45 minutes while USFDA guidance document on Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances recommends dissolution criterion as Q=80% in 30 minutes	At initial stage firm adopted specification from BP General chapter "Appendix XII B. Annex X: Recommendation on dissolution testing" which states that "at least 80% of active substance is released within a specified time, typically 45min or less (75% Q value). However dissolution specification was revised on 29 Jan 2020 before the testing of 3rd month stability interval from 45 min to 30min as per CDER report of USFDA approved reference product Glyxambi (NDA 206-073).

Decision: Approved with innovators specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

Registration applications of drugs for which stability study data is submitted for exemption from onsite verification of stability data

373.	Name and address of manufacturer / Applicant	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.

	Brand Name +Dosage Form + Strength	Jarlina Tablets 25mg+5mg
	Diary No. Date of R& I & fee	Dy No. 776 dated 11.01.2019 , Rs: 50,000/- 10-12-2018
	Composition	Each film coated tablet contains: Empagliflozin…….25mg Linagliptin….5mg
	Pharmacological Group	Anti diabetic
	Type of Form	Form 5-D
	Finished Product Specification	Manufacturer Specs.
	Pack size & Demanded Price	As per country requirement
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved Glyxambi
	Me-too status	Linjardy 25/5mg tablet (Reg No 112052) by M/s CCl Lab, Lahore
	GMP status	GMP inspection conduced on 07/07/2022 Tablet (General & General Antibiotic) section approved dated 29.10.2022

STABILITY STUDY DATA			
Drug	Jarlina Tablets 25mg+5mg		
Name of Manufacturer	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.		
Manufacturer of API	Empagliflozin: Anhui Youcare kaiyue Pharmaceutical Co.Ltd, CHINA	Linagliptin Ruyuan HEC Pharm Co., Ltd, CHINA	
API Lot No.	Empagliflozin 20181001002	Linagliptin S204A-RD201712201	
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 18 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6,9,12,18(months)		
Batch No.	19PD-202	19PD-212	19PD-211
Batch Size	2500 Tablets	2500 Tablets	2500 Tablet
Manufacturing Date	09-2019	09-2019	09-2019
Date of Initiation	06.02.2020	06.02.2020	06.02.2020
No. of Batches	03		
Date of Submission	22-09-2021 (Dy No. 2603 PEC, DRAP)		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION			
DOCUMENTS / DATA PROVIDED BY THE APPLICANT			
S. No.	Documents To Be Provided	Status	

1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product for Tapendol (Tapentadol) Tablets 75mg & 100mg on 11th March, 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th – 16th May 2019. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software. Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Empagliflozin: Firm has submitted COA of Empagliflozin (Batch # 20181001002) from M/s Anhui Youcare Kaiyue Pharmaceutical Co. Ltd., China. COA (Batch # 20181001002) from M/s The Searle Company Limited is also submitted. Linagliptin: Firm has submitted COA of Linagliptin (Batch # S204A-RD201712201) from Ruyuan HEC Pharma Co. Ltd., China. Copy of COA (Batch # S204A-RD201712201) from M/s The Searle Company Limited is also submitted.
3.	Method used for analysis of API from both API Manufacturer & Finished Product manufacturer	Submitted
4.	Stability study data of API from API manufacturer	Empagliflozin: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 36 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches Linagliptin: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 36 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Empagliflozin: Firm has submitted copy of GMP certificate by M/s Anhui Youcare Kaiyue Pharmaceutical Co. Ltd., China issued by Anhui Food and Drug Administration of the People's Republic of China. The certificate is valid till 05-03-2023. Linagliptin: Firm has submitted copy of GMP certificate of Ruyuan HEC Pharma Co. Ltd., China issued by Shaoguan Food and Drug Administration, China. The certificate is valid till 06-01-2024.

<table>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Firm has submitted import License No. 0010/19-DRAP dated 01-01-2019 confirming import of 1Kg Empagliflozin from M/s Anhui Youcare Kaiyue Pharmaceutical Co. Ltd., China for Batch # 20181001002.
Firm has submitted import License No. 0546/18-DRAP dated 14-02-2018 confirming import of 0.5Kg Linagliptin from M/s Ruyuan HEC Pharma Co. Ltd., China for Batch # S204A-RD201712201</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Submitted</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Firm has submitted that same excipients has been used as used by innovator ‘GLYXAMBI Tablets 25mg + 5mg’. However, there is only difference in film coating materials Therefore, Drug-excipients compatibility studies were not performed.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has manufactured three stability batches of Empagliflozin + Linagliptin Tablets 25mg + 5mg and has submitted copy of complete batch manufacturing. Details are as under:
<table>
<tr><td colspan="3">Jarlina Tablets 25mg+5mg</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Date</td></tr>
<tr><td>19PD-202</td><td>2500 Tablets</td><td>September 2019</td></tr>
<tr><td>19PD-212</td><td>2500 Tablets</td><td>September 2019</td></tr>
<tr><td>19PD-211</td><td>2500 Tablets</td><td>September 2019</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “GLYXAMBI”. The details are as follows:
<table>
<tr><td>Feature</td><td>Reference product</td><td>Product of M/s The Searle Company</td></tr>
<tr><td>Brand name</td><td>GLYXAMBI Tablets 25mg + 5mg</td><td>Jarlina Tablets 25mg+5mg</td></tr>
<tr><td>Batch No.</td><td>803794A</td><td>19PD-202</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer

The Average % release of both Drug substances in all three mediums is more than 85% at 15 minutes hence there is no need to calculate f2 value. The CDP of Jarlina Tablets</td></tr>
</table>

		25mg+5mg against GLYXAMBI Tablets 25mg + 5mg shows equivalence.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of stability chambers.

Remarks of Evaluator:

Sr No.	Observations	Firm's response (dated 25th October, 2022)
1	Analytical Method Validation studies to be submitted by the firm.	Detailed analytical testing method along with validation studies are submitted including validation parameters such as accuracy, precision, system suitability, range, robustness and specificity
2	Justification shall be provided for selection of acceptance criteria of dissolution i.e NLT 80% (75% Q value) after 45 minutes while USFDA guidance document on Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances recommends dissolution criterion as Q=80% in 30 minutes	At initial stage firm adopted specification from BP General chapter "Appendix XII B. Annex X: Recommendation on dissolution testing" which states that "at least 80% of active substance is released within a specified time, typically 45min or less (75% Q value). However dissolution specification was revised on 24 Jan 2020 before the testing of 3rd month stability interval from 45 min to 30min as per CDER report of USFDA approved reference product Glyxambi (NDA 206-073).

Decision: Approved with innovators specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

Registration applications of drugs for which stability study data is submitted for exemption from onsite verification of stability data

374.	Name and address of manufacturer / Applicant	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.
	Brand Name +Dosage Form + Strength	Anzo D MR Capsule
	Diary No. Date of R& I & fee	Dy No. 2368 (PEC DRAP) Dated 17.10.2022 (duplicate) Rs: 50,000/- 22-12-2017

	Composition	Each modified release capsule contains: Diclofenac sodium…….75mg Omeprazole…….20mg
	Pharmacological Group	Anti-arthritis Anti-ulcer
	Type of Form	Form 5-D
	Finished Product Specification	Innovator's Specs.
	Pack size & Demanded Price	As per DPC
	Approval status of product in Reference Regulatory Authorities.	EMA Approved Diotop 75 mg / 20 mg modified release hard capsules
	Me-too status	Not Applicable
	GMP status	GMP inspection conduced on 07/07/2022 Capsule (General & General Antibiotic) section approved.

STABILITY STUDY DATA			
Drug	Anzo D MR Capsule		
Name of Manufacturer	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.		
Manufacturer of API	Diclofenac Sodium MR pellets : M/s Alphamed Formulations Private Limited	Omeprazole delayed release pellets: M/s Alphamed Formulations Private Limited	
API Lot No.	RD0149-017	8000201-010	
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6,9,12,18(months)		
Batch No.	20PD-271	20PD-272	20PD-273
Batch Size	2500 cap	2500 cap	2500 cap
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	26-10.2020	26-10.2020	26-10.2020
No. of Batches	03		
Date of Submission	10-01-2022 (Dy No. 57 PEC, DRAP)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
S. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product for Tapendol (Tapentadol) Tablets 75mg & 100mg on 11th March, 2019.

		Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th – 16th May 2019. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software. Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Diclofenac sodium MR pellets 35%: Firm has submitted COA of Diclofenac sodium MR pellets 35% (Batch No. RD0149-017) from M/s ALPHAMED FORMULATIONS PRIVATE LIMITED. COA (Batch No. RD0149-017)) from M/s The Searle Company Limited is also submitted. Omeprazole Delayed release pellets 20%w/w: Firm has submitted COA of Omeprazole Delayed release pellets 20%w/w (Batch No. 8000201-010.) from M/s ALPHAMED FORMULATIONS PRIVATE LIMITED. COA (Batch No. 8000201-010.)) from M/s The Searle Company Limited is also submitted
3.	Method used for analysis of API from both API Manufacturer & Finished Product manufacturer	Submitted
4.	Stability study data of API from API manufacturer	Diclofenac sodium MR pellets 35%: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 36 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches Omeprazole Delayed release pellets 20%w/w: The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 36 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. L.Dis.No:93420/TS/2022 by M/s ALPHAMED FORMULATIONS PRIVATE LIMITED issued by Drugs Control Administration Government of Telangana. The certificate is valid till 15-08-2023. ..

<table>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Diclofenac sodium pellets 35%:
Firm has submitted import License dated 02-12-2019 confirming import of 5Kg Diclofenac sodium MR pellets 35% w/w from M/s ALPHAMED FORMULATIONS PRIVATE LIMITED for Batch # RD0149-017.

Omeprazole Delayed release pellets 20%w/w
Firm has submitted import License dated 02-12-2019 confirming import of 1.8Kg Omeprazole Delayed release pellets 20%w/w from M/s ALPHAMED FORMULATIONS PRIVATE LIMITED for Batch # 8000201-010.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Submitted</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Since there is only encapsulation of pellets carried out at FPP mfg site, no additional excipients are required hence compatibility studies are not performed.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has manufactured three stability batches of Anzo D MR Capsule and has submitted copy of complete batch manufacturing. Details are as under:
<table>
<tr><td colspan="3">Anzo D MR Capsule (75mg+20mg)</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Date</td></tr>
<tr><td>20PD-271</td><td>2500 capsules</td><td>October 2020</td></tr>
<tr><td>20PD-272</td><td>2500 capsules</td><td>October 2020</td></tr>
<tr><td>20PD-273</td><td>2500 capsules</td><td>October 2020</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product against Aristo 75/20 capsule :
<table>
<tr><td>Feature</td><td>Reference product</td><td>Product of M/s The Searle Company</td></tr>
<tr><td>Brand name</td><td>Aristo capsule 75mg + 20mg</td><td>Anzo D MR capsule</td></tr>
<tr><td>Batch No.</td><td>1394180100</td><td>20PD-271</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:

1. pH 1.2 HCl buffer (omeprazole)
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
4. purified water (diclofenac sodium)</td></tr>
</table>

		on the basis of similarity factor (f2) result i.e NLT 50 of dissolution profile of both API in test product and reference product, both products are similar.
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of stability chambers.

Remarks of Evaluator:

- Permission/approval for manufacturing omeprazole delayed release pellets from relevant DCA.
- Analytical Method Validation studies to be submitted by the firm.
- Justify selection of Aristo 75/20 capsule for conducting comparative dissolution profile. Give details of aforementioned brand i.e manufacturer, approval status etc
- Whether omeprazole pellets are tested in acetate medium or not, its not clear in profile. Clarify the results/release profile of each API tested in different mediums and conclude results accordingly, in CDP report
- Innovator (EMA approved) product is Each modified release capsule contains 75 mg diclofenac sodium (25 mg as gastroresistant pellets and 50 mg as prolonged release pellets) and 20 mg of omeprazole (gastro-resistant pellets) however MR pellets of diclofenac sodium used by the firm has to be clarified in this regard.
- Method of analytical testing to be submitted from pellets manufacturer.
- Drug excipient computability (carried out by pellets manufacturer) to be submitted.
- Justification to be provided for selection of acceptance criteria of dissolution (Q value, dissolution time, sampling time and medium etc)

Decision: Registration Board deferred the application for above mentioned shortcomings within 6 months.

375.	Name, address of Applicant / Marketing Authorization Holder	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.
	Name, address of Manufacturing site.	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐Domestic and Export sales
	Dy. No. and date of submission	Dy. No 6369 dated 08-03-2022

	Details of fee submitted	PKR 75,000/-: dated 08/02/2022
	The proposed proprietary name / brand name	PRU-CIC 1mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Prucalopride……..1mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-constipation agent
	Reference to Finished product specifications	N.A
	Proposed Pack size	As per DPC
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	USFDA approved Motegrity Tablet
	For generic drugs (me-too status)	Not applicable
	GMP status of the Finished product manufacturer	GMP inspection conduced on 07/07/2022
	Name and address of API manufacturer.	M/s Symed Labs Limited, India Address: Symed Labs Limited (UNIT-VI) Sy. No. 744 & 745 and 750 to 753, Mandolla gudem (Village), Choutuppal (Mandal), Yadadri District – 508252 Telangana, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, physical form, solubility, manufacturers, description of manufacturing process and controls, characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, characterization, impurities, specifications, analytical procedures and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 24 Months Batches: (6PCS0010817, 6PCS0020817, 6PCS0030817)

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (6PCS0010817, 6PCS0020817, 6PCS0030817)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, batch formula, pharmaceutical development and analytical procedure, analytical method validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator product i.e. Resolor 1mg tablet (by M/s. Takeda UK Ltd) by performing quality tests (Appearance, Disintegration time, Assay, content uniformity, Dissolution and impurity testing)
	Analytical method validation/verification of product	Method validation studies have been submitted including Linearity, Accuracy, and Precision including Repeatability & Intermediate Precision, Robustness and Specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Symed Labs Limited Address: Symed Labs Limited (UNIT-VI) Sy. No. 744 & 745 and 750 to 753, Mandolla gudem (Village), Choutuppal (Mandal), Yadadri District – 508252 Telangana, India		
API Lot No.	6PCS0010420		
Description of Pack (Container closure system)	Alu/Alu blisters		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3,6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20PD-331	20PD-332	20PD-333
Batch Size	2500 tablets	2500 tablets	2500 tablets
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	01-2021	01-2021	01-2021
No. of Batches	03		

Administrative Portion		
	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Tapendol (Tapentadol) Tablets 75mg & 100mg on 11th March, 2019. Further, the said panel inspection report was discussed in 289th

		Drug Registration Board meeting held on 14th – 16th May 2019. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software. Related manufacturing area, equipment, personnel and utilities are GMP compliant..
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate (65931/TS/2021) issued to M/s Symed Labs Limited (UNIT-VI) Sy. No. 744 & 745 and 750 to 753, Mandolla gudem (Village), Choutuppal (Mandal), Yadadri District – 508252 Telangana, India issued by Drug Control Administration, Government of Telangana valid till 14-09-2022 is submitted
	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of following invoices specifying: 0.070kg of Prucalopride Succinate (invoice # 2907/20) Batch No. 6PCS0010420 attested by AD (I&E), Karachi dated 24-09-2020 is submitted
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

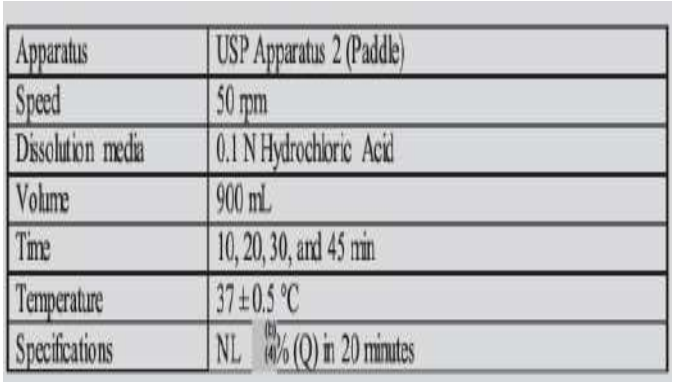
Remarks of Evaluator:

Section#	**Observations**	**Firm's response (dated 20th October, 2022)**
1.6.5	GMP certificate issued to M/s Symed Labs Limited (UNIT-VI) India Is valid till 14-09-2022. Hence valid GMP certificate for the manufacturer of	Firm submitted document from Drug Substance manufacturer i.e M/s Symed Labs Limited (UNIT-VI) India, stating "***GMP certificate is under renewal and expected to be received by end of October 2022."***

<table>
<tr><td></td><td>Prucalopride Succinate to be submitted .</td><td></td></tr>
<tr><td>3.2.P.5.1</td><td>MHRA Public assessment report of the reference product recommends dissolution specifications as “More than 80% dissolved in 10 minute”, whereas firm has submitted dissolution specifications as “Not less than 80% (Q=75%) in 20 minutes.

USFDA guidance document on Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances recommends dissolution medium as “500 mL of 0.1N HCl in aqueous medium” whereas dissolution medium volume used by the firm is 900ml

Justification to be provided for selection of dissolution parameters i.e
Acceptance criteria and volume of dissolution medium.</td><td>Firm has taken the dissolution specification from FDA assessment report of innovator “Motegrity tablet”
NDA 210166 which specify following dissolution parameters:

 
<table><tr><td>Apparatus</td><td>USP Apparatus 2 (Paddle)</td></tr><tr><td>Speed</td><td>50 rpm</td></tr><tr><td>Dissolution media</td><td>0.1 N Hydrochloric Acid</td></tr><tr><td>Volume</td><td>900 mL</td></tr><tr><td>Time</td><td>10, 20, 30, and 45 min</td></tr><tr><td>Temperature</td><td>37 ± 0.5 °C</td></tr><tr><td>Specifications</td><td>NL [illegible]% (Q) in 20 minutes</td></tr></table>
Firm took above mentioned specification and tested accordingly from initial stage to onward.</td></tr>
<tr><td>3.2.P.2</td><td>Batch No. of Resolor 1mg tablet used for pharmaceutical equivalence has not been mentioned.

Results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 to be submitted.</td><td>Firm has submitted CDP report now (No CDP-114/21-R)
Wherein CDP has been performed as follows:

<table><tr><td>Feature</td><td>Reference product</td><td>Product of M/s The Searle Company</td></tr><tr><td>Brand name</td><td>Resolor 1mg Tablet</td><td>Pru-cic 1mg tablet</td></tr><tr><td>Batch No.</td><td>KLL1P02</td><td>20PD-331</td></tr></table>Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer

The Average % release of both Drug substances in all three mediums is more than 85% at 15 minutes hence product is categorized as very rapidly</td></tr>
</table>

		dissolving drug, there is no need to calculate f2 value. The CDP of Pru-cic 1mg tablet against Resolor 1mg Tablet shows equivalence.

Decision: Approved with innovator's specifcations. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

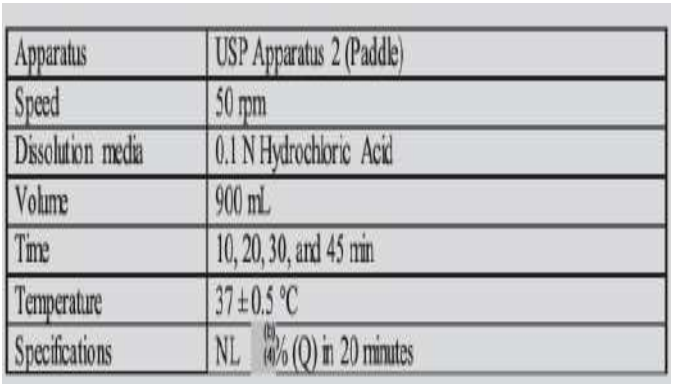
376.	Name, address of Applicant / Marketing Authorization Holder	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.
	Name, address of Manufacturing site.	M/s The Searle Company Limited F-319, S.I.T.E., Karachi, Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐Domestic and Export sales
	Dy. No. and date of submission	Dy. No 6370 dated 08-03-2022
	Details of fee submitted	PKR 75,000/-: dated 08/02/2022
	The proposed proprietary name / brand name	PRU-CIC 2 mg tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Prucalopride……..2mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-constipation agent
	Reference to Finished product specifications	N.A
	Proposed Pack size	As per DPC
	Proposed unit price	As per DPC
	The status in reference regulatory authorities	USFDA approved Motegrity Tablet
	For generic drugs (me-too status)	Not applicable
	GMP status of the Finished product manufacturer	GMP inspection conduced on 07/07/2022
	Name and address of API manufacturer.	M/s Symed Labs Limited, India

		Address: Symed Labs Limited (UNIT-VI) Sy. No. 744 & 745 and 750 to 753, Mandolla gudem (Village), Choutuppal (Mandal), Yadadri District – 508252 Telangana, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, physical form, solubility, manufacturers, description of manufacturing process and controls, characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, characterization, impurities, specifications, analytical procedures and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Stability study conditions:** Real time: 30°C ± 2°C / 75% ± 5%RH for 24 Months Batches: (6PCS0010817, 6PCS0020817, 6PCS0030817) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (6PCS0010817, 6PCS0020817, 6PCS0030817)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, batch formula, pharmaceutical development and analytical procedure, analytical method validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator product i.e. Resolor 2mg tablet (by M/s. Takeda UK Ltd) by performing quality tests (Appearance, Disintegration time, Assay, content uniformity, Dissolution and impurity testing)

	Analytical method validation/verification of product	Method validation studies have been submitted including Linearity, Accuracy, and Precision including Repeatability & Intermediate Precision, Robustness and Specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Symed Labs Limited Address: Symed Labs Limited (UNIT-VI) Sy. No. 744 & 745 and 750 to 753, Mandolla gudem (Village), Choutuppal (Mandal), Yadadri District – 508252 Telangana, India		
API Lot No.		6PCS0010420		
Description of Pack (Container closure system)		Alu/Alu blisters		
Stability Storage Condition		Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 3,6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		20PD-334	20PD-335	20PD-336
Batch Size		2500 tablets	2500 tablets	2500 tablets
Manufacturing Date		12-2020	12-2020	12-2020
Date of Initiation		01-2021	01-2021	01-2021
No. of Batches		03		
Administrative Portion				
	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Tapendol (Tapentadol) Tablets 75mg & 100mg on 11th March, 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th – 16th May 2019. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software. Related manufacturing area, equipment, personnel and utilities are GMP compliant..		
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate (65931/TS/2021) issued to M/s Symed Labs Limited (UNIT-VI) Sy. No. 744 & 745 and 750 to 753, Mandolla gudem (Village), Choutuppal (Mandal), Yadadri District – 508252 Telangana, India issued by Drug Control Administration, Government of Telangana valid till 14-09-2022 is submitted		

	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of following invoices specifying: 0.070kg of Prucalopride Succinate (invoice # 2907/20) Batch No. 6PCS0010420 attested by AD (I&E), Karachi dated 24-09-2020 is submitted
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Firm has submitted audit trail record of product testing of HPLC.
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Section#	**Observations**	**Firm's response (dated 20th October, 2022)**
1.6.5	GMP certificate issued to M/s Symed Labs Limited (UNIT-VI) India Is valid till 14-09-2022. Hence valid GMP certificate for the manufacturer of Prucalopride Succinate to be submitted	Firm submitted document from Drug Substance manufacturer i.e M/s Symed Labs Limited (UNIT-VI) India, stating "***GMP certificate is under renewal and expected to be received by end of October 2022."***
3.2.P.5.1	MHRA Public assessment report of the reference product recommends dissolution specifications as "More than 80% dissolved in 10 minute", whereas firm has submitted dissolution specifications as "Not less than 80% (Q=75%) in 20 minutes. USFDA guidance document on Dissolution Testing and Acceptance Criteria for Immediate-Release Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances recommends dissolution medium as "500 mL of 0.1N HCl in aqueous medium" whereas dissolution medium volume used by the firm is 900ml	Firm has taken the dissolution specification from FDA assessment report of innovator "Motegrity tablet" NDA 210166 which specify following dissolution parameters:  Firm took above mentioned specification and tested accordingly from initial stage to onward.

<table>
<tr><td></td><td>Justification to be provided for selection of dissolution parameters i.e
Acceptance criteria and volume of dissolution medium.</td><td></td></tr>
<tr><td>3.2.P.2</td><td>Batch No. of Resolor 2mg tablet used for pharmaceutical equivalence has not been mentioned.

Results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 to be submitted.</td><td>Firm has submitted CDP report now (No CDP-115/21-R)
Wherein CDP has been performed as follows:

<table><tr><td>Feature</td><td>Reference product</td><td>Product of M/s The Searle Company</td></tr><tr><td>Brand name</td><td>Resolor 2mg Tablet</td><td>Pru-cic 2mg tablet</td></tr><tr><td>Batch No.</td><td>LFL6T00</td><td>20PD-334</td></tr></table>Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer

The Average % release of both Drug substances in all three mediums is more than 85% at 15 minutes hence product is categorized as very rapidly dissolving drug, there is no need to calculate f2 value. The CDP of Pru-cic 2mg tablet against Resolor 2mg Tablet shows equivalence.</td></tr>
<tr><td colspan="3">Decision: Approved with innovator’s specifcations. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.
• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.
• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application</td></tr>
</table>

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the pharmaceutical i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year. In compliance to the aforementioned decision of the Board, the following firm have achieved the benchmark of more than 100,000 USD during the fiscal Year 2020-2021 and submitted their applications as communicated by Assistant Director (PR-I/EFD) vide letter No No.F.1-6/2019-PR-I (EFD dated 06th October 2022.

Registration applications of drugs for which stability study data is submitted for exemption from onsite verification of stability data

377.	Name and address of manufacturer / Applicant	M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan.
	Brand Name +Dosage Form + Strength	Sacuval 50mg Tablets
	Diary No. Date of R& I & fee	Dy No. 1809 (dated 17.10.2016) Rs: 50,000/- 17-10-2016
	Composition	Each film coated tablet contains: Sacubitril…….24.3mg

		Valsartan…….25.7mg
	Pharmacological Group	Sacubitril: Angiotensin Receptor Neprilysin Inhibitor (ARNI) Valsartan: Angiotensin II receptor blocker (ARBs)
	Type of Form	Form 5-D
	Finished Product Specification	Manufacturer Specs.
	Pack size & Demanded Price	Rs 15000/- for 10's Rs 45000/- for 30's
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved Entresto tablet 24/26
	Me-too status	Savesto 50 tablet (Reg No 093110) by M/s Getz Pharma (Pvt) Ltd, Karachi
	GMP status	GMP conducted on 17-06-2021. (valid till 3rd June 2023)

STABILITY STUDY DATA			
Drug	Sacuval 50mg Tablets		
Name of Manufacturer	M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan..		
Manufacturer of API	Nantong Chanyoo Pharmatech Co., Ltd No. 2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, P.R China.		
API Lot No.	Sacubitril+ Valsartan (LCZ696) RD-LCZ696-201906241		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 18 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6,9,12 (months)		
Batch No.	TR-559	TR-560	TR-561
Batch Size	2000 Tablets	2000 Tablets	2000 Tablet
Manufacturing Date	11-2019	11-2019	11-2019
Date of Initiation	02-12-2019	02-12-2019	02-12-2019
No. of Batches	03		
Date of Submission	21-04-2021 (Dy No. 1137 PEC, DRAP)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION			
DOCUMENTS / DATA PROVIDED BY THE APPLICANT			
S. No.	Documents To Be Provided	Status	
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product for Glyzia XR (Sitagliptin/Metfrormin HCl) Tablets 50/500 & 50/1000 on 26th September, 2018. Further, the said panel inspection report was discussed in 285th Drug Registration Board meeting held on 3rd-4th October,2018. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber.. Related manufacturing area, equipment, personnel and utilities are GMP compliant.	
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted COA of API (Batch No. RD-LCZ696-201906241) from M/s Nantong Chanyoo Pharmatech Co., Ltd China. COA (Batch No. RD-LCZ696-201906241) from M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan is also submitted.	
3.	Method used for analysis of API from both API Manufacturer & Finished Product manufacturer	Submitted	
4.	Stability study data of API from API manufacturer	The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 24 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches: RD-LCZ696-201709181, RD-LCZ696-201709241, RD-LCZ696-201710091,	
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate of M/s Nantong Chanyoo Pharmatech Co., Ltd China., China issued by People's Republic of China NANTONG JIANGSU. The certificate is valid till 05-05-2022.	
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted import License No. 2299-DRAP dated 19-08-2019 confirming import of 5.3Kg Sacubitril+ Valsartan from M/s	

<table>
<tr><td></td><td></td><td>Nantong Chanyoo Pharmatech Co., Ltd China for Batch No. RD-LCZ696-201906241.</td><td></td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Submitted</td><td></td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Submitted</td><td></td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Firm has submitted that same excipients has been used as used by innovator “Enestro Tablets 24.3mg + 25.7mg” by M/s Novertis Pharmaceuticals UK Ltd. Therefore, Drug-excipients compatibility studies were not performed.</td><td></td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has manufactured three stability batches of Sacuval 50mg Tablets 24.3mg + 25.7mg and has submitted copy of complete batch manufacturing. Details are as under:
<table>
<tr><td colspan="3">Sacuval Tablets 24.3mg+25.7mg</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. D</td></tr>
<tr><td>TR-559</td><td>2000 Tablets</td><td>Novem 2019</td></tr>
<tr><td>TR-560</td><td>2000 Tablets</td><td>Novem 2019</td></tr>
<tr><td>TR-561</td><td>2000 Tablets</td><td>Novem 2019</td></tr>
</table></td><td></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “Uperio 200mg tablet”. The details are as follows:
<table>
<tr><td>Feature</td><td>Reference product by M/s Novartis pharma Pakistan Ltd</td><td>Test product by M/s AGP Limited</td></tr>
<tr><td>Brand name</td><td>Entresto 50mg tablet</td><td>Sacuval 50mg Tablet</td></tr>
<tr><td>Batch No.</td><td>TW 724</td><td>TR-560</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
On the basis of similarity factor (f2) result i.e NLT 50 of dissolution profile of both API Sacubitril and</td><td></td></tr>
</table>

		Valsartan in test product and reference product, both products are similar.	
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted	
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of stability chambers.	
Remarks of Evaluator:			

S.no.	Observation	Reply
1.	Drug Substance used in reference product is "sacubitril valsartan sodium salt complex' while Drug Substance used in instant application as "sacubitril valsartan complex", salt form to be clarified.	Firm has used Sacubitril / Valsartan so complex in applied formulation. The sa claim mentioned has been verified fron
2.	The absence of a test for water content has to be justified since water content may increase above 60% RH condition, however slightly increased water content observed during stability studies had no impact on product performance.	Stability results of water in the raw mat showing any significant change at high (75%) of accelerated condition that is v water content not incorporated in the pr specification. Moreover, as per EMA A report, during stability studies water co no impact on product performance.
3.	Identification test has not been performed by using IR method since the individual active substance and the co-crystal complex are readily distinguished by IR method. Identification test of innovator product (Entresto) has been performed using both IR and HPLC technique.	IR method are used for the Identificatio raw material while in product only HPL used. HPLC method is also well established identification technique in pharmacopo products.
4.	If both the test and innovator / reference product show more than 85% dissolution within 15minutes, the profiles are considered similar in that particular medium and hence calculation of f2 factor is not required. Both Test product and reference products show more than 85% dissolution (both sacubitril and valsartan) within 15minutes in pH 4.5 Acetate buffer and pH 6.8 Phosphate buffer medium then why f2 factor has been calculated.	A f2 calculation required for pH 1.2 HC result, same default calculation templat other mediums. Hence both results sim factor more than 50 or results showing 85% dissolution within 15minutes conc satisfactory.

5.	GMP Certificate of M/s Nantong Chanyoo Pharmatech Co., Ltd China., issued by People's Republic of China NANTONG JIANGSU is valid till 05-05-2022. Submit valid/updated GMP status of API manufacturer.	Firm has submitted copy of DML (No Su 20160512) (valid till 02.12.2025) issued by Jiangsu Drug Administration.		

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

Registration applications of drugs for which stability study data is submitted for exemption from onsite verification of stability data

378.	Name and address of manufacturer / Applicant	M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan.
	Brand Name +Dosage Form + Strength	Sacuval 100mg Tablets
	Diary No. Date of R& I & fee	Dy No. 1799 (dated 17/10/2016), Rs: 50,000/- 17-10-2016
	Composition	Each film coated tablet contains: Sacubitril…….48.6mg Valsartan…….51.4mg
	Pharmacological Group	Sacubitril: Angiotensin Receptor Neprilysin Inhibitor (ARNI) Valsartan: Angiotensin II receptor blocker (ARBs)
	Type of Form	Form 5-D
	Finished Product Specification	Manufacturer Specs.
	Pack size & Demanded Price	Rs 30,000/- for 10's Rs 90,000/- for 30's
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved Entresto tablet 49/51
	Me-too status	Savesto 100 tablet (Reg No 093111) by M/s Getz Pharma (Pvt) Ltd, Karachi
	GMP status	GMP conducted on 17-06-2021. (valid till 3rd June 2023)

STABILITY STUDY DATA	
Drug	Sacuval 100mg Tablets
Name of Manufacturer	M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan..
Manufacturer of API	Nantong Chanyoo Pharmatech Co., Ltd No. 2 Tonghai Si Road, Yangkou Chemical Industrial Park, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, P.R China.China
API Lot No.	Sacubitril+ Valsartan (LCZ696) RD-LCZ696-201906241
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton

Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 18 months
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6,9,12 (months)

Batch No.	TR-556	TR-557	TR-558
Batch Size	2000 Tablets	2000 Tablets	2000 Tablet
Manufacturing Date	11-2019	11-2019	11-2019
Date of Initiation	27-11-2019	27-11-2019	27-11-2019
No. of Batches	03		
Date of Submission	21-04-2021 (Dy No. 1136 PEC, DRAP)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
S. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product for Glyzia XR (Sitagliptin/Metfrormin HCl) Tablets 50/500 & 50/1000 on 26th September, 2018. Further, the said panel inspection report was discussed in 285th Drug Registration Board meeting held on 3rd-4th October,2018. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber.. Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted COA of API (Batch No. RD-LCZ696-201906241) from M/s Nantong Chanyoo Pharmatech Co., Ltd China. COA (Batch No. RD-LCZ696-201906241) from M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan is also submitted.
3.	Method used for analysis of API from both API Manufacturer & Finished Product manufacturer	Submitted
4.	Stability study data of API from API manufacturer	The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 24 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches: RD-LCZ696-201709181, RD-LCZ696-201709241, RD-LCZ696-201710091,
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate of M/s Nantong Chanyoo Pharmatech Co., Ltd China., China issued by People's Republic of China NANTONG JIANGSU. The certificate is valid till 05-05-2022.

<table>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Firm has submitted import License No. 2299-DRAP dated 19-08-2019 confirming import of 5.3Kg Sacubitril+ Valsartan from M/s Nantong Chanyoo Pharmatech Co., Ltd China for Batch No. RD-LCZ696-201906241.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Submitted</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Firm has submitted that same excipients has been used as used by innovator “Enestro Tablets 48.6mg + 51.4mg” by M/s Novertis Pharmaceuticals UK Ltd. Therefore, Drug-excipients compatibility studies were not performed.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has manufactured three stability batches of Sacuval Tablet 48.6mg + 51.4mg and has submitted copy of complete batch manufacturing. Details are as under:
<table>
<tr><td colspan="3">Sacuval Tablets 48.6mg+51.4mg</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Date</td></tr>
<tr><td>TR-556</td><td>2000 Tablets</td><td>November 2019</td></tr>
<tr><td>TR-557</td><td>2000 Tablets</td><td>November 2019</td></tr>
<tr><td>TR-558</td><td>2000 Tablets</td><td>November 2019</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “Uperio 200mg tablet”. The details are as follows:
<table>
<tr><td>Feature</td><td>Reference product by M/s Novartis pharma Pakistan Ltd</td><td>Test product by M/s AGP Limited</td></tr>
<tr><td>Brand name</td><td>Entresto 100mg tablet</td><td>Sacuval 100mg Tablet</td></tr>
<tr><td>Batch No.</td><td>TW 892</td><td>TR-557</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer

On the basis of similarity factor (f2) result i.e NLT 50 of dissolution profile of both API Sacubitril and Valsartan in test product and reference product, both products are similar.</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
</table>

14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of stability chambers.

Remarks of Evaluator:

S.no.	Observation	Reply
1.	Drug Substance used in reference product is "sacubitril valsartan sodium salt complex' while Drug Substance used in instant application as "sacubitril valsartan complex", salt form to be clarified.	Firm has used Sacubitril / Valsartan sodium salt complex in applied formulation. The same API claim mentioned has been verified from BMR.
2.	The absence of a test for water content has to be justified since water content may increase above 60% RH condition, however slightly increased water content observed during stability studies had no impact on product performance.	Stability results of water in the raw material not showing any significant change at higher RH (75%) of accelerated condition that is why test of water content not incorporated in the product specification. Moreover, as per EMA Assessment report, during stability studies water content had no impact on product performance.
3.	Identification test has not been performed by using IR method since the individual active substance and the co-crystal complex are readily distinguished by IR method. Identification test of innovator product (Entresto) has been performed using both IR and HPLC technique.	IR method are used for the Identification in the raw material while in product only HPLC method used. HPLC method is also well established identification technique in pharmacopoeial products.
4.	If both the test and innovator / reference product show more than 85% dissolution within 15minutes, the profiles are considered similar in that particular medium and hence calculation of f2 factor is not required. Both Test product and reference products show more than 85% dissolution (both sacubitril and valsartan) within 15minutes in pH 4.5 Acetate buffer and pH 6.8 Phosphate buffer medium then why f2 factor has been calculated.	A f2 calculation required for pH 1.2 HCl buffer result, same default calculation template used in other mediums. Hence both results similarity factor more than 50 or results showing more than 85% dissolution within 15minutes conclusion is satisfactory.
5.	GMP Certificate of M/s Nantong Chanyoo Pharmatech Co., Ltd China., issued by People's Republic of China NANTONG JIANGSU is valid till 05-05-2022. Submit valid/updated GMP status of API manufacturer.	Firm has submitted copy of DML (No Su 20160512) (valid till 02.12.2025) issued by Jiangsu Drug Administration.

Decision: Approved with Innovator's specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

Registration applications of drugs for which stability study data is submitted for exemption from onsite verification of stability data

379.	Name and address of manufacturer / Applicant	M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan.
	Brand Name +Dosage Form + Strength	Sacuval 200mg Tablets
	Diary No. Date of R& I & fee	Dy No. 1800 (dated 17/10.2016), Rs: 50,000/- 17-10-2016
	Composition	Each film coated tablet contains: Sacubitril…….97.2mg Valsartan…….102.8mg
	Pharmacological Group	Sacubitril: Angiotensin Receptor Neprilysin Inhibitor (ARNI) Valsartan: Angiotensin II receptor blocker (ARBs)
	Type of Form	Form 5-D
	Finished Product Specification	Manufacturer Specs.
	Pack size & Demanded Price	Rs 60,000/- for 10's Rs 180,000/- for 30's
	Approval status of product in Reference Regulatory Authorities.	USFDA Approved Entresto tablet 97/103
	Me-too status	Savesto 200 tablet (Reg No 093112) by M/s Getz Pharma (Pvt) Ltd, Karachi
	GMP status	GMP conducted on 17-06-2021. (valid till 3rd June 2023)

STABILITY STUDY DATA			
Drug	Sacuval 200mg Tablets		
Name of Manufacturer	M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan..		
Manufacturer of API	Nantong Chanyoo Pharmatech Co., Ltd China		
API Lot No.	Sacubitril+ Valsartan (LCZ696) RD-LCZ696-201906241		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	Real time : 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 18 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6,9,12 (months)		
Batch No.	TR-544	TR-545	TR-546
Batch Size	2000 Tablets	2000 Tablets	2000 Tablet
Manufacturing Date	11-2019	11-2019	11-2019
Date of Initiation	26-11-2019	26-11-2019	26-11-2019
No. of Batches	03		

Date of Submission	21-04-2021 (Dy No. 1135 PEC, DRAP)	
DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
S. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Firm has referred to onsite inspection report of their product for Glyzia XR (Sitagliptin/Metfrormin HCl) Tablets 50/500 & 50/1000 on 26th September, 2018. Further, the said panel inspection report was discussed in 285th Drug Registration Board meeting held on 3rd-4th October,2018. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber.. Related manufacturing area, equipment, personnel and utilities are GMP compliant.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted COA of API (Batch No. RD-LCZ696-201906241) from M/s Nantong Chanyoo Pharmatech Co., Ltd China. COA (Batch No. RD-LCZ696-201906241) from M/s AGP Limited B-23 S.I.T.E., Karachi, Pakistan is also submitted.
3.	Method used for analysis of API from both API Manufacturer & Finished Product manufacturer	Submitted
4.	Stability study data of API from API manufacturer	The firm has submitted copy of accelerated, 06 Months (40°C ± 2°C & 75±5%RH) & long term, 24 Months (30°C ± 2°C & 65±5%RH) stability study reports of 03 batches: RD-LCZ696-201709181, RD-LCZ696-201709241, RD-LCZ696-201710091,
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate of M/s Nantong Chanyoo Pharmatech Co., Ltd China., China issued by People's Republic of China NANTONG JIANGSU. The certificate is valid till 05-05-2022.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted import License No. 2299-DRAP dated 19-08-2019 confirming import of 5.3Kg Sacubitril+ Valsartan from M/s Nantong Chanyoo Pharmatech Co., Ltd China for Batch No. RD-LCZ696-201906241.
7.	Protocols followed for conduction of stability study	Submitted
8.	Method used for analysis of FPP	Submitted

<table>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Firm has submitted that same excipients has been used as used by innovator ‘Enestro Tablets 97.2mg + 102.8mg’ by M/s Novertis Pharmaceuticals UK Ltd. Therefore, Drug-excipients compatibility studies were not performed.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has manufactured three stability batches of Sacuval 200mg Tablets 97mg + 103mg and has submitted copy of complete batch manufacturing. Details are as under:
<table>
<tr><td colspan="3">Sacuval Tablets 97.2mg+102.8mg</td></tr>
<tr><td>Batch No.</td><td>Bach size</td><td>Mfg. Date</td></tr>
<tr><td>TR-544</td><td>2000 Tablets</td><td>November 2019</td></tr>
<tr><td>TR-545</td><td>2000 Tablets</td><td>November 2019</td></tr>
<tr><td>TR-546</td><td>2000 Tablets</td><td>November 2019</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “Uperio 200mg tablet”. The details are as follows:
<table>
<tr><td>Feature</td><td>Reference product by M/s Novartis pharma Pakistan Ltd</td><td>Test product by M/s AGP Limited</td></tr>
<tr><td>Brand name</td><td>Uperio 200mg tablet</td><td>Sacuval Tablets 97.2mg+102.8mg</td></tr>
<tr><td>Batch No.</td><td>TT213</td><td>TR545</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer

On the basis of similarity factor (f2) result i.e NLT 50 of dissolution profile of both API Sacubitril and Valsartan in test product and reference product, both products are similar.</td></tr>
<tr><td>12.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted</td></tr>
<tr><td>13.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
</table>

14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of stability chambers.

Remarks of Evaluator:

S.no.	Observation	Reply
1.	Drug Substance used in reference product is "sacubitril valsartan sodium salt complex' while Drug Substance used in instant application as "sacubitril valsartan complex", salt form to be clarified.	Firm has used Sacubitril / Valsartan sodium salt complex in applied formulation. The same API claim mentioned has been verified from BMR.
2.	The absence of a test for water content has to be justified since water content may increase above 60% RH condition, however slightly increased water content observed during stability studies had no impact on product performance.	Stability results of water in the raw material not showing any significant change at higher RH (75%) of accelerated condition that is why test of water content not incorporated in the product specification. Moreover, as per EMA Assessment report, during stability studies water content had no impact on product performance.
3.	Identification test has not been performed by using IR method since the individual active substance and the co-crystal complex are readily distinguished by IR method. Identification test of innovator product (Entresto) has been performed using both IR and HPLC technique.	IR method are used for the Identification in the raw material while in product only HPLC method used. HPLC method is also well established identification technique in pharmacopoeial products.
4.	GMP Certificate of M/s Nantong Chanyoo Pharmatech Co., Ltd China., issued by People's Republic of China NANTONG JIANGSU is valid till 05-05-2022. Submit valid/updated GMP status of API manufacturer.	Firm has submitted copy of DML (No Su 20160512) (valid till 02.12.2025) issued by Jiangsu Drug Administration.

Decision: Approved with Innovator's specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.**

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the pharmaceutical i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year.

In compliance to the aforementioned decision of the Board, the following firm have achieved the benchmark of more than 100,000 USD during the fiscal Year 2020-2021 and submitted their applications for priority consideration/ evaluation as communicated by Assistant Director (PR-I/EFD) vide letter No No.F.1-6/2019-PR-I (EFD dated 06th October 2022.

380.	Name, address of Applicant / Marketing Authorization Holder	M/s. SAMI Pharmaceuticals (Pvt.) Ltd. F-95, Off Hub River Road, S.I.T.E., Karachi – 75730, Pakistan
	Name, address of Manufacturing site.	M/s. SAMI Pharmaceuticals (Pvt.) Ltd. F-95, Off Hub River Road, S.I.T.E., Karachi – 75730, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 10233 dated 21/04/2022
	Details of fee submitted	PKR 75,000/-: dated 23/09/2021
	The proposed proprietary name / brand name	LAGITA DOUBLE ACTION Chewable Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Chewable Tablet contains: Sodium Alginate BP……250mg Sodium Bicarbonate BP…..106.5mg Calcium Carbonate BP…..187.5mg
	Pharmaceutical form of applied drug	One layer of the tablet is colored pink with a slightly mottled appearance, with the other layer being white, Flat, Circular, bilayer tablet with beveled edges
	Pharmacotherapeutic Group of (API)	Antacid
	Reference to Finished product specifications	Innovators Specs.
	Proposed Pack size	48’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Gaviscon Double Action Mint flavor Chewable Tablets by Reckitt Benckiser Healthcare (UK) Limited, MHRA Approved
	For generic drugs (me-too status)	N/A
	GMP status of the Finished product manufacturer	GMP Certificate issued date 28-08-2019 Tablet (General/General antibiotic) section is approved dated 22.06.2018
	Name and address of API manufacturer.	Sodium Alginate: QingDao Bright Moon Seaweed Group Co. Ltd NO.777, Mingyue Road, Huangdao District Qingdao China Sodium Bicarbonate:

		Solvay Peroxythai Limited 1, I-3A Road, Tambol Map Ta Phut, Amphur Muang, Rayong 21150, Thailand Calcium Carbonate: Sudeep Pharma Private Limited Plot No. 129/1/A, G.I.D.C., Estate, Nandesari - 391 340. Dist. Vadodara.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, characterization, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, characterization, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Sodium Alginate Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (H051708011, H051708013, H051708012) Sodium bicarbonate Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (MTP25417, MTP27317, MTP28017) Calcium Carbonate Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (17B/CP/030, 17B/CP/031, 17B/CP/032)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, pharmaceutical development, impurities, individual impurity and total impurity, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator product i.e. GAVISCON double Action Tablet by M/s. Reckitt Benckiser Healthcare (UK) Ltd. (batch no. 107801) by performing quality tests (Appearance, Average weight, Taste, Raft strength, Acid neutralizing capacity, Firability, Assay, Microbial Limit Test CDP not required here since formulation is antacid preparation which has non systemic use. .
	Analytical method validation/verification of product	Method validation studies have been submitted including Linearity, Accuracy, and Precision including Repeatability & Intermediate Precision, Robustness and Specificity.

STABILITY STUDY DATA			
Manufacturer of API	Sodium alginate: QingDao Bright Moon Seaweed Group Co. Ltd Sodium bicarbonate: Solvay Peroxythai Limited Calcium carbonate: Sudeep Pharma Private Limited		
API Lot No.	Sodium alginate: H052002087 Sodium bicarbonate: MTP01820 Calcium carbonate: 18C/CP/080		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 2, 3, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Lab-04	Lab-05	Lab-06
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	18-02-2021	18-02-2021	18-02-2021
No. of Batches	03		
Administrative Portion			

	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted reference of last onsite panel inspection for instant dosage form conducted during last two years i.e. EMPOLI (Empagliflozin) 10mg & 25mg Tablets which was presented in 290th meeting of the registration board & hence approved & registered by registration board Date of inspection: 13th June 2019. The inspection report confirms following points • The HPLC software is 21CFR Compliant • Audit trail on the testing reports is available. • Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Sodium alginate: Copy of GMP certificate No. SD20180790 issued to Qingdao Bright moon Seaweed Group Co., Ltd valid till 23/10/2023. Sodium bicarbonate: Copy of GMP certificate No. 1-2-07-17-20-00013 issued to Solvay Peroxythai Limited valid till 25/08/2022 Calcium carbonate: Copy of GMP certificate No. 20051985 issued to Sudeep Pharma Private Limited valid till 17/05/2023
	Documents for the procurement of API with approval from DRAP (in case of import).	Sodium Alginate: Attached copy of commercial invoice (Invoice# BMM20080 dated 27th March 2020, with received quantity i.e. 5000Kgs) for the purchase of Sodium Alginate from Qingdao Bright Moon Seaweed Group Co. Ltd. with attestation of DRAP dated 19th May 2020 Sodium Bicarbonate: Attached copy of commercial invoice (with received quantity i.e. 24Kgs) for the purchase of Sodium Bicarbonate from Solvay Peroxythai Limited with courier slip dated 14th March 2020 Calcium Carbonate: Attached copy of commercial invoice (Invoice# SPPL/EX021/18-19 dated 17th April 2018, with received quantity i.e. 12 Kg for the purchase of Calcium Carbonate from Sundeep Pharma PrivateLimited with attestation of DRAP dated 30th April 2018

	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted complete record of testing of all batches along with raw data sheets and summary data sheets. Chromatograms are not applicable since spectroscopic method are used for analysis of drugs.
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of digital data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

Sr.#	Observation	Reply
	Good Manufacturing Practice (GMP) certificate of the Drug Substance / API (sodium bicarbonate) manufacturer with valid period of time.	Copy of GMP certificate No. 1-2-07-17-20-00013 issued to Solvay Peroxythai Limited valid till 25/08/2022 is provided. Firm has submitted notification from Food and Drug Administration, Thailand Wherein it is stated that GMP certificate of manufacturer issued by FDA that expires before 31st Dec,2022 are considered valid till 31st Dec,2022 due to ongoing threat of COVI-19 pandemic.
	Updated GMP status of FPP manufacturer to be submitted.	Firm has submitted GMP certificate dated 03.08.2022 valid till 2 years.
	The information on tablet hardness and disintegration is not provided (as recommended by USFDA guidance document on quality attributes of chewable tablet). Justify it	**Firm has submitted specification of hardness and disintegration as follows** **Disintegration time 35 min** **Hardness NLT 7Kp and NMT 15Kp** **While USFDA recommends that hardness for chewable tablets be kept low (<12 kp). A higher hardness value (>12 kp) may be considered if justified.**
	Detailed analytical procedures used for testing the drug product should be provided.	Complied
	Documents for the procurement of API with approval from DRAP is required. Only commercial invoices are provided under this section.	Not complied. **Firm has submitted commercial invoice (of sodium bicarbonate) only. Batch No/Lot No is not verifiable. Clearance from DRAP is**

		also required for all three drug substances. **Furthermore, CoA of relevant batch from DS manufacturer and FPP manufacturer is required for all three drug substances.**
	CoA at each time interval is required in stability data.	Complied

Decision: Registration Board considered the case deferred the request for following observations:

- **Specification of hardness i.e NLT 7Kp and NMT 15Kp to be justified. Since USFDA recommends hardness for chewable tablets as <12 kp.**
- **Commercial invoices and DRAP clearance certificate of all drug substances along with CoA of relevant batches (from both Drug Substance and Finished Product manufacturer).**
- **Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin**

Registration applications of newly granted DML or New section (Human)
New DML
M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat CLB in its 282nd meeting held on 31st August 2021, has considered and approved the grant of DML by way of Formulation with following 3 sections:
Tablet Section (General)
Capsule Section (General)
Cream/ointment section (General)

381.	Name, address of Applicant / Marketing Authorization Holder	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Name, address of Manufacturing site.	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25524 (R&I) DRAP, dated 09/09/2022
	Details of fee submitted	PKR 30,000/- dated 22/08/2022
	The proposed proprietary name / brand name	Transa 250mg capsule

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Tranexamic acid…….250mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Anti fibrinolytic
	Reference to Finished product specifications	JP specification
	Proposed Pack size	2×10's
	Proposed unit price	As per Policy
	The status in reference regulatory authorities	PMDA (Japan) approved
	For generic drugs (me-too status)	Transamin 250mg capsule by M/s Hilton pharma, Karachi.
	GMP status of the Finished product manufacturer	DML grant inspection report not provided Capsule section (General) is approved dated 14.09.2021
	Name and address of API manufacturer.	Changzhou Yinsheng Pharmaceutical Co., Ltd. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, control of excipients, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months Batches:(100301, 100302, 100303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls,

		process validation studies, specifications, analytical procedure and validation studies batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence was determined against Transamin 250mg capsule (Batch No 141899) by M/s Hilton Pharma. Quality parameters such as identification, dissolution and assay were compared against Transa 500mg capsule (Batch No CP-02-T250 RT) CDP has been performed against the same brand that is Transamin 250mg capsule (Batch No 141899 in Acid media (pH 1.0-1.2) in Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range. Complete CDP report is not provided
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Changzhou Yinsheng Pharmaceutical Co., Ltd. China		
API Lot No.	2111002		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	500mg capsule		
Batch No.	CP-01-T250	CP-02-T250	CP-03-T250
Batch Size	5000 cap	5000 cap	5000 cap
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	29-03-2022	29-03-2022	29-03-2022
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. JS20170680 of Changzhou Yinsheng Pharmaceutical Co., Ltd. China issued by China Food and Drug Administration. The certificate is valid till 20-06-2022.
	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Observation	Reply (dated 30.10.2022)
	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided	Firm has submitted clarification regarding GMP of API manufacturer that Chinese Drug Regulatory Authority has declared that they will not issue new GMP from 31st Dec,2019 and authority has refused for renewal. DML# Su 20160123 valid till 16-12-2025 has been verified form the website of NMP China: https://www.nmpa.gov.cn/datasearch/home-index.html?79QlcAyHig6m=1670181120509#category=yp
	GMP status/inspection report of FPP manufacturer to be submitted.	Inspection report for grant of DML has been provided (dated 24.08.2021)
	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along	Provided

<table>
<tr><td></td><td>with Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacture.</td><td></td></tr>
<tr><td></td><td>Detailed analytical procedures for the testing of drug substance to be provided by Drug Product manufacturer</td><td>Provided</td></tr>
<tr><td></td><td>Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer to be provided</td><td>Provided</td></tr>
<tr><td></td><td>For testing of Pharmacopeial Drug Substance, the use of primary reference standard is recommended, justify use of working standard for Tranexamic acid</td><td>Firm has submitted copy of CoA of working standard (Tranexamic acid batch no. 2108005) and clarified that The primary working standard has been given to us by API manufacturer has already been qualified with the reference working standard</td></tr>
<tr><td></td><td>Detailed CDP report to be provided wherein values for f1 and f2 are calculated along with results conclusion.</td><td>Firm has submitted CDP report now Wherein CDP has been performed as follows:
<table><tr><td>Feature</td><td>Reference product by M/s Hilton</td><td>Product of M/s Akhsah</td></tr><tr><td>Brand name</td><td>Transamin 250mg cap</td><td>Transa 250mg cap</td></tr><tr><td>Batch No.</td><td>141899</td><td>CP-02-T250</td></tr></table>Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
The values for f1 and f2 are in the acceptable range.</td></tr>
<tr><td></td><td>Uniformity of dose is not provided in finished product specification and stability studies.</td><td>Provided calculation of uniformity of dose for all three stability batches CP-01-T250, CP-02-T250, CP-03-T250</td></tr>
<tr><td></td><td>Documents for the procurement of API</td><td>Provided copy of commercial invoice (Invoice# FNDL21-8165 dated 14th January 2022, with received quantity i.e. 14Kg) for the purchase of Tranexamic acid</td></tr>
</table>

	with approval from DRAP is required	from Changzhou Yinsheng Pharmaceutical Co., Ltd. China with attestation of DRAP dated 17th Feb 2022

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

382.	Name, address of Applicant / Marketing Authorization Holder	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Name, address of Manufacturing site.	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25525 (R&I) DRAP, dated 09/09/2022
	Details of fee submitted	PKR 30,000/- dated 22/08/2022
	The proposed proprietary name / brand name	Transa 500mg capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Tranexamic acid…….500mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Anti fibrinolytic
	Reference to Finished product specifications	JP specification
	Proposed Pack size	2×10’s
	Proposed unit price	As per Policy
	The status in reference regulatory authorities	PMDA (Japan) approved
	For generic drugs (me-too status)	Transamin 500mg capsule by M/s Hilton pharma, Karachi.
	GMP status of the Finished product manufacturer	DML grant inspection report not provided

		Capsule section (General) is approved dated 14.09.2021
	Name and address of API manufacturer.	Changzhou Yinsheng Pharmaceutical Co., Ltd. China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, control of excipients, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for impurity, specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months Batches:(100301, 100302, 100303)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, process validation studies, specifications, analytical procedure and validation studies batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence was determined against Transamin 500mg capsule (Batch No 143474) by M/s Hilton Pharma. Quality parameters such as identification, dissolution and assay were compared against Transa 500mg capsule (Batch No CP-01-T500) CDP has been performed against the same brand that is Transamin 500mg capsule (Batch No 143474) in Acid media (pH 1.0-1.2) in Acetate Buffer (pH 4.5) &

		Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range. CDP report is not submitted.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Changzhou Yinsheng Pharmaceutical Co., Ltd. China		
API Lot No.	2111002		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	500mg capsule		
Batch No.	CP-01-T500	CP-02-T500	CP-03-T500
Batch Size	5000 cap	5000 cap	5000 cap
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	29-03-2022	29-03-2022	29-03-2022
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. JS20170680 of Changzhou Yinsheng Pharmaceutical Co., Ltd. China issued by China Food and Drug Administration. The certificate is valid till 20-06-2022.
	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Observation	Reply (dated 30.10.2022)
	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided	Firm has submitted clarification regarding GMP of API manufacturer that Chinese Drug Regulatory Authority has declared that they will not issue new GMP from 31st Dec,2019 and authority has refused for renewal. DML# Su 20160123 valid till 16-12-2025 has been verified form the website of NMP China: https://www.nmpa.gov.cn/datasearch/home-index.html?79QlcAyHig6m=1670181120509#category=yp
	GMP status/inspection report of FPP manufacturer to be submitted.	Inspection report for grant of DML has been provided (dated 24.08.2021)
	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacture.	Provided
	Detailed analytical procedures for the testing of drug substance to be provided by Drug Product manufacturer	Provided
	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer to be provided	Provided

<table>
<tr><td></td><td>For testing of Pharmacopeial Drug Substance, the use of primary reference standard is recommended, justify use of working standard for Tranexamic acid</td><td>Firm has submitted copy of CoA of working standard (Tranexamic acid batch no. 2108005) and clarified that The primary working standard has been given to us by API manufacturer has already been qualified with the reference working standard</td></tr>
<tr><td></td><td>Detailed CDP report to be provided wherein values for f1 and f2 are calculated along with results conclusion.</td><td>Firm has submitted CDP report now Wherein CDP has been performed as follows:
<table>
<tr><td>Feature</td><td>Reference product by M/s Hilton</td><td>Product of M/s Akhsah</td></tr>
<tr><td>Brand name</td><td>Transamin 500mg cap</td><td>Transa 500mg cap</td></tr>
<tr><td>Batch No.</td><td>143474</td><td>CP-02-T500</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
The values for f1 and f2 are in the acceptable range.</td></tr>
<tr><td></td><td>Uniformity of dose is not provided in finished product specification and stability studies.</td><td>Provided calculation of uniformity of dose for all three stability batches CP-01-T500, CP-02-T500, CP-03-T500</td></tr>
<tr><td></td><td>Documents for the procurement of API with approval from DRAP is required</td><td>Provided copy of commercial invoice (Invoice# FNDL21-8165 dated 14th January 2022, with received quantity i.e. 14Kg) for the purchase of Tranexamic acid from Changzhou Yinsheng Pharmaceutical Co., Ltd. China with attestation of DRAP dated 17th Feb 2022</td></tr>
</table>

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

383.	Name, address of Applicant / Marketing Authorization Holder	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Name, address of Manufacturing site.	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Status of the applicant	☒ Manufacturer ☐ Importer

		☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25523 (R&I) DRAP, dated 09/09/2022
	Details of fee submitted	PKR 30,000/- dated 22/08/2022
	The proposed proprietary name / brand name	Elox 250mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Levofloxacin hemihydrate eq to Levofloxacin……..….250mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Fluoroquinolone
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1×10’s
	Proposed unit price	As per Policy
	The status in reference regulatory authorities	USFDA approved
	For generic drugs (me-too status)	Leflox 250mg tablet by M/s Getz pharma, Pakistan.
	GMP status of the Finished product manufacturer	DML grant inspection report not provided Capsule section (General) is approved dated 14.09.2021
	Name and address of API manufacturer.	Zhejiang East-Asia Pharmaceutical Co Ltd
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, control of excipients, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and

		controls, tests for impurity, specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(DC-0401-1203001, DC-0401-1203002, DC-0401-1203003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, process validation studies, specifications, analytical procedure and validation studies batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence was determined against Leflox 250mg tablet by M/s Getz pharma, Pakistan. (Batch No 1G016) Quality parameters such as identification, dissolution and assay were compared against Elox 250mg Tablet (Batch No TB-01-E250) CDP has been performed against the same brand that is Leflox 250mg tablet by M/s Getz pharma, Pakistan (Batch No 1G016) in Acid media (pH 1.0-1.2) in Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range. CDP report is not provided.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Zhejiang East-Asia Pharmaceutical Co Ltd China
API Lot No.	DC-004-2110012
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Strength	250mg Tablet		
Batch No.	TB-01-E250	TB-02-E250	TB-03-E250
Batch Size	5000 tab	5000 tab	5000 tab
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	24-03-2022	24-03-2022	24-03-2022
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted
	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Observation	Reply (dated 30.10.2022)
	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided	Firm has submitted clarification regarding GMP of API manufacturer that Chinese Drug Regulatory Authority has declared that they will not issue new GMP from 31st Dec,2019 and authority has refused for renewal.
	GMP status/inspection report of FPP manufacturer to be submitted.	Inspection report for grant of DML has been provided (dated 24.08.2021)
	Compatibility of the Drug Substance(s) with excipients is not provided. Since excipients used in applied product are different from innovator/reference product.	***IPA has been used along with Povidone. IPA get evaporated and dried granules get mixed with API.***

<table>
<tr><td></td><td></td><td>sodium starch glycolate has been used as disintegrant instead of croscarmillose sodium, which is used by innovator, both has same functions.

Remarks:
Drug excipients compatibility studies is required for sodium starch glycolate, PVPK30 and silicon dioxide.</td></tr>
<tr><td></td><td>Detailed analytical procedures for the testing of drug substance to be provided by Drug Product manufacturer</td><td>Provided</td></tr>
<tr><td></td><td>Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer to be provided</td><td>Provided</td></tr>
<tr><td></td><td>For testing of Pharmacopeial Drug Substance, the use of primary reference standard is recommended, justify use of working standard for Levofloxacin</td><td>Firm has submitted copy of CoA of working standard (Levofloxacin hemihydrate batch no. WS-ZFSX-202101) and clarified that
The primary working standard has been given to us by API manufacturer has already been qualified with the reference working standard</td></tr>
<tr><td></td><td>Detailed CDP report to be provided wherein values for f1 and f2 are calculated along with results conclusion.</td><td>Firm has submitted CDP report now Wherein CDP has been performed as follows:
<table>
<tr><td>Feature</td><td>Reference product by M/s Getz pharma</td><td>Product of M/s Akhsah</td></tr>
<tr><td>Brand name</td><td>Leflox 250mg tablet</td><td>Elox 250mg tablet</td></tr>
<tr><td>Batch No.</td><td>1G016</td><td>TB-01-E250</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
The Average % release of Drug substances in all three mediums is more than 85% at 15 minutes hence there is no need to calculate f2 value. Whereas firm has calculated both f1 and f2. The</td></tr>
</table>

		values for f1 and f2 are in the acceptable range.
	Uniformity of dose is not provided in finished product specification and stability studies.	Provided calculation of uniformity of dose for all three stability batches TB-01-E250, TB-02-E250 TB-03-E250
	Documents for the procurement of API with approval from DRAP is required	Provided copy of commercial invoice (Invoice# LEV220113-L dated 13th January 2022, with received quantity i.e. 12Kg) for the purchase of Levofloxacin hemihydrate from Zhejiang East-Asia Pharmaceutical Co Ltd. China with attestation of DRAP dated 02/03/2022

Decision: Deferred for following:

- **Justification of difference in qualitative composition of excipients of applied product from innovator.**
- **Valid DML/GMP certificate/approval of API in the name of Zhejiang East-Asia Pharmaceutical Co Ltd China issued by concerned regulatory authority of China.**

384.	Name, address of Applicant / Marketing Authorization Holder	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Name, address of Manufacturing site.	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25526 (R&I) DRAP, dated 09/09/2022
	Details of fee submitted	PKR 30,000/- dated 22/08/2022
	The proposed proprietary name / brand name	Expel 5mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Escitalopram Oxalate eq. to Escitalopram……..….5mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-depressant
	Reference to Finished product specifications	USP specification

	Proposed Pack size	1×14's
	Proposed unit price	As per Policy
	The status in reference regulatory authorities	USFDA approved
	For generic drugs (me-too status)	Estar 5mg tablet by M/s Pharmevo, Karachi
	GMP status of the Finished product manufacturer	DML grant inspection report not provided Tablet section (General) is approved dated 14.09.2021
	Name and address of API manufacturer.	Zhejiang Haisen Pharmaceutical Co Ltd
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, control of excipients, list of reference standard used, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (3619102201, 3619102202 3619102203) DC-0401-1203002, DC-0401-1203003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, process validation studies, specifications, analytical procedure and verification studies batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence was determined against Estar 5mg tablet by M/s Pharmevo, Pvt Ltd (Batch No 1M031) Quality parameters such as identification, dissolution

		and assay were compared against Expel 5mg Tablet (Batch No TB-01-E5) CDP has been performed against the same brand that is Estar 5mg tablet by M/s Pharmevo, Pvt Ltd (Batch No 1M031) in Acid media (pH 1.0-1.2) in Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range. CDP report is not submitted
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Haisen Pharmaceutical Co Ltd China		
API Lot No.	3621050212		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	5mg Tablet		
Batch No.	TB-01-E5	TB-02-E5	TB-03-E5
Batch Size	5138 tab	5138 tab	5138 tab
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	12-03-2022	12-03-2022	12-03-2022
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted
	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided

	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Observation	Reply (dated 01.11.2022)
	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided	Firm has provided copy of GMP certificate (No. ZJ20190082) issuance dated 22.07.2019 valid till 21.07.2024 by China Food and Drug Administration.
	GMP status/inspection report of FPP manufacturer to be submitted.	Inspection report for grant of DML has been provided (dated 24.08.2021)
	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacture.	Complied. .
	Detailed analytical procedures for the testing of drug substance to be provided by Drug Product manufacturer	Complied.
	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer to be provided	Complied.
	Specifications of primary / secondary reference standard including source and lot number for primary reference standard to be provided	Firm has submitted copy of CoA of working standard (Escitalopram oxalate, batch no. WS-3621) For testing of Pharmacopoeial Drug Substance, the use of primary reference standard is recommended, use of working standard to be justified.
	Stability data of Drug Substance has been submitted for 6 months only.	complied.

<table>
<tr><td></td><td></td><td>Real time stability data submitted for three batches: (3619102201, 3619102202 3619102203) for the period of 24 months at 30.°C ± 2°C / 75% ± 5%RH.</td></tr>
<tr><td></td><td>Detailed CDP report to be provided wherein values for f1 and f2 are calculated along with results conclusion.</td><td>Firm has submitted CDP report now Wherein CDP has been performed as follows:
<table>
<tr><td>Feature</td><td>Reference product by M/s PharmEvo</td><td>Product of M/s Akhsah</td></tr>
<tr><td>Brand name</td><td>Estar 5mg tablet</td><td>Expel 5mg tablet</td></tr>
<tr><td>Batch No.</td><td>1M031</td><td>TB-01-E5</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
The values for f1 and f2 are in the acceptable range.</td></tr>
<tr><td></td><td>Uniformity of dose is not provided in finished product specification and stability studies.</td><td>Provided calculation of uniformity of dose for all three stability batches TB-01-E5, TB-02-E5, TB-03-E5</td></tr>
<tr><td></td><td>Documents for the procurement of API with approval from DRAP is required</td><td>Provided copy of commercial invoice (Invoice# ZHP8220126 dated 26th January 2022, with received quantity i.e. 0.3Kg) for the purchase of Escitalopram oxalate from Zhejiang Haisen Pharmaceutical Co Ltd China with attestation of DRAP dated 02/03/2022</td></tr>
</table>

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

385	Name, address of Applicant / Marketing Authorization Holder	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat
	Name, address of Manufacturing site.	M/s Akhsah Pharmaceuticals (Pvt) Ltd, Plot No. 47, Street No S-10,RCCI,Industrial estate, Rawat

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25527 (R&I) DRAP, dated 09/09/2022
	Details of fee submitted	PKR 30,000/- dated 22/08/2022
	The proposed proprietary name / brand name	Expel 10mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Escitalopram Oxalate eq. to Escitalopram……..……..….10mg
	Pharmaceutical form of applied drug	Tablet
	Pharmacotherapeutic Group of (API)	Anti-depressant
	Reference to Finished product specifications	USP specification
	Proposed Pack size	1×14’s
	Proposed unit price	As per Policy
	The status in reference regulatory authorities	USFDA approved
	For generic drugs (me-too status)	Estar 10mg tablet by M/s Pharmevo, Karachi
	GMP status of the Finished product manufacturer	DML grant inspection report not submitted Tablet section (General) is approved dated 14.09.2021
	Name and address of API manufacturer.	Zhejiang Haisen Pharmaceutical Co Ltd
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, control of excipients, list of reference standard used, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for

		impurity & related substances, specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 6 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (3619102201, 3619102202 3619102203) DC-0401-1203002, DC-0401-1203003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, process validation studies, specifications, analytical procedure and verification studies batch analysis and justification of specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence was determined against Estar 10mg tablet by M/s pharmevo, Pvt Ltd (Batch No 1G016) Quality parameters such as identification, dissolution and assay were compared against Expel 10mg Tablet (Batch No TB-01-E10) CDP has been performed against the same brand that is Estar 10mg tablet by M/s Pharmevo, Pvt Ltd (Batch No 1G016) in Acid media (pH 1.0-1.2) in Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range. CDP report is not submitted
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Zhejiang Haisen Pharmaceutical Co Ltd China
API Lot No.	3621050212
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×14's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	10mg Tablet		
Batch No.	TB-01-E10	TB-02-E10	TB-03-E10
Batch Size	5000 tab	5000 tab	5000 tab
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	12-03-2022	12-03-2022	12-03-2022
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	Not applicable
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted
	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Observation	Reply (dated 01.11.2022)
	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided	Firm has provided copy of GMP certificate (No. ZJ20190082) issuance dated 22.07.2019 valid till 21.07.2024 by China Food and Drug Administration.
	GMP status/inspection report of FPP manufacturer to be submitted.	Inspection report for grant of DML has been provided (dated 24.08.2021)
	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (COA)	complied.

<table>
<tr><td></td><td>of the same batch from Drug Substance / API manufacture.</td><td></td></tr>
<tr><td></td><td>Detailed analytical procedures for the testing of drug substance to be provided by Drug Product manufacturer</td><td>complied.</td></tr>
<tr><td></td><td>Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer to be provided</td><td>complied.</td></tr>
<tr><td></td><td>Specifications of primary / secondary reference standard including source and lot number for primary reference standard to be provided</td><td>Firm has submitted copy of CoA of working standard (Escitalopram oxalate, batch no. WS-3621)

For testing of Pharmacopoeial Drug Substance, the use of primary reference standard is recommended, use of working standard to be justified.</td></tr>
<tr><td></td><td>Stability data of Drug Substance has been submitted for 6 months only.</td><td>complied.

Real time stability data submitted for three batches: (3619102201, 3619102202 3619102203) for the period of 24 months at 30°C ± 2°C / 75% ± 5%RH.</td></tr>
<tr><td></td><td>Detailed CDP report to be provided wherein values for f1 and f2 are calculated along with results conclusion.</td><td>Firm has submitted CDP report now Wherein CDP has been performed as follows:
<table>
<tr><td>Feature</td><td>Reference product by M/s PharmEvo</td><td>Product of M/s Akhsah</td></tr>
<tr><td>Brand name</td><td>Estar 10mg tablet</td><td>Expel 10 mg tablet</td></tr>
<tr><td>Batch No.</td><td>1G016</td><td>TB-01-E10</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
The values for f1 and f2 are in the acceptable range.</td></tr>
<tr><td></td><td>Uniformity of dose is not provided in finished product specification and stability studies.</td><td>Provided calculation of uniformity of dose for all three stability batches TB-01-E10, TB-02-E10, TB-03-E10</td></tr>
<tr><td></td><td>Documents for the procurement of API with approval from DRAP is required</td><td>Provided copy of commercial invoice (Invoice# ZHP8220126</td></tr>
</table>

		dated 26th January 2022, with received quantity i.e. 0.3Kg) for the purchase of Escitalopram oxalate from Zhejiang Haisen Pharmaceutical Co Ltd China with attestation of DRAP dated 02/03/2022

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

Registration applications of newly granted DML or New section (Human)
New Section:
M/s Hudson Pharma (Pvt) Limited D-93, North West Industrial zone , Port Qasim Karachi

CLB in its 283rd meeting held on 28th October 2021, has considered and approved the grant of following additional sections/facility:

- **Injectable ampoule BF (Steroid)-New**
- **Capsule Section (General)-New**

386.	Name, address of Applicant / Marketing Authorization Holder	M/s Hudson Pharma (Pvt) Limited D-93, North West Industrial zone , Port Qasim Karachi
	Name, address of Manufacturing site.	M/s Hudson Pharma (Pvt) Limited D-93, North West Industrial zone , Port Qasim Karachi
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27740 (R&I) DRAP, dated 23/09/2022
	Details of fee submitted	PKR 75,000/- dated 22/08/2022
	The proposed proprietary name / brand name	Actonide Suspension for Nebulisation 1mg/2ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 2 ml Respule contains: Budesonide…….1mg
	Pharmaceutical form of applied drug	Suspension for inhalation

	Pharmacotherapeutic Group of (API)	Corticosteroid
	Reference to Finished product specifications	BP specification
	Proposed Pack size	1mg/2ml (2mlx10's)
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA approved Pulmicort Inhalation Suspension 1mg/2ml (Manufacturer: AstraZeneca)
	For generic drugs (me-too status)	Not Available
	GMP status of the Finished product manufacturer	GMP inspection conducted on 07th October 2021 Additional section Injectable ampoule BF (Steroid) approved on 24.11.2021
	Name and address of API manufacturer.	Industriale Chimica S.R.L Via E.H Grieg,13-21047 SARONNO (VA)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, control of excipients, list of reference standard used, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for impurity A, D, K, L & related substances specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 5 years. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (080377, 080488, 080492)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, process validation studies, specifications, analytical procedure and verification studies batch analysis and justification of

		specification, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence was determined against Pulmicort 1mg/2ml inhalation suspension by Astrazeneca (Batch No PBLF) Quality parameters such as identification, Ph, Epimer A and assay were compared against Actonide Suspension for Nebulisation 1mg/2ml (Batch No SB-BU-NU-01)
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Industriale Chimica S.R.L Via E.H Grieg,13-21047 SARONNO (VA)		
API Lot No.	PR182023		
Description of Pack (Container closure system)	LDPE ampoule		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Strength	1mg/2ml		
Batch No.	SB-BU-NU-01	SB-BU-NU-02	SB-BU-NU-03
Batch Size	1000 ampoules	1000 ampoules	1000 ampoules
Manufacturing Date	01-2022	01-2022	01-2022
Date of Initiation	21-01-2022	21-01-2022	21-01-2022
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Brinzoson eye drops (dated 08th October, 2020). Further, the said panel inspection report was discussed in 297th Drug Registration Board meeting held on 12th – 15th January 2021. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Chambers

<table>
<tr><td></td><td></td><td>are controlled and monitored through data logger..
Related manufacturing area, equipment, personnel and utilities are GMP compliant</td></tr>
<tr><td></td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>GMP certificate of Industriale Chimica S.R.L Via E.H Grieg,13-21047 SARONNO (VA) based on inspection conducted on 21.09.2018 (valid till 3 years) by AIFA.</td></tr>
<tr><td></td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Firm has submitted import License No. 0567/19 DRAP dated 21-02-2019 confirming import of 0.39Kg Budesonide micronised from M/s Industriale Chimica S.R.L for Batch No. PR182023
<table>
<tr><td colspan="4">Budesonide</td></tr>
<tr><td>Batch No.</td><td>Date of import</td><td>Invoice No.</td><td>Quantity Import</td></tr>
<tr><td>PR182023</td><td>20-02-2019</td><td>CS-19/01540</td><td>0.390Kg</td></tr>
</table></td></tr>
<tr><td></td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Submitted
Water loss test was also performed for semi permeable container closure system, which was found within acceptable range.</td></tr>
<tr><td></td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td>Submitted</td></tr>
<tr><td></td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Submitted</td></tr>
</table>

Remarks of Evaluator:

Sr.#	Observation	Reply
	Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance / API manufacturer issued by concerned regulatory authority of country of origin to be provided	Firm has referred to notice from EMA regarding MEDICINAL PRODUCTS FOR HUMAN USE DURING THE COVID-19 PANDEMIC wherein it is written that: The validity of GMP certificates for manufacturing sites of active substances and/or finished products located outside the EEA should be extended until the end of 2023 without the need for further action from the holder of the certificate,
	Specifications of primary / secondary reference standard including source and lot number for primary reference standard to be provided	Specifications of Budesonide Working standard (internal code A-3736) from INDUSTRIALE

		CHIMICA Srl Via E.H. Grieg 13, Saronno are provided.
	For testing of Pharmacopoeial Drug Substance, the use of primary reference standard is recommended, justify use of working standard for Budesonide	Budesonide Working Standard (A-3736) is identified by comparison of its IR spectrum with those obtained from Standard supplied by Pharmacopoeia European (batch 4,0, internal code A-3769). The obtained spectra are perfectly identical and superimposable.

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

M/s Caraway Pharmaceuticals, RCCI Rawat, Islamabad.

CLB in its 287th meeting held on 24th June 2022, has considered and approved the renewal of DML of already approved section. Moreover, following amendment has been approved:

Liquid vial section(infusion) changed into syrup on first floor

387.	Name, address of Applicant / Marketing Authorization Holder	M/s Caraway Pharmaceuticals, RCCI Rawat, Islamabad.
	Name, address of Manufacturing site.	M/s Caraway Pharmaceuticals, Plot 12, Street N-3 RCCI Rawat Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27124 dated 20 /09/2022
	Details of fee submitted	PKR 30,000/-: dated 20/09/2022
	The proposed proprietary name / brand name	Licide Syrup 2.5mg/5mL
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5mL contains; Levocetirizine Dihydrochloride ……2.5mg
	Pharmaceutical form of applied drug	Syrup
	Pharmacotherapeutic Group of (API)	Anti-histaminic (Piperazine derivative)
	Reference to Finished product specifications	Innovator's Specs.

	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	XYZAL oral solution 2.5/5mL USFDA Approved.
	For generic drugs (me-too status)	Concidol L Syrup by M/s Convell Laboratories Registration No. 079350
	GMP status of the Finished product manufacturer	Last inspection conducted on 22-02-2022 Syrup section approved on 04.07.2022
	Name and address of API manufacturer.	M/s Metrochem API Private Limited India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Levocetirizine Dihydrochloride is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 25°C ± 2°C / 65% ± 5% RH for 60 months. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(LCZ/A/200801001, LCZ/A/200801002,LCZ/A/200801003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is

		T-Day syrup by GSK Pakistan by performing quality tests (Physical Appearance, Identification pH, Volume & Assay).		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Metrochem API Private Limited India		
API Lot No.		LVHPC20280		
Description of Pack (Container closure system)		Amber color PET bottle (60ml) packed in unit carton (1's)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0,3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		T-031	T-032	T-033
Batch Size		250 Bottles	250 Bottles	250 Bottles
Manufacturing Date		08-2021	08-2021	08-2021
Date of Initiation		04-08-2021	04-08-2021	04-08-2021
No. of Batches		03		
Administrative Portion				
	Reference of previous approval of applications with stability study data of the firm (if any)	Not provided		
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. . L.Dis.No.HMF07-14051/305/2020-TECH-DCA Dated:18.08.2020 issued by Govt of Andhra Pradesh DCA valid up to three years		
	Documents for the procurement of API with approval from DRAP (in case of import).	Levocetirizine Dihydrochloride invoice no. DE/20/104 Dated:31.10.2020 is attached as proof of procurement of API (10Kg) Batch No LVHPC20280 from Metrochem API Pvt. Ltd India.		
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	The firm has submitted Data of stability batches supported by attested respective documents like chromatograms, raw data sheets, COA, summary data sheets etc.		
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted Compliance Record of HPLC software 21CFR & audit trail reports on product testing.		
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).		

Remarks of Evaluator:

Sr.#	Observation	Reply
	Formulation approved in RRA is mentioned as "oral solution" while dosage form mentioned by the firm in instant application is "syrup" hence dosage form should be standardized on line with RRA along with fee.	Firm has revised dosage form as per RRA (from syrup to oral solution) **without fee.**
	Stability data (real time) of Drug Substance has been submitted with 25°C ± 2°C / 65% ± 5% RH condition which is not as per WHO zone IV-A. Submit real time stability study data of drug substance as per zone IV-A or else submit the following as per the decision of 290th meeting of Registration Board: Record of data logger for the storage conditions throughout the transportation. Real term stability studies data of the product for at least 1 year along with degradation studies in the finished pharmaceutical product	Firm has submitted stability data of drug substance as per zone IV-A conditions as follows: Batch No: LVU-P/19001 LVU-P/19002 LVU-P/19003 40°C ± 2°C / 75% ± 5% RH for 36 months 30°C ± 2°C / 65% ± 5% RH for 36months
	Proposed container closure system (PET) suitability testing to be submitted as per pharmacopeia. Moreover, description is required regarding suitability of the container closure system for the storage, transportation (shipping) and use of the FPP (e.g. choice of materials, protection from moisture and light, compatibility of the materials with the FPP)	Firm has submitted suitability testing of PET bottle as per USP general monograph <661> Including thermal analysis, heavy metals testing and IR spectroscopic analysis.
	Documents for the procurement of API with approval from DRAP is required. Only commercial invoices are provided under this section.	Not complied Firm has again submitted invoice no. DE/20/104 Dated:31.10.2020 is attached as proof of procurement of API (10Kg) Batch No LVHPC20280 from Metrochem API Pvt. Ltd India. Approval from DRAP is required.
	For testing of Pharmacopeial Drug Substance, the use of primary reference standard is recommended, justify use of working standard for Levocetirizine Dihydrochloride.	Firm has submitted USP reference standard of Levocetirizine Dihydrochloride 200mg (lot No R170Q0) which is used in API testing and for batch release.
	Compatibility of the Drug Substance(s) with excipients is not provided (mainly alpha tocopherol and mannitol) which are not used in reference product.	Firm has submitted compatibility testing of alpha tocopherol and mannitol with drug substance using HPLC

		method. There was no significant change in % quantity of drug at storage condition 60°C ± 2°C
	Reference of previous approval of applications with stability study data of the firm (if any)	**Not provided**

Decision: Deferred for following observations:

- **DRAP clearance certificate of drug substance (Levocetirizine Dihydrochloride) along with commercial invoice, CoA (from both Drug Substance/Drug Product manufacturer) of relevant batch no. is required**
- **Submission of applicable fee that is Rs. 7,500/- for revision of dosage form (from syrup to oral solution) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021**

Item No. X: Agenda of Evaluator (Dr. Sidra Khalid)

388.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33256 dated 08/12/2021
	Details of fee submitted	PKR 30,000/-: dated 17/11/2021
	The proposed proprietary name / brand name	Nalbim Injection 10mg/ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1ml ampoule contains: Nalbuphine HCl …….10mg
	Pharmaceutical form of applied drug	Clear, colourless liquid free from foreign particles filled in clear glass ampoule USP further packed in secondary carton.
	Pharmacotherapeutic Group of (API)	Morphinan derivatives
	Reference to Finished product specifications	Getz Pharma Specs.
	Proposed Pack size	1ml x 1's, 1ml x 5's & 1ml x 10's
	Proposed unit price	Rs. 100/- (1ml x 1's) Rs. 500/- (1ml x 5's) Rs. 1000/- (1ml x 10's)

	The status in reference regulatory authorities	Nalbuphine HCl Injection 10mg/ml by M/s Hospira, Inc., USA. USFDA Approved.
	For generic drugs (me-too status)	Kinz Injection 10mg/ml by M/s SAMI Pharmaceutical (Pvt.) Ltd, Karachi. (Reg. No. 018686)
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Liquid Injectable (General) section approved.
	Name and address of API manufacturer.	SpecGx LLC 3600 North Second Street St. Louis, Missouri 63147. USA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its Validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Nalbuphine HCl is not present in any pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (0907000789, 0907000790, 0907000791)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Kinz Injection 10mg/ml by M/s SAMI Pharmaceutical

		(Pvt.) Ltd, by performing quality tests (Appearance, Assay, pH and deliverable volume). CDP is not applicable.	
	Analytical method validation/verification of product	Method Validation studies have submitted including system suitability, specificity, linearity, accuracy, precision, robustness, stability of solution and range.	
STABILITY STUDY DATA			
Manufacturer of API	SpecGx LLC 3600 North Second Street St. Louis, Missouri 63147. USA		
API Lot No.	2002000117		
Description of Pack (Container closure system)	Clear glass USP ampoule, packed in unit carton with packaging insert. (1ml x 1's, 1ml x 5's & 1ml x 10's).		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 9 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9 (Months)		
Batch No.	564DS01	565DS02	566DS03
Batch Size	1500 Ampoules	1500 Ampoules	1500 Ampoules
Manufacturing Date	30.11.2020	30.11.2020	30.11.2020
Date of Initiation	21.12.2020	21.12.2020	21.12.2020
No. of Batches	03		
Administrative Portion			
	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine (Ebastine) Tablets 10mg & 20mg on 6th May, 2019. Further, the said panel inspection report was discussed in 289th Drug Registration Board meeting held on 14th – 16th May 2019. The case was approved and the inspection report confirms following points: The HPLC software is 21CFR Compliant as per record available with the firm. Audit trail on the testing reports is available. Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well. Related manufacturing area, equipment, personnel and utilities are GMP compliant.	
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	API manufacturer of Nalbuphine HCl that is SpecGx LLC is USFDA approved source and validity of their site registration is till 31/12/2022. Link for FDA Inspection Classification Database is as follows:	

<table>
<tr><td></td><td></td><td>https://datadashboard.fda.gov/ora/cd/inspections.htm</td></tr>
<tr><td></td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted.
<table>
<tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr>
<tr><td>2002000117</td><td>19027101</td><td>0.5000 Kg</td><td>03-11-2020</td></tr>
</table></td></tr>
<tr><td></td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td></tr>
<tr><td></td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td>Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.</td></tr>
<tr><td></td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).</td></tr>
<tr><td colspan="3">Remarks OF Evaluator:
<table>
<tr><th>S No</th><th>Section #.</th><th>Deficiencies</th><th>Reply</th></tr>
<tr><td></td><td>3.2.S.4.3</td><td>Submit data of verification of analytical procedure of drug substance as per the guidance document approved by Registration Board which specifies that “Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as noncompendial drug substance(s) shall be submitted”</td><td>Analytical Method Verification studies including system suitability, specificity, linearity, repeatability and range performed by the Drug Product manufacturer. Further, with reference to ICH Guidelines “VALIDATION OF ANALYTICAL PROCEDURES: TEXT AND METHODOLOGY Q2 (R1)” it is mentioned in section 4.1.1 Drug Substance “accuracy may be inferred once precision, linearity and specificity have been established”. This is bring to your kind attention that since we have performed method verification studies as per ICH Q2 (R1) therefore,</td></tr>
</table></td></tr>
</table>

			requirement of accuracy is not applicable.
	3.2.S.4.2	Justify how the developed formulation is declared similar in quality with the comparator product since the values of pH (3.00-4.5)are outside the acceptable limit defined by FDA approved innovator product.	This is to inform you that our benchmark innovator product (for both strength) is NUBAIN Injection by M/s Par Pharmaceutical USA, which is USFDA approved product. The pH values as mentioned in prescribing information of NUBAIN Injection range is 3.5 – 3.7 which is target pH value. However, pH ranges as provided by NUBAIN Injection is 3.0 – 4.5 as mentioned in Rx list of NUBAIN Injection and prescribing information of Nalbuphine Injection by M/s Hospira Inc. USA. This is to bring to your kind attention that NUBAIN Solution for Injection as approved by Austrian Agency for Health and Food Safety has mentioned pH value range of 3.0 – 4.0 in their approved prescribing information. This is to bring to your kind attention that Lapainol Solution for Injection as approved by Health Products Regulatory Authority (HPRA) Ireland has mentioned pH value range of 3.0 – 4.2 in their approved prescribing information.
	3.2.P	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance /Active Pharmaceutical Ingredient manufacture	Results of analysis of relevant batch (es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance Active Pharmaceutical Ingredient manufacture is provided

	3.2.S.4	The excipients are different from the reference product justification is needed in this regard	This is to inform you that our benchmark innovator product (for both strength) is NUBAIN Injection by M/s Par Pharmaceutical USA, which is USFDA approved product. We have developed the formulation for our product Nalbim Injection 10mg/ml & Nalbim Injection 20mg/ml by using the same excipients as used in benchmark product.
		The Name of manufacture is mentioned as SpecGx LLC 3600 North Second Street St. Louis, Missouri 63147. USA but on all documents, name is mentioned as Mallinckrodt pharmaceuticals. Provide the relationship.	SpecGx LLC and Mallinckrodt's are same entity. Mallinckrodt's Specialty Generics and API business' changed their legal name to SpecGx LLC in 2017. The manufacturer declares that "The Mallinckrodt logo and trade names will remain on all product labels".

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

389.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33257 dated 08/12/2021

	Details of fee submitted	PKR 30,000/-: dated 08/12/2021
	The proposed proprietary name / brand name	Nalbim Injection 20mg/ml
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1ml ampoule contains: Nalbuphine HCl…….20mg
	Pharmaceutical form of applied drug	Clear, colorless liquid free from foreign particles filled in clear glass ampoule USP further packed in secondary carton.
	Pharmacotherapeutic Group of (API)	Morphinan derivatives
	Reference to Finished product specifications	Getz Pharma Specs.
	Proposed Pack size	1ml x 1's, 1ml x 5's & 1ml x 10's
	Proposed unit price	Rs. 150/- (1ml x 1's) Rs. 750/- (1ml x 5's) Rs. 1500/- (1ml x 10's)
	The status in reference regulatory authorities	Nalbuphine HCl Injection 20mg/ml by M/s Hospira, Inc., USA. USFDA Approved.
	For generic drugs (me-too status)	Kinz Injection 20mg/ml by M/s SAMI Pharmaceutical (Pvt.) Ltd, Karachi. (Reg. No. 018687)
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Liquid Injectable (General) section approved.
	Name and address of API manufacturer.	SpecGx LLC 3600 North Second Street St. Louis, Missouri 63147. USA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its Validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Nalbuphine HCl is not present in any pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container

		closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (0907000789, 0907000790, 0907000791)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Kinz Injection 20mg/ml by M/s SAMI Pharmaceutical (Pvt.) Ltd, by performing quality tests (Appearance, Assay, pH and deliverable volume). CDP is not applicable.
	Analytical method validation/verification of product	Method Validation studies have submitted including system suitability, specificity, linearity, accuracy, precision, robustness, stability of solution and range.

STABILITY STUDY DATA			
Manufacturer of API	SpecGx LLC 3600 North Second Street St. Louis, Missouri 63147. USA		
API Lot No.	2002000117		
Description of Pack (Container closure system)	Clear glass USP ampoule, packed in unit carton with packaging insert. (1ml x 1's, 1ml x 5's & 1ml x 10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 9 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9 (Months)		
Batch No.	565DS01	565DS02	565DS03
Batch Size	1500 Ampoules	1500 Ampoules	1500 Ampoules
Manufacturing Date	30.11.2020	30.11.2020	30.11.2020
Date of Initiation	21.12.2020	21.12.2020	21.12.2020
No. of Batches	03		

Administrative Portion		
	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product for Estine (Ebastine) Tablets 20mg & 20mg on 6th May, 2019. Further, the said panel

<table>
<tr><td></td><td></td><td>inspection report was discussed in 289th Drug Registration Board meeting held on 14th – 16th May 2019. The case was approved and the inspection report confirms following points:
The HPLC software is 21CFR Compliant as per record available with the firm.
Audit trail on the testing reports is available.
Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
Related manufacturing area, equipment, personnel and utilities are GMP compliant.</td></tr>
<tr><td></td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>API manufacturer of Nalbuphine HCl that is SpecGx LLC is a USFDA approved source and validity of their site registration is till 31/12/2022.

Link for FDA Inspection Classification Database is as follows:

https://datadashboard.fda.gov/ora/cd/inspections.htm</td></tr>
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<tr><td></td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td>Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.</td></tr>
<tr><td></td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).</td></tr>
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<table>
<tr><th>S No</th><th>Section #.</th><th>Deficiencies</th><th>Reply</th></tr>
<tr><td></td><td>3.2.S.4.3</td><td>Submit data of verification of analytical procedure of drug substance as per the guidance document approved by Registration Board which specifies that “Analytical Method Verification studies including</td><td>Analytical Method Verification studies including system suitability, specificity, linearity, repeatability and range performed by the Drug Product manufacturer.</td></tr>
</table></td></tr>
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		specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as noncompendial drug substance(s) shall be submitted"	Further, with reference to ICH Guidelines "VALIDATION OF ANALYTICAL PROCEDURES: TEXT AND METHODOLOGY Q2 (R1)" it is mentioned in section 4.1.1 Drug Substance "accuracy may be inferred once precision, linearity and specificity have been established". This is bring to your kind attention that since we have performed method verification studies as per ICH Q2 (R1) therefore, requirement of accuracy is not applicable.
	3.2.S.4.2	Justify how the developed formulation is declared similar in quality with the comparator product since the values of pH (3.00-4.5) are outside the acceptable limit defined by FDA approved innovator product.	This is to inform you that our benchmark innovator product (for both strength) is NUBAIN Injection by M/s Par Pharmaceutical USA, which is USFDA approved product. The pH values as mentioned in prescribing information of NUBAIN Injection range is 3.5 – 3.7 which is target pH value. However, pH ranges as provided by NUBAIN Injection is 3.0 – 4.5 as mentioned in Rx list of NUBAIN Injection and prescribing information of Nalbuphine Injection by M/s Hospira Inc. USA. This is to bring to your kind attention that NUBAIN Solution for Injection as approved by Austrian Agency for Health and Food Safety has mentioned pH value range of 3.0 – 4.0 in their approved prescribing information. This is to bring to your kind attention that Lapainol Solution for Injection as approved by Health Products Regulatory Authority (HPRA) Ireland

			has mentioned pH value range of 3.0 – 4.2 in their approved prescribing information.
	3.2.P	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance /Active Pharmaceutical Ingredient manufacture	Results of analysis of relevant batch (es) of Drug Substance performed by Drug Product manufacturer used during product deve lopment and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance Active Pharmaceutical Ingredient manufacture is provided
	3.2.S.4	The excipients are different from the reference product justification is needed in this regard	This is to inform you that our benchmark innovator product (for both strength) is NUBAIN Injection by M/s Par Pharmaceutical USA, which is USFDA approved product. We have developed the formulation for our product Nalbim Injection 10mg/ml & Nalbim Injection 20mg/ml by using the same excipients as used in benchmark product.
		The Name of manufacture is mentioned as SpecGx LLC 3600 North Second Street St. Louis, Missouri 63147. USA but on all documents, name is mentioned as Mallinckrodt pharmaceuticals. Provide the relationship.	SpecGx LLC and Mallinckrodt's are same entity. Mallinckrodt's Specialty Generics and API business' changed their legal name to SpecGx LLC in 2017. The manufacturer declares that "The Mallinckrodt logo and trade names will remain on all product labels".

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

Priority Registration applications of Export Facilitation

Assistant Director PR-I/EFD vide letter NO.1-6/2019-PR-I (EFD) dated 18-06-2021 has informed that Reg. Board in its 263rd meeting held on 29-30th November 2016 decided to grant registration on priority basis to the pharmaceutical firms/manufacturers who have shown appreciable performance in export of pharmaceuticals. The Board further decided to consider one molecule for each 50,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year. In compliance to the aforementioned decision of the Board, the following firms have achieved the benchmark of USD 656,218.90/- during FY 2020-21. Following applications submitted by the firms for priority consideration/ evaluation in lieu of export facilitation are submitted before the Board for its consideration please:

390.	Name and address of manufacturer / Applicant	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Redupres-S 49/51 mg Tablet
	Composition	Each film coated tablet contains: Sacubitril……..48.6 mg Valsartan…..…51.4 mg (as sacubitril valsartan sodium salt complex).
	Diary No. Date of R& I & fee	Dy. No 24324 dated 13-12-2017 Rs.50,000/- Dated 13-12-2017
	Pharmacological Group	Angiotensin II receptor blocker
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's, 14"s As per SRO
	Approval status of product in Reference Regulator Authorities	Entresto™ (sacubitril/valsartan) Tablets, 97/103, 49/51, and 24/26 mg (USFDA)
	Me-too status	NA
	GMP status	03.08.2017, The firm is operating at an acceptable level of compliance of GMP requirements at the time of inspection.
	Remarks of the Evaluator	Assay is by HPLC method The firm didn't provide detailed dissolution method, 2ndly It shall justify the dissolution specification NLT 80%(Q) after 45 minutes, since the USFDA review document of the innovator product specify dissolution specifications i.e NLT (Q) after 25 minutes. Revise the dissolution specifications to NLT (Q after 25 minutes as per the reference product and as per the decision of 293rd meeting of Registration Board. GMP certificate by API manufacturer Not provided by Guangdong Province. But the city Reference and working standard missing

STABILITY STUDY DATA	
Drug	Redupres-S 49/51 mg Tablet

Name of Manufacturer	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi		
Manufacturer of API	sacubitril/valsartan: M/s Zhuhai Rundu Pharmaceutical Co., Ltd, China Address: No 6,North airport Road Sanzao Town, Jinwan District Zhuhai, Guangdong province China		
API Lot No.	sacubitril/valsartan: 57318060103		
Description of Pack (Container closure system)	As per SRO		
Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%		
Time Period	Real time: 6 months Accelerated:6 months		
Frequency	Accelerated: 0,1,2,3,4, 6 (month) Real Time: 0,3,6 (month)		
Batch No.	375DS01	375DS02	375DS03
Batch Size	1500	1500	1500
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	14-10-2020	14-10-2020	14-10-2020
No. of Batches	03		
Date of Submission	2/June/2021 (15245)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr. No.	Documents to Be Provided	Status
	Reference of previous approval of applications with stability study data of the firm	A panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting. Audit trail on the testing reports cannot be made as audit trail was not activated.
	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	For Sacubitral/Valsartin: The firm has submitted COA from both API Zhuhai Rundu Pharmaceutical Co. Ltd China No.6, North Airport Road, Sanzao Town, Jinwan District, Guangdong, China and FPP manufacturer
	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Yes
	Stability study data of API from API manufacturer	Provided (for zone IV-B)
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Sacubitril/Valsartan: The firm has provided copy of Certificate of GMP compliance issued to M/s Zhuhai food and Drug administration, valid Up to 21-12-2021. Not provided by Guangdong Province.

<table>
<tr><td></td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Sacubitril/Valsartan:
Copy of commercial invoice has been submitted issued by ADC, Karachi DRAP.
Import quantity: 3.3 kg
Impurities: Provided
Address of Exporter (Head office): M/s Zhuhai Rundu Pharmaceutical Co. Ltd China No.6, North Airport Road,Sanzao Town, Jinwan District, Guangdong, China</td></tr>
<tr><td></td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td></td><td>Method used for analysis of FPP</td><td>Yes (same as API manufacturer)</td></tr>
<tr><td></td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA
(Formulation of applied drug product is qualitatively similar to that of innovator Brand)</td></tr>
<tr><td></td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted photocopy of Batch Manufacturing Orders of following 03 Batches:
<table>
<tr><td>Batch No.</td><td>Batch Size</td><td>Mfg. Date</td></tr>
<tr><td>375DS01</td><td>1500</td><td>10-2020</td></tr>
<tr><td>375DS02</td><td>1500</td><td>10-2020</td></tr>
<tr><td>375DS03</td><td>1500</td><td>10-2020</td></tr>
</table></td></tr>
<tr><td></td><td>Record of comparative dissolution data (where applicable)</td><td>Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “Uperio 100 mg Tablets” The details are as follows:
<table>
<tr><td colspan="2">Reference product</td><td colspan="2">Test Product</td></tr>
<tr><td>Product name</td><td>Uperio 100 mg Tablets</td><td>Product name</td><td>Sacubitril/Valsartan tablet</td></tr>
<tr><td>Batch #</td><td>TEJ85</td><td>Batch #</td><td>375DS01</td></tr>
<tr><td>Mfg date</td><td>05-2019</td><td>Mfg date</td><td>10-2020</td></tr>
</table>
Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer</td></tr>
<tr><td></td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Yes</td></tr>
</table>

	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

REMARKS OF EVALUATOR

Sr. No.	Observations/Documents Required	Status of Document/Justifications
1.	The firm didn't provide detailed dissolution method, 2ndly It shall justify the dissolution specification NLT 80% (Q) after 45 minutes, since the USFDA review document of the innovator product specify dissolution specifications i.e. NLT (Q) after 25 minutes. Revise the dissolution specifications to NLT (Q) after 25 minutes as per the reference product as per the decision of 293rd meeting of Registration Board.	The revise Finished Product Specification as per the reference product is submitted without submission of any fee
2.	Submitted GMP Certificate of supplier of API has been issued by M/s. Zhuhai Food and Drug Administration, instead of Provincial Drug Regulatory Authority. Clarification is required for this regard.	The valid GMP Certificate of API Manufacturer M/s. Zhuhai Rundu Pharmaceutical Co. Ltd., (Vali till 13-11-2021) issued by the China Food and Drug Administration is provided
3.	Firm has not submitted documents for procurement of reference and impurity standards.	The documents for procurement of reference and impurity standards is provided
4.	Valid DML of FPP should be provided as provided one is expired.	The valid DML # 000105 (by way of formulation) renewed w.e.f. 12-07-2019 and valid upto 11-07-2024 is attached
	In Reference of previous approval of application with stability study data firm provides the panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting but the Audit trail of the testing reports cannot be made as audit trail was not activated. So, on that base exemption could be granted.	We in this regard would like to state that our latest GMP Inspection report carried out by the DRAP Panel for our new drug "Novasept 7.1% Gel" on 27th October 2020 (Report enclosed herewith) confirms the availability of audit trials on the testing report. Copy of Inspection Report of Novasept Gel is product

<table>
<tr><td></td><td>Comparative Dissolution Profile.</td><td>We are also enclosing Firm has submitted Comparative dissolution study of their product with Innovator's Brand "Uperio 100 mg Tablets" The details are as follows:
<table>
<tr><td colspan="2">Reference product</td><td colspan="2">Test Product</td></tr>
<tr><td>Product name</td><td>Uperio 100 mg Tablets</td><td>Product name</td><td>Sacubitril/Valsartan tablet</td></tr>
<tr><td>Batch #</td><td>TEJ85</td><td>Batch #</td><td>375DS01</td></tr>
<tr><td>Mfg date</td><td>05-2019</td><td>Mfg date</td><td>10-2020</td></tr>
</table>
Comparative dissolution studies have been done in 3 mediums</td></tr>
<tr><td colspan="3">Decision of 316th meeting: Deferred for consideration on turn as product development data was submitted on 11/06/2021</td></tr>
<tr><td colspan="3">Firm has submitted fee of Rs 7500/- dated 31.10.2022 to revise Finished Product Specification as per the reference product.</td></tr>
<tr><td colspan="3">Decision: Approved with innovator's specifications.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.</td></tr>
<tr><td rowspan="11">391.</td><td>Name and address of manufacturer / Applicant</td><td>M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi</td></tr>
<tr><td>Brand Name +Dosage Form + Strength</td><td>Redupres-S 24/26 mg Tablet</td></tr>
<tr><td>Composition</td><td>Each film coated tablet contains:
Sacubitril……..24.3mg
Valsartan…..…25.7 mg
(as sacubitril valsartan sodium salt complex).</td></tr>
<tr><td>Diary No. Date of R& I & fee</td><td>Dy. No 24322 dated 13-12-2017 Rs.50,000/- (#0709180) Dated 13-12-2017</td></tr>
<tr><td>Pharmacological Group</td><td>Angiotensin II receptor blocker</td></tr>
<tr><td>Type of Form</td><td>Form 5</td></tr>
<tr><td>Finished product Specifications</td><td>Manufacturer specifications</td></tr>
<tr><td>Pack size & Demanded Price</td><td>10's, 14"s As per SRO</td></tr>
<tr><td>Approval status of product in Reference Regulator Authorities</td><td>Entresto™ (sacubitril/valsartan) Tablets, 97/103, 49/51, and 24/26 mg (USFDA)</td></tr>
<tr><td>Me-too status</td><td>NA</td></tr>
<tr><td>GMP status</td><td>03.08.2017, The firm is operating at an acceptable level of compliance of GMP requirements at the time of inspection.</td></tr>
</table>

	Remarks of the Evaluator	Assay is by HPLC method The firm didn't provide detailed dissolution method, 2ndly It shall justify the dissolution specification NLT 80%(Q) after 45 minutes, since the USFDA review document of the innovator product specify dissolution specifications i.e NLT (Q) after 25 minutes. Revise the dissolution specifications to NLT (Q after 25 minutes as per the reference product and as per the decision of 293rd meeting of Registration Board. GMP certificate by API manufacturer Not provided by Guangdong Province. But the city Reference and working standard missing Certificate for NMDA provided

STABILITY STUDY DATA			
Drug	Redupres-S 24/26 mg Tablet		
Name of Manufacturer	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi		
Manufacturer of API	Sacubitril/valsartan: M/s Zhuhai Rundu Pharmaceutical Co., Ltd, China Address: No 6, North airport Road Sanzao Town, Jinwan District Zhuhai, Guangdong province China		
API Lot No.	sacubitril/valsartan: 57318060103		
Description of Pack (Container closure system)	As per SRO		
Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%		
Time Period	Real time: 6 months Accelerated:6 months		
Frequency	Accelerated: 0,1,2,3,4, 6 (month) Real Time: 0,3,6 (month)		
Batch No.	374DS01	374DS02	374DS03
Batch Size	1500	1500	1500
Manufacturing Date	10-2020	10-2020	10-2020
Date of Initiation	14-10-2020	14-10-2020	14-10-2020
No. of Batches	03		
Date of Submission	28/5/2021 (14567)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
Sr. No.	Documents to Be Provided	Status
	Reference of previous approval of applications with stability study data of the firm	A panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting.

<table>
<tr><td></td><td>Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.</td><td>For Sacubitral/Valsartin:
The firm has submitted COA from both API Zhuhai Rundu Pharmaceutical Co. Ltd China No.6, North Airport Road, Sanzao Town, Jinwan District, Guangdong, China and FPP manufacturer</td></tr>
<tr><td></td><td>Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer</td><td>Yes</td></tr>
<tr><td></td><td>Stability study data of API from API manufacturer</td><td>Provided (for zone IV-B)</td></tr>
<tr><td></td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Sacubitril/Valsartan:
The firm has provided copy of Certificate (Certificate# …) of GMP compliance issued to M/s Zhuhai food and Drug administration, valid Up to 21-12-2021.
Not provided by Guangdong Province.</td></tr>
<tr><td></td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>Sacubitril/Valsartan:
Copy of commercial invoice has been submitted issued by ADC, Karachi DRAP.
Import quantity: 3.3 kg
Impurities: Provided
Address of Exporter (Head office): M/s Zhuhai Rundu Pharmaceutical Co. Ltd China No.6, North Airport Road,Sanzao Town, Jinwan District, Guangdong, China</td></tr>
<tr><td></td><td>Protocols followed for conduction of stability study</td><td>Yes</td></tr>
<tr><td></td><td>Method used for analysis of FPP</td><td>Yes (same as API manufacturer)</td></tr>
<tr><td></td><td>Drug-excipients compatibility studies (where applicable)</td><td>NA
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<tr><td>374DS03</td><td>1500</td><td>10-2020</td></tr>
</table></td></tr>
<tr><td></td><td>Record of comparative dissolution data (where applicable)</td><td>No
Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “Uperio 100 mg Tablets” The details are as follows:</td></tr>
</table>

		<table><tr><td colspan="2">Reference product</td><td colspan="2">Test Product</td></tr><tr><td>Product name</td><td>Uperio 100 mg Tablets</td><td>Product name</td><td>Sacubitril/Valsartan tablet</td></tr><tr><td>Batch #</td><td>TEJ85</td><td>Batch #</td><td>375DS01</td></tr><tr><td>Mfg date</td><td>05-2019</td><td>Mfg date</td><td>10-2020</td></tr></table> Comparative dissolution studies have been performed in following mediums: 1. pH 1.2 HCl buffer 2. pH 4.5 Acetate buffer 3. pH 6.8 Phosphate buffer Comparative dissolution studies for other strengths not performed. It has been performed with competitor product Uperio 100 mg by Novartis for higher strength i.e. Sita/Met XR 100/1000 mg as formulation is dose proportional)
	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Yes
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	No
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	No

REMARKS OF EVALUATOR

Sr. No.	Observations/Documents Required	Status of Document/Justifications
1.	The firm didn't provide detailed dissolution method, 2ndly It shall justify the dissolution specification NLT 80% (Q) after 45 minutes, since the USFDA review document of the innovator product specify dissolution specifications i.e. NLT (Q) after 25 minutes. Revise the dissolution specifications to NLT (Q) after 25 minutes as per the reference product as per the decision of 293rd meeting of Registration Board.	The revise Finished Product Specification as per the reference product is submitted without submission of any fee
2.	Submitted GMP Certificate of supplier of API has been issued by M/s. Zhuhai Food and Drug Administration, instead of Provincial Drug Regulatory Authority. Clarification is required for this regard.	The valid GMP Certificate of API Manufacturer M/s. Zhuhai Rundu Pharmaceutical Co. Ltd., (Vali till 13-11-2021) issued by the China Food and Drug Administration is provided

<table>
<tr><td>3.</td><td>Firm has not submitted documents for procurement of reference and impurity standards.</td><td>The documents for procurement of reference and impurity standards is provided</td></tr>
<tr><td>4.</td><td>Valid DML of FPP should be provided as provided one is expired.</td><td>The valid DML # 000105 (by way of formulation) renewed w.e.f. 12-07-2019 and valid upto 11-07-2024 is attached</td></tr>
<tr><td></td><td>In Reference of previous approval of application with stability study data firm provides the panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting but the Audit trail of the testing reports cannot be made as audit trail was not activated. So, on that base exemption could be granted.</td><td>We in this regard would like to state that our latest GMP Inspection report carried out by the DRAP Panel for our new drug “Novasept 7.1% Gel” on 27th October 2020 (Report enclosed herewith) confirms the availability of audit trials on the testing report. Copy of Inspection Report of Novasept Gel is product</td></tr>
<tr><td></td><td>Comparative Dissolution Profile.</td><td>We are also enclosing Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “Uperio 100 mg Tablets” The details are as follows:
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<tr><td>Product name</td><td>Uperio 100 mg Tablets</td><td>Product name</td><td>Sacubitril/Valsartan tablet</td></tr>
<tr><td>Batch #</td><td>TEJ85</td><td>Batch #</td><td>375DS01</td></tr>
<tr><td>Mfg date</td><td>05-2019</td><td>Mfg date</td><td>10-2020</td></tr>
</table>
Comparative dissolution studies have been done in 3 mediums</td></tr>
</table>

Decision of 316th meeting: Deferred for consideration on turn as product development data was submitted on 11/06/2021

Firm has submitted fee of Rs 7500/- dated 31.10.2022 to revise Finished Product Specification as per the reference product

Decision: Approved with innovator’sspecifcations.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.

392.	Name and address of manufacturer / Applicant	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Redupres-S 97/103 mg Tablet

	Composition	Each film coated tablet contains: Sacubitril……..97.2 mg Valsartan…..…102.8 mg (as sacubitril valsartan sodium salt complex)
	Diary No. Date of R& I & fee	Dy. No 24322 dated 13-12-2017 Rs.50,000/-(#0709182) Dated 13-12-2017
	Pharmacological Group	Angiotensin II receptor blocker
	Type of Form	Form 5
	Finished product Specifications	Manufacturer specifications
	Pack size & Demanded Price	10's, 14"s As per SRO
	Approval status of product in Reference Regulator Authorities	Entresto™ (sacubitril/valsartan) Tablets, 97/103, 49/51, and 24/26 mg (USFDA)
	Me-too status	NA
	GMP status	03.08.2017, The firm is operating at an acceptable level of compliance of GMP requirements at the time of inspection.
	Remarks of the Evaluator	Assay of ……..is by HPLC method The firm didn't provide detailed dissolution method, 2ndly It shall justify the dissolution specification NLT 80%(Q) after 45 minutes, since the USFDA review document of the innovator product specify dissolution specifications i.e NLT (Q) after 25 minutes. Revise the dissolution specifications to NLT (Q after 25 minutes as per the reference product and as per the decision of 293rd meeting of Registration Board. GMP certificate by API manufacturer Not provided by Guangdong Province. But the city Reference and working standard missing Certificate for NMDA provided

STABILITY STUDY DATA	
Drug	Redupres-S 97/103 mg Tablet
Name of Manufacturer	M/s. Nabiqasim Industries (Pvt). Ltd., 17/24, Korangi Industrial Area, Karachi
Manufacturer of API	sacubitril/valsartan: M/s Zhuhai Rundu Pharmaceutical Co., Ltd, China Address: No 6, North airport Road Sanzao Town, Jinwan District Zhuhai, Guangdong province China
API Lot No.	sacubitril/valsartan: 57318060103
Description of Pack (Container closure system)	As per SRO
Stability Storage Condition	Real time: 30°C ± 2° C / 75% ± 5% RH Accelerated: 40 °C ± 2 °C/75% ± 5%
Time Period	Real time: 6 months Accelerated:6 months

Frequency		Accelerated: 0,1,2,3,4, 6 (month) Real Time: 0,3,6 (month)	
Batch No.		376DS01	376DS02	376DS03
Batch Size		1500	1500	1500
Manufacturing Date		10-2020	10-2020	10-2020
Date of Initiation		14-10-2020	14-10-2020	14-10-2020
No. of Batches		03		
Date of Submission		11 June 2021 (11251)		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT			
Sr. No.	Documents to Be Provided		Status
	Reference of previous approval of applications with stability study data of the firm		A panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting.
	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.		For Sacubitral/Valsartin: The firm has submitted COA from both API Zhuhai Rundu Pharmaceutical Co. Ltd China No.6, North Airport Road, Sanzao Town, Jinwan District, Guangdong, China and FPP manufacturer
	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer		Yes
	Stability study data of API from API manufacturer		Provided (for zone IV-B)
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.		Sacubitril/Valsartan: The firm has provided copy of Certificate (Certificate# …) of GMP compliance issued to M/s Zhuhai food and Drug administration, valid Up to 21-12-2021. Not provided by Guangdong Province.
	Documents for the procurement of API with approval from DRAP (in case of import).		Sacubitril/Valsartan: Copy of commercial invoice has been submitted issued by ADC, Karachi DRAP. Import quantity: 3.3 kg Impurities: Provided Address of Exporter (Head office): M/s Zhuhai Rundu Pharmaceutical Co. Ltd China No.6, North Airport Road,Sanzao Town, Jinwan District, Guangdong, China
	Protocols followed for conduction of stability study		Yes
	Method used for analysis of FPP		Yes (same as API manufacturer)
	Drug-excipients compatibility studies (where applicable)		NA (Formulation of applied drug product is qualitatively similar to that of innovator Brand)

<table>
<tr><td></td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted photocopy of Batch Manufacturing Orders of following 03 Batches:<table><tr><td>Batch No.</td><td>Batch Size</td><td>Mfg. Date</td></tr><tr><td>376DS01</td><td>1500</td><td>10-2020</td></tr><tr><td>376DS02</td><td>1500</td><td>10-2020</td></tr><tr><td>376DS03</td><td>1500</td><td>10-2020</td></tr></table></td></tr>
<tr><td></td><td>Record of comparative dissolution data (where applicable)</td><td>No
Firm has submitted Comparative dissolution study of their product with Innovator’s Brand “Uperio 100 mg Tablets” The details are as follows:<table><tr><td colspan="2">Reference product</td><td colspan="2">Test Product</td></tr><tr><td>Product name</td><td>Uperio 100 mg Tablets</td><td>Product name</td><td>Sacubitril/Valsartan tablet</td></tr><tr><td>Batch #</td><td>TEJ85</td><td>Batch #</td><td>375DS01</td></tr><tr><td>Mfg date</td><td>05-2019</td><td>Mfg date</td><td>10-2020</td></tr></table>Comparative dissolution studies have been performed in following mediums:
1. pH 1.2 HCl buffer
2. pH 4.5 Acetate buffer
3. pH 6.8 Phosphate buffer
Comparative dissolution studies for other strengths not performed. It has been performed with competitor product Uperio 100 mg by Novartis for higher strength i.e. Sita/Met XR 100/1000 mg as formulation is dose proportional)</td></tr>
<tr><td></td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Yes</td></tr>
<tr><td></td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>No</td></tr>
<tr><td></td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>No</td></tr>
</table>

REMARKS OF EVALUATOR

Sr. No.	Observations/Documents Required	Status of Document/Justifications
1.	The firm didn't provide detailed dissolution method, 2ndly It shall justify the dissolution specification NLT 80% (Q) after 45 minutes, since the USFDA review document of the innovator product specify dissolution specifications i.e. NLT (Q) after 25 minutes. Revise the dissolution specifications to NLT (Q) after 25 minutes as per the reference product as per the decision of 293rd meeting of Registration Board.	The revise Finished Product Specification as per the reference product is submitted without submission of any fee
2.	Submitted GMP Certificate of supplier of API has been issued by M/s. Zhuhai Food and Drug Administration, instead of Provincial Drug Regulatory Authority. Clarification is required for this regard.	The valid GMP Certificate of API Manufacturer M/s. Zhuhai Rundu Pharmaceutical Co. Ltd., (Vali till 13-11-2021) issued by the China Food and Drug Administration is provided
3.	Firm has not submitted documents for procurement of reference and impurity standards.	The documents for procurement of reference and impurity standards is provided
4.	Valid DML of FPP should be provided as provided one is expired.	The valid DML # 000105 (by way of formulation) renewed w.e.f. 12-07-2019 and valid upto 11-07-2024 is attached
	In Reference of previous approval of application with stability study data firm provides the panel inspection of Sofosbuvir 400 mg tablet conducted on 26th October 2020 and approved in 297 meeting but the Audit trail of the testing reports cannot be made as audit trail was not activated. So, on that base exemption could be granted.	We in this regard would like to state that our latest GMP Inspection report carried out by the DRAP Panel for our new drug "Novasept 7.1% Gel" on 27th October 2020 (Report enclosed herewith) confirms the availability of audit trials on the testing report. Copy of Inspection Report of Novasept Gel is product

<table>
<tr><td></td><td>Comparative Dissolution Profile.</td><td>We are also enclosing Firm has submitted Comparative dissolution study of their product with Innovator's Brand "Uperio 100 mg Tablets" The details are as follows:
<table>
<tr><td colspan="2">Reference product</td><td colspan="2">Test Product</td></tr>
<tr><td>Product name</td><td>Uperio 100 mg Tablets</td><td>Product name</td><td>Sacubitril/Valsartan tablet</td></tr>
<tr><td>Batch #</td><td>TEJ85</td><td>Batch #</td><td>375DS01</td></tr>
<tr><td>Mfg date</td><td>05-2019</td><td>Mfg date</td><td>10-2020</td></tr>
</table>
Comparative dissolution studies have been done in 3 mediums</td></tr>
<tr><td colspan="3">Decision of 316th meeting: Deferred for consideration on turn as product development data was submitted on 11/06/2021</td></tr>
<tr><td colspan="3">Firm has submitted fee of Rs 7500/- dated 31.10.2022 to revise Finished Product Specification as per the
reference product</td></tr>
<tr><td colspan="3">Decision: Approved with innovator's specifcations.
Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.</td></tr>
</table>

Case no. 02 Registration applications of drugs for which stability study data is submitted
Registration applications for Form 5F

a) Form 5F Import (Human)

393.	Name, address of Applicant / Importer	M/s Al-Habib Pharmaceuticals, Plot #81, block B, SMCHS, Karachi.
	Details of Drug Sale License of importer	DSL No.: 1245 Address:Al- Habib Pharmaceuticals, 81-B, block B, SMCHS, Karachi. Godown: 1. Plot No. 10 sector 25 KIA, Karachi 2. HT-8, Landhi Industrial Area, Karachi Validity: 18/05/2022 Status: Drug License by way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Laboratories IMA S.A.I.C, Palpa 2862, Ciudad Autonoma de Buenos Aires, Argentina.

	Name, address of manufacturer(s)	M/s Laboratorios IMA S.A.I.C, Palpa 2862, Ciudad Autonoma de Buenos Aires, Argentina.
	Name of exporting country	Argentina
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	CoPP: Original legalized CoPP (certificate No. 191106) valid till 30-10-2021 issued by National Institute of Drugs, Argentina. The applied product is available for free sale in exporting country. The facilities and operations conform to WHO-GMP.
	Details of letter of authorization / sole agency agreement	Notarized copy of sole agency agreement is submitted whereby M/s Laboratorios IMA S.A.I.C, authorizes M/s Al-Habib Pharmaceuticals to Import and commercialize different products including Gemcitabine 1000mg injection.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No.22751: 20-08-2021
	Details of fee submitted	PKR 100,000 Dated: 29-03-2021 Differential fee : PKR 50,000 Dated : 05-07-2021
	The proposed proprietary name / brand name	GEMSTAR 200 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Gemcitabine HCl ……. 200 mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Anti-Cancer (Nucleoside) (L01BC05)
	Reference to Finished product specifications	USP
	Proposed Pack size	1 Vial

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Gemzar® 200 mg injection (USFDA Approved) by Eli Lilly
	For generic drugs (me-too status)	Gemzar® 200 mg injection by Eli Lilly Pakistan (PvtP Ltd
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Hetero Labs Limited Survey.No.10, I.D.A., Gaddapotharam Village, Jinnaram Mandal, Medak District, Andhra Pradesh, INDIA
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 25°C ± 2°C. The stability study data is till 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established against the reference product Gemzar® 200mg injection by Eli Lilly

	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type I, amber glass vial 50 ml Bromobutyl elastomeric stopper. Aluminum capsule with flip off closure.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches 24 months real time stability data at 30°C ± 2°C / 65% ± 5%RH of 03 batches 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 03 batches

Evaluation by PEC:

S No	Section #.	Deficiencies	Response
	1.33	Importer shall provide valid Certificate of Pharmaceutical Product (CoPP) / Free Sale certificate issued by relevant regulatory authority in the country of origin and name of exporting country.	Original legalized CoPP (certificate No. 191106) valid till 30-10-2021 issued by National Institute of Drugs, Argentina. The applied product is available for free sale in exporting country. The facilities and operations conform to WHO-GMP. Firm submitted that "This get expired during its period in R& I that's why as per rule it will be considered as valid"
	1.33	The GMp of shanghai acebright pharma co ltd. China is provided as API manufacture but at some place Hetero Labs Limited Survey.No.10, I.D.A., Gaddapotharam Village, Jinnaram Mandal, Medak District, Andhra Pradesh, INDIA is mentioned as API manufacturer clarification is needed in this regard.	Hetero Labs Limited Survey.No.10, I.D.A., Gaddapotharam Village, Jinnaram Mandal, Medak District, Andhra Pradesh, INDIA is API manufacturer, its GMP is provided
	1.33	The GMP certificate of Laboratories IMA SAIC Argentina issued by National administration of drug, food and medical devices (ANMAT)is valid till 2 April 2021. Provides Valid GMP	The GMP certificate of Laboratories IMA SAIC Argentina issued by National administration of drug, food and medical devices (ANMAT) valid till 3 April 2022 is provided
	2.3.S	On API stability both IMA lab and hetro lab is mentioned justify	No justification is given

Decision 321st meeting: Clarification regarding the site wherein stability studies of drug substance have been performed, since in submitted stability sheets both IMA lab and Hetro lab is mentioned.

REMARKS OF EVALUATOR:

Firm has submitted clarification that Finished product manufacturer is IMA lab that's why they have mentioned their name on every page of dossier , whereas the API manufacturer is Hetro lab and they have performed the stability studies at their own site.

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

394.	Name, address of Applicant / Importer	M/s Al-Habib Pharmaceuticals, Plot #81, block B, SMCHS, Karachi.
	Details of Drug Sale License of importer	DSL No.: 1245 Address: Al-Habib Pharmaceuticals, 81-B, block B, SMCHS, Karachi. Godown: 1. Plot No. 10 sector 25 KIA, Karachi 2. HT-8, Landhi Industrial Area, Karachi Validity: 18/05/2022 Status: Drug License by way of wholesale
	Name and address of marketing authorization holder (abroad)	M/s Laboratories IMA S.A.I.C, Palpa 2862, Ciudad Autonoma de Buenos Aires, Argentina.
	Name, address of manufacturer(s)	M/s Laboratories IMA S.A.I.C, Palpa 2862, Ciudad Autonoma de Buenos Aires, Argentina.
	Name of exporting country	Argentina
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	COPP: Original legalized CoPP (certificate No. 191106) valid till 30-10-2021 issued by National Institute of Drugs, Argentina. The applied product is available for free sale in exporting country. The facilities and operations conform to WHO-GMP.
	Details of letter of authorization / sole agency agreement	Notarized copy of sole agency agreement is submitted whereby M/s Laboratories IMA S.A.I.C, authorizes M/s Al-Habib Pharmaceuticals to Import and commercialize different products including Gemcitabine 200 mg injection.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales

	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 22752 Dated: 20-08-2021
	Details of fee submitted	PKR 100,000 Dated: 29-03-2021 Differential fee: PKR 50,000 Dated : 05-07-2021 (#98092840732), 100000 PKR, (#1954777) dated 29-03-2021
	The proposed proprietary name / brand name	GEMSTAR 1000 mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Gemcitabine HCl (as free base) ……. 1000 mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Anti-Cancer (Nucleoside) (L01BC05)
	Reference to Finished product specifications	USP
	Proposed Pack size	Type I amber glass 14 ml, 1 Vial
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Gemzar® 1000mg injection (USFDA Approved) by Eli Lilly
	For generic drugs (me-too status)	Gemzar® 100mg injection by Eli Lilly Pakistan (Pvt) Ltd
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Hetero Labs Limited Survey.No.10, I.D.A., Gaddapotharam Village, Jinnaram Mandal, Medak District, Andhra Pradesh, INDIA
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated as well as real time conditions. The real time stability data is conducted at 25°C ± 2°C. The stability study data is till 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established against the reference product Gemzar® 1000mg injection by Eli Lilly (Batch # 1G00216-1)
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type I, amber glass vial 14 ml Bromobutyl elastomeric stopper. Aluminum capsule with flip off closure.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches 24 months real time stability data at 30°C ± 2°C / 70% ± 5%RH of 03 batches 06 month accelerated stability data 40°C ± 2°C / 75% ± 5%RH of 03 batches (Batch# 34001/B, 34002/B, 34003/B)

Evaluation by PEC:

S No	Section #.	Deficiencies	Response
	1.33	Importer shall provide valid Certificate of Pharmaceutical Product (CoPP) / Free Sale certificate issued by relevant regulatory authority in the country of origin and name of exporting country.	Original legalized CoPP (certificate No. 191106) valid till 30-10-2021 issued by National Institute of Drugs, Argentina. The applied product is available for free sale in exporting country. The facilities and operations conform to WHO-GMP. Firm submitted that "This get expired during its period in R& I that's why as per rule it will be considered as valid"
	1.33	The GMp of shanghai acebright pharma co ltd. China is provided as API manufacture but at some place Hetero Labs Limited Survey.No.10, I.D.A., Gaddapotharam Village, Jinnaram Mandal, Medak District, Andhra Pradesh, INDIA is mentioned as API manufacturer clarification is needed in this regard.	Hetero Labs Limited Survey.No.10, I.D.A., Gaddapotharam Village, Jinnaram Mandal, Medak District, Andhra Pradesh, INDIA is API manufacturer, its GMP is provided
	1.33	The GMP certificate of Laboratories IMA SAIC Argentina issued by National administration of drug, food and medical devices (ANMAT)is valid till 2 April 2021. Provides Valid GMP	The GMP certificate of Laboratories IMA SAIC Argentina issued by National administration of drug, food and medical devices (ANMAT) valid till 3 April 2022 is provided
	2.3.S	On API stability both IMA lab and hetro lab is mentioned justify	No justification is given

Decision 321st meeting: Clarification regarding the site wherein stability studies of drug substance have been performed, since in submitted stability sheets both IMA lab and Hetro lab is mentioned.

REMARKS OF EVALUATOR:
Firm has submitted clarification that Finished product manufacturer is IMA lab that's why they have mentioned their name on every page of dossier , whereas the API manufacturer is Hetro lab and they have performed the stability studies at their own site.

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

395.	Name, address of Applicant / Marketing Authorization Holder	ATCO Laboratories Limited Address: B-18,S.I.T.E., Karachi - 75700,Karachi.Sindh
	Name, address of Manufacturing site.	ATCO Laboratories Limited

		Address: B-18,S.I.T.E., Karachi - 75700,Karachi.Sindh
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29426 dated 28/10/2021
	Details of fee submitted	PKR 150,000/-: dated 04/10/2021
	The proposed proprietary name / brand name	ITRACONAZOLE CAPSULE 100MG
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Itraconazole Pellets equivalent to Itraconazole MS 100mg (Itraconazole Pellets 22.2% w/w)
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Azole Antifungal agent.
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	1s, 4s, 7s, 10s, 14s, 20s, 28s & 30s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Itraconazole 100mg Capsules Accord-UK Ltd.
	For generic drugs (me-too status)	Sporanox Capsule Janssen-Cilag Pty Ltd
	GMP status of the Finished product manufacturer	GMP Certificate issued on 06 November 2020 valid till 05 November 2022.
	Name and address of API manufacturer.	Source of Pellets: ALPHAMED FORMULATIONS PVT., LIMITED Survey No.225, Sampanbole Village, Shamirpet Mandal, Medchal Malkajgiridistrict Telangana - 500 101, India Corporate office: Metrochem API Private Limited. Flat no. 302, Bhanu Enclave, Sunder nagar, Erragadda, Hyderabad-500038 Telangana state, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 32 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (BBA15001,BBA15002,BBA15003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Aspin pharma, by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand, in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Source of Pellets: ALPHAMED FORMULATIONS PVT., LIMITED Survey No.225, Sampanbole Village, Shamirpet Mandal, Medchal Malkajgiridistrict Telangana - 500 101, India
API Lot No.	8000200-022
Description of Pack	ALU-ALU Blister in printed carton

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0,3,6 (Months)		
Batch No.	N0374B	N0375B	N0376B
Batch Size	6000capsules	6000capsules	6000capsules
Manufacturing Date	15/12/2020	15/12/2020	15/12/2020
Date of Initiation	24/12/2020	24/12/2020	24/12/2020
No. of Batches	03		
Administrative Portion			
	Reference of previous approval of applications with stability study data of the firm (if any)	Rofl 500mg tablet Approved in DRB 277 held on 27-29 December 2017.	
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP issued by (Drug Control Administration, Government of Telangana CFDA valid till 29/08/2022.	
	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted	
	Data of stability batches will be supported by attested respective documents like chromatograms,Raw data sheets, COA, summary data sheets etc.	Submitted	
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted	
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted	

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

396.	Name and address of manufacturer / Applicant	M/S High –Q Pharmaceuticals, Plot No ; 224/23 Korangi Industrial Area, Karachi.
	Brand Name +Dosage Form + Strength	Platlo Plus 75mg/75mg Tablet
	Composition	Each film coated tablet contain Clopidogrel (as bisulfate) (USP)…….75mg

<table>
<tr><td></td><td></td><td>Acetylsalicylic acid (as enteric coated pellets)….75mg</td></tr>
<tr><td></td><td>Diary No. Date of R& I & fee</td><td>Dy.No.10448; 31-07-2017; Rs.20,000/- (31-07-2017)</td></tr>
<tr><td></td><td>Pharmacological Group</td><td>Anti-Platelet aggregation</td></tr>
<tr><td></td><td>Type of Form</td><td>Form 5</td></tr>
<tr><td></td><td>Finished product Specifications</td><td>Manufacturer’s specification</td></tr>
<tr><td></td><td>Pack size & Demanded Price</td><td>10’s, 14’s, 28’s, ; As per SRO</td></tr>
<tr><td></td><td>Approval status of product in Reference Regulatory Authorities</td><td>CoPlavix Tablet Of (TGA Approved)</td></tr>
<tr><td></td><td>Me-too status</td><td>Clodril Plus Tablet M/s Macter International</td></tr>
<tr><td></td><td>GMP status</td><td>Last GMP inspection was conducted on 30 June 2021
and the report shows good GMP.</td></tr>
<tr><td></td><td>Remarks of the Evaluator</td><td>1st letter: 04th June, 2018
Reminder letter: 9th October, 2018
Latest GMP inspection report (conducted within the period of last one year).
Source of pellets of Acetyl salicylic acid (In case of imported source remaining Rs: 80000/- fee)
GMP certificate of source of pellets
Stability study of 3 batches of pellets
Certificate of analysis of pellets</td></tr>
<tr><td></td><td>Previous decision(s) 296</td><td>Deferred for following:
Registration Board deferred the case for:
• Latest GMP inspection report (conducted within the period of last three year).
• Source of pellets of Acetyl salicylic acid (In case of imported source remaining Rs: 80000/- fee)
• GMP certificate of source of pellets, stability data and COA of pellets.
• Clarification of the dosage of the Innovator product, whether bilayer tablet or otherwise.</td></tr>
<tr><td></td><td>Remarks of evaluator:</td><td>
<table>
<tr><th>S#</th><th>Query</th><th>Response</th></tr>
<tr><td>1</td><td>Latest GMP inspection report (conducted within the period of last three year).</td><td>Last GMP inspection was conducted on 30 June 2021
and the report shows good GMP.</td></tr>
<tr><td>2</td><td>Source of pellets of Acetyl salicylic acid (In case of imported source remaining Rs: 80000/- fee)</td><td>Source is Surge lab Pakistan</td></tr>
<tr><td>3</td><td>GMP certificate of source of pellets, stability data and COA of pellets. GMP certificate of source of pellets, stability data and COA of pellets</td><td>Source is Surge lab Pakistan</td></tr>
</table>
</td></tr>
</table>

		4 | Clarification of the dosage of the Innovator product, whether bilayer tablet or otherwise. | Highnoon is making this table by compression and then film coating is done, in TGA biconcave coated tablet is mentioned.
	Previous Decision 312	Deferred for revision of formulation and manufacturing method as per reference product and confirmation of availability of bilayered machine
	Remarks of Evaluator VII	The Inspection report dated 6 July 2021 confirms the availability of bilayer machine. In TGA Australia the dosage form is described as biconvex tablet film coated not bilayered detailed method of manufacturing is also submitted by the firm.
	Decision of 313th meeting: Deferred for deliberation in forthcoming meeting regarding approval of the applied formulation as bi-layered and /or plain tablet.	
	Remarks of Evaluator xx: Formulations approved in reference countries (EMA /TGA) are bi layered tablet in which clopidogrel hydrogen sulfate is included in one layer and aspirin is in another layer. Firm has submitted revised formulation as per "EMA assessment report" (along with fee of Rs 30,000/- dated 19.10.2022) as follows: Each film coated bi layered tablet contains: Clopidogrel (as bisulfate) (USP)…….75mg Acetylsalicylic acid ……..75mg	
Decision: Approved as follows: **Each film coated bi layered tablet contains:** **Clopidogrel (as bisulfate) (USP)…….75mg** **Acetylsalicylic acid ……..75mg**		

Deferred case of 316th meeting:

397. Name and address of manufacturer / Applicant	M/s Cure Laboratories. Plot # 11,12,NS-2 RCCI, Industrial Estate, Rawat, Islamabad By M/s Vision Pharmaceuticals. Plot # 22,23, Industrial Triangle, Kahuta Road, Islamabad
Brand Name +Dosage Form + Strength	Esocure 40mg Injection
Composition	Each vial contains: Esomeprazole as Sodium…40mg
Diary No. Date of R& I & fee	Form-5 Dy.No 13942 dated 06-03-2019 Rs.50,000/- Dated 06-03-2019 (#0807480)
Pharmacological Group	Proton pump inhibitor
Form	Form-5
Finished product Specifications	Manufacturing specifications
Pack size & Demanded Price	As per SRO
Approval status of product in Reference Regulatory Authorities	Nexium IV 40mg/vial injection by M/s ASTRAZENECA PHARMS (USFDA approved)
Me-too status	Esold 40mg/vial Injection of M/s Weather Folds Pharmaceutical, Reg No. 74824
GMP status	M/S Vision: GMP Certificate issued on 08.05.2018.

Remarks of Evaluator VII	The applicant has submitted that they are not having any manufacturing on contract basis from any firm. Currently the firm have 3 Sections.
Remarks of Evaluator VII	Total sections: 3 Total products on toll: No
Previous decision (296)	Deferred for consideration on its turn
Decision of 316th meeting: Deferred as already deferred for capacity assessment (manufacturing and testing facility etc) of M/s vision in 313th meeting of Registration Board, For "Dry Powder Injection section (General)" & "Dry Powder Injection section (Steroid)", notified vide letter No. F.15-1/2022-PEC dated 08-03-2022.	
Decision: Approved with innovator specifications. Registration letter will be issued after submission of 7500/- fee for correction/pre-approval change ,as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
Name and address of manufacturer / Applicant	M/s Cure Laboratories. Plot # 11,12,NS-2 RCCI, Industrial Estate, Rawat, Islamabad By M/s Vision Pharmaceuticals Plot # 22,23, Industrial Triangle, Kahuta Road, Islamabad
Brand Name +Dosage Form + Strength	P-Role 40mg Injection
Composition	Each vial contains: Omeprazole as Sodium……40mg
Diary No. Date of R& I & fee	Form-5 Dy.No 13942 dated 06-03-2019 Rs.50,000/- Dated 06-03-2019 (#0807479)
Pharmacological Group	Proton pump inhibitor
Form	Form-5
Finished product Specifications	Manufacturing specifications
Pack size & Demanded Price	As per SRO
Approval status of product in Reference Regulatory Authorities	Omeprazole 40mg Powder for Solution for Infusion by M/s Sandoz Limited, MHRA Approved.
Me-too status	RISEK 40MG INJECTION. Reg. No. 45617
GMP status	M/S Vision: GMP Certificate issued on 08.05.2018.
Remarks of Evaluator VII	The applicant has submitted that they are not having any manufacturing on contract basis from any firm. Currently the firm have .. sections.
Remarks of Evaluator VII	Total sections: 3 Total products on toll: No
Previous decision (296)	Deferred for consideration on its turn
Decision of 316th meeting: Deferred as already deferred for capacity assessment (manufacturing and testing facility etc) of M/s vision in 313th meeting of Registration Board, For "Dry Powder Injection section (General)" & "Dry Powder Injection section (Steroid)", notified vide letter No. F.15-1/2022-PEC dated 08-03-2022.	
Decision: Approved with innovator specifications. Registration letter will be issued after submission of 7500/- fee for correction/pre-approval change ,as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	
Name and address of manufacturer / Applicant	M/s Cure Laboratories. Plot # 11,12,NS-2 RCCI, Industrial Estate, Rawat, Islamabad By M/s Vision Pharmaceuticals. Plot # 22,23, Industrial Triangle, Kahuta Road, Islamabad
Brand Name +Dosage Form + Strength	Quantum 5mg Injection

Composition	Each ampoule contains: Cholecalciferol …5mg
Diary No. Date of R& I & fee	Form-5 Dy.No 13942 dated 06-03-2019 Rs.50,000/- Dated 06-03-2019 (#0807483)
Pharmacological Group	Vitamin D3 analogue
Form	Form-5
Finished product Specifications	Manufacturing specifications
Pack size & Demanded Price	1 ml As per SRO
Approval status of product in Reference Regulatory Authorities	Vitamin D3 Good 200,000 IU / 1 ml IM solution for injection of (ANSM France approved)
Me-too status	D-Tres 5mg/ml Injection by M/s Sami (Reg#076115)
GMP status	M/S Vision: GMP inspection dated 11-2-2019 concluding good GMP compliance
Remarks of Evaluator VII	Each Ampoule (1ml) Contains: Cholecalciferol (Vitamin D3)…200,000 IU Eq. to 5mg/ml
Remarks of Evaluator VII	Total sections: 3 Total products on toll: No
Previous decision (296)	Deferred for consideration on its turn
Decision 316th meeting: Deferred according to the decision of 313th meeting of Registration Board, for capacity assessment of manufacturing and testing facility of M/s Vision Pharmaceuticals Pvt. Ltd. For "Dry Powder Injection vial section (General)" & "Dry Powder Injection section (Steroid)", notified vide letter No. F.15-1/2022-PEC dated 08-03-2022.	
Remarks of Evaluator xx: Registration Board has discussed the capacity assessment inspection report in details in 320th meeting. Deliberations were made on used and available manufacturing and quality control capacity keeping in view all registered product and currently applied products. After thorough deliberation, the Board decided to allow contract manufacturing from M/s Vision Pharmaceuticals (Pvt) Ltd Plot No. 22 – 23, Industrial Triangle Kahuta Road, Islamabad for following sections: • Sterile Dry Powder Injection Vial (General) • Sterile Dry Powder Injection Vial (Steroid	
Decision: Approved with innovator specifications. Registration letter will be issued after submission of 7500/- fee for correction/pre-approval change ,as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	

Deferred case of 285th meeting:

398.	M/s Global Pharmaceuticals, Islamabad	Vorzol 200mg Dry powder Injection Each vial contains:- Voriconazole ……..200 mg (Antifungal)	Form 5-D 16-06-2011 Dy.No.2120 Rs.15000/= Rs.5000/= 26-03-2015 1's As Per SRO	Vfend Infusion by PF Prism (USFDA Approved) Vorif by Ferozsons Last inspection report 23-24-08-2016 Overall cGMP compliance is	Deferred for confirmation of me too status as reported reference is in-correct. (M-265) Deferred for evidence of approval of manufacturing facility of "Dry	The firm has changed the application from Form-5D to Form-5 The firm has submitted me-too reference as "Vivid Injection of S.J. & G. Fazul Ellahie, Karachi (Reg # 070582)".

				considered as good.	powder Lyophilized injection" by Central Licensing Board. (M-278)	The firm has changed the application from local manufacture to contract manufacturing from M/s Vision Pharma, Islamabad. Differential fee of Rs. 30,000/- (deposit slip# 0742858) dated 28-08-2018 has been submitted.
Decision of 285th meeting : Deferred for following: Submission of remaining fee of Rs. 20,000/- for contract manufacturing. Evidence of manufacturing facility for ready to fill powder.						
Remarks of Evaluator: Now the firm has submitted differential fee of Rs 20,000/- for contract manufacturing and evidence of section approval (vide letter No F.1-26/2009-Lic (Vol-1) dated 07th June 2021) wherein "sterile dry powder injection (general)" of M/s Vision Pharma, Islamabad is confirmed.						
Decision: Deferred for evidence of availability of required manufacturing facility of "Dry Powder Injection (Lyophilisation)" from CLB since innovator drug product is manufactured by way of Lyophilisation.						

Veterinary:

399.	Name and address of manufacturer / Applicant	M/s. Elko Organization (Pvt) Ltd , Plot No. 27 & 28, sector 12-B North Karachi Industrial Area, Karachi
	Brand Name +Dosage Form + Strength	Link injection
	Diary No. Date of R& I & fee	Dy.No.24288, 12-6-7, Rs. 15,000/- (12,july 2018), 5000 (12 july 2018)
	Composition	Each ml contains: - Buserelin acetate…0.0042mg eq to 0.004mg Buserelin
	Pharmacological Group	Gonadotropin releasing hormone analogues
	Type of Form	Form-5
	Finished Product Specification	In house
	Pack size & Demanded Price	5ml; Decontrolled
	Approval status of product in Reference Regulatory Authorities.	Busol – 0.004 mg/ml solution for injection aniMedica GmbH, UK
	Me-too status	Conceptal Injection of Star Laboratories (Pvt) Ltd, Lahore (Reg # 058939).

	GMP status	Routine GMP inspection conducted on 13-06-2017 & 06-07-2017 concluded that the firm is operating at good level of GMP compliance as of today
	Remarks of the Evaluator.	VET
	Decision of 285th meeting:	Deleted since it is not priority
	Remarks of Evaluator:'	Firm has submitted the reference of already registered product "LINK INJECTION (50ml) (Reg No 084981)" and stated that 5ml pack size is more economical for the farmers, it has much priority for firm to market the said drug for poor farmers. Generc version: Conceptal Injection of Star Laboratories (Pvt) Ltd, Lahore (Reg # 058939).
	Decision: Deferred for opinion of Veterinary expert committee.	

400. Name and address of manufacturer / Applicant	M/s Star laboratories (Pvt) Ltd. 23 kilometer, multan road, Lahore
Brand Name +Dosage Form + Strength	Montel Paedrtric 4 mg tablet
Diary No. Date of R& I & fee	Form-5 Dy.No 462 dated 27-1-2014 Rs. 20,000
Composition	Each tablet contains: Montelukast as sodium…4 mg
Pharmacological Group	Leutkotriene Receptor Antagonist
Type of Form	Form-5
Finished Product Specification	Innovators
Pack Size & Demanded Price	As per SRO
Approval Status of Product in Reference Regulatory Authorities.	Singulair 4 mg chewable tablets (USFDA)
Me-too Status	Bronsecur of Pfizer Laboratories Ltd
Remarks of the Evaluator.	Latest GMP inspection report was required, the shortcoming was communicated to firm on 11.12.2018. Now the firm has submitted copy of GMP inspection report conducted on 21.01.2020 to 24.01.2020 wherein GMP was at satisfactory level.
Decision: Approved with USP specifications. Registration letter will be issued after submission of 7500/- fee for correction/pre-approval change ("Each Chewable tablet" in label claim & USP specification), as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.	

401.	Name, address of Applicant / Marketing Authorization Holder	M/s Himark Laboratories Private Limited Lahore
	Name, address of Manufacturing site.	M/s Himark Laboratories Private Limited Plot 37-A, Sundar Industrial Estate Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Prod-uct (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale

		☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13410 dated 02 June 2022
	Details of fee submitted	PKR 30,000/-: dated: 11 Feb 2022
	The proposed proprietary name / brand name	Himox 400 mg film coated tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Moxifloxacin as hydrochloride .... 400 mg
	Pharmaceutical form of applied drug	White to off-white color oblong shaped film coated tablet
	Pharmacotherapeutic Group of (API)	Fluoroquinolones
	Reference to Finished product specifications	USP
	Proposed Pack size	1 ×5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	AVELOX 400mg tablet M/S Bayer Health Care Inc. (USFDA Approved).
	For generic drugs (me-too status)	Mofest 400 mg tablet by M/s Sami Pharmaceuticals (Pvt.) Ltd. Reg. No. 050745
	GMP status of the Finished product manufacturer	New license granted on 26/09/2019 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	Pharmagen Limited Ferozepur Rd, Sue Aasal, Kasur
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability
	Module III (Drug Substance)	Firm has submitted detailed drug substance data related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 6 months accelerated and 36 months real time data of 3 batches of drug substance.
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted pharmaceutical equivalence study of trial formulation (B # T-70) with comparator product MOXIGET 400mg Tablet (B # 205F31) of M/s GETZ pharma. The results of the quality tests of both products fall within the specifications and are comparable. The firm has performed comparative dissolution profile in pH 1.2, acetate buffer pH 4.5 and phosphate buffer 6.8. The results showed that similarity factor f2 was above 50 in three media.
	Analytical method validation/verification of product	Firm has submitted report of verification studies of analytical method for the drug substance. Firm has submitted report of validation of analytical method for the drug product.

STABILITY STUDY DATA	
Manufacturer of API	Pharmagen Limited Lahore, Pakistan
API Lot No.	00510711/002/2021
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×5's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No.	T-70	T-71	T-72
Batch Size	2000 tab	2000 tab	2000 tab
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	20-06-2021	20-06-2021	20-06-2021
No. of Batches	03		

Administrative Portion

	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate Ref. No. 06/2019-DRAP (AD/607409-530) Dated 11-01-2019.
	Documents for the procurement of API with approval from DRAP (in case of import).	API (Moxifloxacin HCl) has been purchase from Pharmagen Limited which is a local manufacturer.
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail has been submitted
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:

S No	Deficiencies (Letter issued dated 15 August 2022)	Reply (dated 19.09.2022)
	Control of drug substance is required	Complied Firm has submitted analytical report and analytical testing methods from both Drug substance and Drug product manufacturer.
	Provide summarized tabulated results of verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer	Complied Analytical verification studies are submitted from finished product manufacturer.
	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance /Active Pharmaceutical Ingredient manufacture	Complied Certificate of Analysis (CoA) of the same batch (no. 00510711/002/2021) from Drug Substance /Active Pharmaceutical Ingredient manufacture is submitted.

	Submitted specifications have different parameters as compare to USP monograph specially in case of dissolution so clarification is required in this regard	Firm has submitted finished product specifications. All quality tests including dissolution acceptance criteria is as per USP monograph.

Decision: Approved

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application**

402.	Name, address of Applicant / Marketing Authorization Holder	M/s Novamed Pharmaceuticals (Pvt.) Ltd Lahore
	Name, address of Manufacturing site.	M/s Novamed Pharmaceuticals (Pvt.) Ltd., 28km Ferozepur Road Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 7175 dated 04/03/2021
	Details of fee submitted	PKR 50,000/-: dated 18/5/2020 (#2004310)
	The proposed proprietary name / brand name	Invid -3 Injection 300,000IU
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Cholecalciferol……..…300,000IU
	Pharmaceutical form of applied drug	Clear colorless oily liquid free from foreign particles
	Pharmacotherapeutic Group of (API)	Fat soluble vitamin, Vitamin-D Analogue (IM injection)
	Reference to Finished product specifications	Manufacturer Specs
	Proposed Pack size	1’s (1ml), 5’s (1ml), 100’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	XARENEL 300,000 IU / ml solution for injection Italy Approved
	For generic drugs (me-too status)	N/A

	GMP status of the Finished product manufacturer	License granted on 08/04/2006 and renewed on 08/04/2021 General liquid section approved and GMP certificate on 06/08/2021
	Name and address of API manufacturer.	Sichuan Province Yuxin Pharmaceutical Co., Ltd. Weicheng Jinhe East Road, Shifang City, Sichuan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C / 65% ± 5% RH for 48 months Accelerated: 25°C ± 2°C / 75% ± 5%RH for 6 months Batches: (B-3-01-130601 , B-3-01-130602 , B-3-01-130603)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the innovator that is Dibase by Abiogen Pharmaceuticals by performing quality tests (Identification, Assay, Dissolution,). CDP has not been applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
	Remarks:	

	The excipient use is XARENEL 300,000 IU / ml solution for injection: refined olive oil for injectable use. The overage added is 25% The membrane filtration is done Particulate matter is counted by particulate counter			
STABILITY STUDY DATA				
Manufacturer of API		Sichuan Province Yuxin Pharmaceutical Co., Ltd. Weicheng Jinhe East Road, Shifang City, Sichuan		
API Lot No.		B-1-51-M190105		
Description of Pack (Container closure system)		USP Type-1 Glass ampoule blistered in Alu - PVC and further packed in unit carton (1's ,5's (1ml)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 1, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		TP-140-T2	TP-140-T3	TP-140-T4
Batch Size		5000 Ampoule	5000 Ampoule	5000 Ampoule
Manufacturing Date		07-2019	07-2019	07-2019
Date of Initiation		25-07-2019	27-07-2019	27-07-2019
No. of Batches		03		
Administrative Portion				
	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has submitted copy of Last inspection Report conducted on 24/01/2018.		
	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SC20160032 issued by CFDA valid till 17/11/2021.		
	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of AD Attested invoice No F 1919090 vide No.5354/2019/DRAP-AD-CD(I&E) dated 16/04/2019 is submitted wherein the permission to import Vitamin D3 API is granted.		
	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted		
	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted		

Remarks OF Evaluator VII:

S. No	Sections	Observations/ Short-comings	Remarks
1.	1.3.4	Valid Drug Manufacturing License (DML) of manufacturer/Applicant shall be submitted as submitted DML was not valid.	Copy of valid DML is submitted
2.	2.3.R.1.1	Provide copy of Batch manufacturing record (BMR) for all the batches of the drug product for which stability study data is provide in module 3 section 3.2.P.8.3.	Copies of Executed/Trial batches & Commercial batch BMR were attracted in 3.2.R. However, Copies of BMR of all the batches of the drug product for which stability study data are provided in 2.3.R.1.1.
3.	3.2.P.8	Stability: on commercial Invoice the quantity mentioned was Vit D3 40MIU but the prepare strength is 300,000IU	As per COA,40MIU is the potency of vitamin D3 i.e 40,000,000 IU/gm , as per label claim of the applied strength the quantity of vitamin d3 with this potency is calculated which is equivalent to vitamin d3 300,000IU (7.5 mg). COA and calculation is attached.
4.	3.2.P.1	The composition contains BHA and Crodamol oil but in the reference product Xarenel 300,000IU/ml solution for injection. The excipient use is refined olive oil for injectable use.	Compatibility of crodamol oil and BHA were performed against Vitamin d3 Active, no interference was observed during the compatibility Analysis
5.	3.2.P.1	Description and composition of the drug product Details of Overage not provide in the formulation	Overage was reflecting in the amount of API /unit, however composition with overage details is attached.
6.	3.2.S.7.3	Justification of the stability of the drug substance at 25˚C±2˚C/ 60%RH±5%RH. In case where the real time stability data of the drug substance is conducted at 25˚C±2˚C/60%RH±5%RH, The firm shall submit the record of data logger for the storage condition throughout the transportation.	Revised Stability Data of new batches is provided
7.	3.2.S.4.1	Specification assay limit is mentioned as 97-103% but	According to USP 42 NF 37 Acceptance criteria limit for

		in USP the limit is from 90-120%.	Cholecalciferol material is 97-103%.Copy of USP monograph is provided for reference.
8.	3.2.P.1	In composition no Overage is mentioned in this section.	Overage was reflecting in the amount of API /unit, however composition with overage details is provided.
9.	2.3.P.3.2	In 2.3.P.3.2 batch formula it is mentioned that after 6 month of accelerated and real time stability studies product is stable so overage will be omitted during commercial validation batches but in the assay, there is a steady decrease in assay limit. Justification is needed about this statement.	Vitamins generally have tendency to degrade. As vitamin D3 is photolytic, thermally unstable and have oxidative nature but at the same time it is a fat-soluble vitamin and more stable with Crodamol Oil, because of this property product show no significant change in assay as defined in guideline.
10.	3.2.A and 3.2R	Appendices and regional information is missing.	Appendices and regional information as per approved checklist of 296th DRB is attached.
11.	3.2.P.8	Justify the result of Assay as all the batches just showed minor decrease in assay results less than which is usually observed in vitamin preparations. Scientific Justification/clarification is required in this regard.	Vitamins generally have tendency to degrade. As vitamin D3 is photolytic, thermally unstable and have oxidative nature but at the same time it is a fat-soluble vitamin and more stable with Crodamol Oil, because of this property product show no significant change in assay as defined in guideline.
12.	3.2.P.2.1.1	As As per relevant guidelines & structure of Form 5F, Comparative assay Pharmaceutical equivalence has to be performed at the time formulation development, while according to your submitted data, it has been performed after commencing stability studies. Justification shall be submitted.	Owing to the prevailed condition of covid throughout the world We had performed PE after formulation development due to unavailability of the Innovator pack. So, as per the need of hour or to overcome this challenge we deviated from the chronological flow. However, we confirm that this deviation will not be repeated.

Decision of 316:
Deferred for the following
The applied product's monograph is present in BP but the specification and methods applied are not according to BP monograph.
Remarks of evaluator VII

In BP monograph method given for assay analysis is by UV spectroscopy while invid-3 was tested by more stringent HPLC method. As a matter of fact, HPLC method exhibited the advantage of high precision and high recovery and high sensitivity
Decision of 321st meeting: Deferred for comparative analysis of drug product specification proposed by the applicant and those recommended by BP monograph of Vitamin D3 injection
Remarks of evaluator XX

Firm has submitted comparative analysis of drug product specification proposed by the applicant and those recommended by BP monograph of Vitamin D3 injection, as follows:

Sr.#	Test Description	Novamed Specifications	B.P Monograph	Gap Analysis
	Label Claim	Each ml contains: Vitamin D3……..300000 I.U (Colecalciferol 7.5mg)	Each ml contains: Vitamin D.…300000 I.U (Colecalciferol 7.5mg)	No changes
	Characteristics	Colorless oily liquid	A pale yellow, oily liquid	Colorless to pale yellow oily liquid
	Identification	HPLC RT Spectrum Wavelength 265nm	UV Spectrophotometry Wavelength 500nm	UV Spectrophotometry Wavelength 500nm
	Assay Test	NLT 95.0% and NMT 125.0% (Release Limit)	NLT 90.0% and NMT 110.0% (Release Limit)	Release Limit based on release criteria given by USP for vitamin assayed by HPLC
	Deliverable Volume	1.0ml-1.15ml	-----	Not Applicable
	Particulate Matter	Visible Particles Sub-visible Particles NMT 6000 Part./ Container of size $\geq 10\mu m$ & $\leq 25\mu m$ & NMT 600 Part./Container of size $\geq 25\mu m$	Visible Particles Sub-visible Particles NMT 6000 Part./ Container of size $\geq 10\mu m$ & $\leq 25\mu m$ & NMT 600 Part./Container of size $\geq 25\mu m$	No change
	Sterility Test	Should be Sterile `	Should be Sterile	No change
	Bacterial Endotoxin Test	NMT 47 EU/ml	Limit not mentioned	Limit not mentioned

Furthermore, firm has submitted rationale of adopting HPLC method due to following reason:

As per BP method, UV spectrophotometer at 500nm and 550nm mentioned, whereas we performed on HPLC method of Analysis (Novamed specs) which is superior technology with respect Accuracy, precision and Linearity. The reason for shifting to HPLC method of analysis is based on;

Very short-range spectrum difference in wavelength (500nm-550nm) and there is possibility of diluent/ethyl oleate will interfere in absorbance at visible region (500nm-550nm). Color Solution which gives false positive results at visible region (500nm-550nm). Method robustness depends upon difference of 500nm and 550nm, while HPLC method provide better quantification with respect to standard and sample spectrum.	
Remarks of evaluator XX	The acceptance criteria of assay in Drug product specification proposed by the firm is NLT 95.0% and NMT 125.0% which is less stringent than acceptance criteria of assay in BP specification i.e NLT 90.0% and NMT 110.0%. **Later on Firm has revised the acceptance criteria as per BP i.e NLT 90.0% and NMT 110.0%(dated 10.11.2022)**
Decision	**Approved with BP specification.** • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application** • **Registration letter will be issued after submission of 7500/- fee for correction/pre-approval change ,as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

Deferred cases of 295th meeting:

403.	Name and address of manufacturer / Applicant	"M/s Aims Pharmaceuticals. Plot # 291, Industrial Triangle, Kahuta Road, Islamabad"
	Brand Name +Dosage Form + Strength	Terbiaim 250mg Tablet
	Diary No. Date of R& I & fee	Dy.No 34340 dated 16-10-2018 Rs.20,000/-
	Composition	Each film coated tablet contains: Terbinafine (as hydrochloride)…250mg
	Pharmacological Group	Antifungal
	Type of Form	Form-5
	Finished Product Specification	USP Specification
	Pack size & Demanded Price	10's: Rs.474.00
	Approval status of product in Reference Regulatory Authorities.	Approved in US-FDA(uncoated tablet)
	Me-too status	Logirid Tablet 250mg of Lowitt Pharmaceutical (Pvt) Ltd,
	GMP status	Dated: 31-05-2018 "The panel unanimously recommended the grant of renewal of DML after thorough and detailed evaluation/inspection."
	Remarks of the Evaluator (VIII)	Reference product is approved as uncoated tablet but you have applied for coated tablet. Submit form 5, master formulation & manufacturing method either in-line with reference product along with requisite fee or evidence of approval of applied drug product as film coated tablet.
	Decision of 295th meeting: Deferred for clarification of applied formulation regarding coated or uncoated tablet is required as submitted master formulation contains ingredients of coating but Outline of method of manufacturing do not contain step of coating.	

	Remarks of Evaluator: Firm has revised formulation/label claim as per reference product as follows: Each tablet contains: Terbinafine (as hydrochloride)…250mg However firm has submitted copy of fee challan and endorsement from DRAP (Rs 5000/- dated 21.02.2020) submitted in this regard.
Decision: Approved as follows: **Each tablet contains:** **Terbinafine (as hydrochloride)…250mg** **Registration letter will be issued after submission of differential fee of 2500/- fee for correction/pre-approval change ,as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with latest GMP inspection report conducted within last three years.**	

404.	Name and address of Manufacturer / Applicant	"M/s Aims Pharmaceuticals. Plot # 291, Industrial Triangle, Kahuta Road, Islamabad"
	Brand Name+ Dosage Form +Strength	Azeskin 200mg Cream
	Composition	"Each Gram Contains: Azelaic Acid…200mg"
	Diary No. Date of R&I & fee	Dy.No 34333 dated 16-10-2018 Rs.20,000/-
	Pharmacological Group	anti-acne preparations for topical use
	Type of Form	Form 5
	Finished Product Specification	Manufacturer's Specification
	Pack Size & Demanded Price	15gm, 30gm: As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved in MHRA(emc)
	Me-too status	Not verifiable.
	GMP status	Date: 31-05-2018 Comments: "The panel unanimously recommended the grant of renewal of DML after thorough and detailed evaluation/inspection."
	Remarks of the Evaluator (VIII)	Approval of section/manufacturing facility by the Central Licensing Board. However, you may submit panel inspection report for renewal of DML verifying the section/manufacturing facility. Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm, as the provided evidence is not verifiable.
	Decision of 295th meeting: Deferred for the following: Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm, as the provided evidence is not verifiable. Approval of section/manufacturing facility by the Central Licensing Board	
	Remarks of Evaluator: Generic version of applied formulation is found as follows: Acnegen cream 20% (Reg No 070195) by M/s Biogen pharma, Rwp Firm has submitted copy of letter (No F.6-1/2009-Lic(M-216) dated 16th March 2008 wherein ointment (general) section is approved	

	Decision: Approved with innovator's specification. Registration letter will be issued after submission of 7500/- fee for correction/pre-approval change ,as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with latest GMP inspection report conduicted within last three years.

405.	Name and address of Manufacturer / Applicant	"M/s Aims Pharmaceuticals. Plot # 291, Industrial Triangle, Kahuta Road, Islamabad"
	Brand Name+Dosage Form+Strength	Aimpride 2mg Tablet
	Composition	"Each Film Coated Tablet Contains: Glimepiride…2mg"
	Diary No. Date of R&I & fee	Dy.No 34348 dated 16-10-2018 Rs.20,000/-
	Pharmacological Group	Sulfonylureas
	Type of Form	Form 5
	Finished Product Specification	USP Specification
	Pack Size & Demanded Price	As per SRO
	Approval status of product in Reference Regulatory Authorities	Approved in USFDA
	Me-too status	Glimera 2mg Tablet of PPP, Karachi
	GMP status	Date: 31-05-2018 Comments: "The panel unanimously recommended the grant of renewal of DML after thorough and detailed evaluation/inspection."
	Remarks of the Evaluator (VIII)	Reference product in approved as uncoated tablet but you have applied for film coated tablet. Submit form 5, master formulation & manufacturing method either in-line with reference product along with submission of requisite fee or evidence of approval of applied drug product as film coated tablet.
	Decision of 295th meeting: Deferred for submission of either evidence of approval of reference product as film coated tablet or otherwise for revision of applied formulation in line with reference product i.e. uncoated tablet alongwith submission of requisite fee, master formulation & manufacturing method.	
	Remarks of Evaluator: Firm has revised formulation/label claim as per reference product as follows: Each tablet contains: Glimepiride…2mg" However firm has submitted copy of fee challan and endorsement from DRAP (Rs 5000/- dated 21.02.2020) submitted in this regard.	
	Decision: Approved as follows: **Each tablet contains:** **Glimepiride…2mg**" **Registration letter will be issued after submission of 2500/- fee for correction/pre-approval change ,as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with latest GMP inspection report conduicted within last three years.**	

406. Name and address of Manufacturer / Applicant	"M/s Aims Pharmaceuticals. Plot # 291, Industrial Triangle, Kahuta Road, Islamabad"
Brand Name+Dosage Form+Strength	Aimpride 4mg Tablet

Composition	"Each Film Coated Tablet Contains: Glimepiride…4mg"
Diary No. Date of R&I & fee	Dy.No 34349 dated 16-10-2018 Rs.20,000/-
Pharmacological Group	Sulfonylureas
Type of Form	Form 5
Finished Product Specification	USP Specification
Pack Size & Demanded Price	As per SRO
Approval status of product in Reference Regulatory Authorities	Approved in USFDA
Me-too status	Glimera 4mg Tablet of PPP, Karachi
GMP status	Date: 31-05-2018 Comments: "The panel unanimously recommended the grant of renewal of DML after thorough and detailed evaluation/inspection."
Remarks of the Evaluator (VIII)	Reference product in approved as uncoated tablet but you have applied for film coated tablet. Submit form 5, master formulation & manufacturing method either in-line with reference product along with submission of requisite fee or evidence of approval of applied drug product as film coated coated tablet.
Decision of 295th meeting: Deferred for submission of either evidence of approval of reference product as film coated tablet or otherwise for revision of applied formulation in line with reference product i.e. uncoated tablet alongwith submission of requisite fee, master formulation & manufacturing method.	
Remarks of Evaluator: Firm has revised formulation/label claim as per reference product as follows: Each tablet contains: Glimepiride…4mg" However firm has submitted copy of fee challan and endorsement from DRAP (Rs 5000/- dated 21.02.2020) submitted in this regard.	
Decision: Approved as follows: **Each tablet contains:** **Glimepiride…4mg**" **Registration letter will be issued after submission of 2500/- fee for correction/pre-approval change ,as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with latest GMP inspection report conduicted within last three years.**	

407. Name and address of Manufacturer / Applicant	"M/s Aims Pharmaceuticals. Plot # 291, Industrial Triangle, Kahuta Road, Islamabad"
Brand Name+ Dosage Form +Strength	Dermera Cream 40mg/0.5mg/0.1mg Cream
Composition	"Each Gram Contains: Hydroquinone…40mg Tretinoin…0.5mg Fluocinolone Acetonide…0.1mg"
Diary No. Date of R&I & fee	Dy.No 34335 dated 16-10-2018 Rs.20,000/-
Pharmacological Group	Anti-fungal
Type of Form	Form 5
Finished Product Specification	USP Specification

Pack Size & Demanded Price	15gm, 30gm: As per SRO
Approval status of product in Reference Regulatory Authorities	Approved in US-FDA
Me-too status	Tricuma Cream Topical of Ciba Pharmaceuticals
GMP status	Date: 31-05-2018 Comments: "The panel unanimously recommended the grant of renewal of DML after thorough and detailed evaluation/inspection."
Remarks of the Evaluator (VIII)	Approval of section/manufacturing facility by the Central Licensing Board. However, you may submit panel inspection report for renewal of DML verifying the section/manufacturing facility.
Decision of 295th meeting: Deferred for approval of section/manufacturing facility by the Central Licensing Board.	
Remarks of Evaluator: Firm has submitted copy of letter (No F.6-1/2009-Lic(M-216) dated 16th March 2008 wherein ointment (general) section is approved	
Decision: Approved. Firm shall submit latest GMP inspection report conduicted within last three years before issuance of registration letter.	

408. Name and address of Manufacturer / Applicant	"M/s Aims Pharmaceuticals. Plot # 291, Industrial Triangle, Kahuta Road, Islamabad"
Brand Name+ Dosage Form +Strength	Vagistat 20mg Cream
Composition	"Each Gram Contains: Butoconazole…20mg"
Diary No. Date of R&I & fee	Dy.No 34332 dated 16-10-2018 Rs.20,000/-
Pharmacological Group	Anti-fungal
Type of Form	Form 5
Finished Product Specification	USP Specification
Pack Size & Demanded Price	15gm, 30gm: As per SRO
Approval status of product in Reference Regulatory Authorities	Approved in Israel (as provided by the firm)
Me-too status	Could not be confirmed
GMP status	Date: 31-05-2018 Comments: "The panel unanimously recommended the grant of renewal of DML after thorough and detailed evaluation/inspection."
Remarks of the Evaluator (VIII)	Approval of section/manufacturing facility by the Central Licensing Board. However, you may submit panel inspection report for renewal of DML verifying the section/manufacturing facility. Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/ approved by the Registration Board in its 275th meeting. Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
Decision of 295th meeting: Deferred for the following: Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.	

Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. Approval of section/manufacturing facility by the Central Licensing Board. However, you may submit panel inspection report for renewal of DML verifying the section/manufacturing facility.
Remarks of Evaluator: Formulation approved in USFDA is Butoconazole nitrate cream 2% hence label claim has to be standardized alongwith fee. **The reference of generic version provided by the firm is not verifiable.** Firm has submitted copy of letter (No F.6-1/2009-Lic(M-216) dated 16th March 2008 wherein ointment (general) section is approved.
Decision: Deferred for Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.

Item No. XI: Agenda of Evaluator (Mr. Umar Latif)

Item no 1: Routine Application on Form 5-F		
409.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan**
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23 Industrial Triangle, kahuta Road, Islamabad-25000, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 23839 dated 31-08-2021
	Details of fee submitted	Rs.20,000/- dated 17-12-2020 Slip no. 2051711
	The proposed proprietary name / brand name	Visoline 0.9% infusion/injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Sodium chloride.…….9mg
	Pharmaceutical form of applied drug	IV Infusion/Injection
	Pharmacotherapeutic Group of (API)	Crystalloid Fluid
	Reference to Finished product specifications	USP specs

	Proposed Pack size	1's, 10ml
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Sodium chloride 0.9% infusion of HOSPIRA (FDA approved)
	For generic drugs (me-too status)	Celine 0.9% Infusion of Surge laboratories Pvt. Ltd.
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 11-02-2019
	Name and address of API manufacturer.	M/s Jiangsu Province Qinfen Co,. Ltd. 28 changxing east road, Economic and Technological Development zone, Nantong Jiangsu Province.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: Temp.: 30°C ± 2°C, RH: 65% ± 5% for 36 month Accelerated: Temp.: 40°C ± 2°C, RH: 75% ± 5%for 6 months Batches: (Na102504, Na104804, Na107905)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The Firm has performed pharmaceutical equivalence of their developed formulation

		Visoline 0.9% injection (B #NPD 912 T-01) with reference product Celine 0.9% injection (B #CLN-054B) of M/s Surge Laboratories Pvt. Ltd. The results showed that both test and comparator products were comparable.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Name**: M/s Jiangsu Province Qinfen Co,. Ltd. **Address**: 28 changxing east road, Economic and Technological Development zone, Nantong Jiangsu Province.		
API Lot No.	200420		
Description of Pack (Container closure system)	LDPE ampoule (10ml) packed in unit carton (1's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	NDP 912 T-01	NDP 912 T-02	NDP 912 T-03
Batch Size	5 liters	5 liters	5 liters
Manufacturing Date	07-2020	07-2020	07-2020
Date of Initiation	16-07-2020	16-07-2020	21-07-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not Provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. JS20170729 issued by China Food & drug Administration valid till 26/11/2022 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of attested ADC (I&E) DRAP, Islamabad dated 02-07-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Provided

<table>
<tr><td>6.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.</td></tr>
<tr><td>Sr No.</td><td>Short-Comings</td><td>Reply from the Firm</td></tr>
<tr><td>a.</td><td>Details regarding the method and testing reports of Endotoxin tests of the drug product are required.
You are using LDPE ampoule, which is a semi-permeable membrane container, how would you justify the performance at both accelerated (40’C, 75%) and real time stability studies (30’C, 65%).</td><td>The firm has provided testing reports for BET.</td></tr>
<tr><td>b.</td><td>You are using LDPE ampoule, which is a semi-permeable membrane container, how would you justify the performance at both accelerated (40’C, 75%) and real time stability studies (30’C, 65%).</td><td>As per ICH guideline stability testing.
If stability for semi-permeable container performed at (30C, 65% real time stability studies and 40C,75% for accelerated, ICH provide the alternative approach for calculation of water loss. For example at a given temperature 40C, the calculated waterloss during storage at NMT 25%RH is the water loss rate measured at 75% RH multiplied by 3, the corresponding water loss ratio is:
<table>
<tr><td>Alternative relative humidity</td><td>Reference</td><td>Ratio of water loss rates at a given temperature.</td></tr>
<tr><td>60%RH</td><td>25%RH</td><td>1.9</td></tr>
<tr><td>60%RH</td><td>40%RH</td><td>1.5</td></tr>
<tr><td>65%RH</td><td>35%RH</td><td>1.9</td></tr>
<tr><td>75%RH</td><td>25%RH</td><td>3.0</td></tr>
</table></td></tr>
<tr><td>c.</td><td>Describe the manufacturing facility along with the section in detail as you have multiple parenteral sections (General)</td><td>We will manufacture in Large Volume parenteral section BFS technology.</td></tr>
<tr><td colspan="3">Remarks of Evaluator:</td></tr>
<tr><td colspan="3">Decision: Approved.
• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.
• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.</td></tr>
<tr><td>410.</td><td>Name, address of Applicant / Marketing Authorization Holder</td><td>M/s Jawa Pharmaceuticals Private Limited
112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,</td></tr>
<tr><td></td><td>Name, address of Manufacturing site.</td><td>M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid-e-Azam Industrial Area Kot</td></tr>
</table>

		Lakhpat, Lahore,
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24076 dated 01-09-2021
	Details of fee submitted	PKR 30,000/-: dated 01-09-2021
	The proposed proprietary name / brand name	Mfor-Sita Tablets JPL 50mg/1000mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Metformin HCL … 1000mg Sitagliptin as phosphate …50mg
	Pharmaceutical form of applied drug	Green, oblong shaped, film coated tablet, embossed "Jawa" on one side-
	Pharmacotherapeutic Group of (API)	Sitagliptin belongs to a class of medicines called DPP-4 inhibitors (dipeptidyl peptidase-4 inhibitors) Metformin belongs to a class of medicines called biguanides.
	Reference to Finished product specifications	In-House
	Proposed Pack size	2 x 7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Janumet Tablet by Merck Sharp & Dohme
	For generic drugs (me-too status)	Janumet Tablet by OBS Pharma Reg No: 066172
	GMP status of the Finished product manufacturer	New license granted on 04-03-2020
	Name and address of API manufacturer.	Metformin HCL: M/s IPCA Laboratories Limited, H-4, M.I.D.C., Waluj Aurangabad (Maharashtra) Pin : 431136, India Sitagliptin as phosphate: M/s Zhejiang Yougtai Pharmaceuticals Co., Ltd, No,1,4th Doughi Zhejiang Provincial and Chemical and Medical Raw Material Base Linhai Zone, Linhai City, Zhejiang Province, 317016, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general

		properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Metformin Hcl & Sitagliptin as phosphate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (Trial 1, Trial 2, Trial 3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Janumet Tablet by Merck Sharp & Dohme B.V., Waarderweg 39, 2031 BN Haarlem, The Netherlands EU/1/08/455/008
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Metformin HCL: M/s IPCA Laboratories Limited, H-4, M.I.D.C., Waluj Aurangabad (Maharashtra) Pin : 431136, India Sitagliptin as phosphate: M/s Zhejiang Yougtai Pharmaceuticals Co., Ltd, No,1,4th Doughi Zhejiang Provincial and Chemical and Medical Raw Material Base Linhai Zone, Linhai City, Zhejiang Province, 317016, China.
API Lot No.	Metformin HCL:20549ML2ARMI Sitagliptin as phosphate: 2036-0001-20196
Description of Pack (Container closure system)	Mfro-Sita tablet supplied Alu alu/aluminum foil blister packs as 2 x 7`s.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 1	Trial 2	Trail 3
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	21-09-2020	25-09-2020	28-09-2020
Date of Initiation	29-09-2020	29-09-2020	29-09-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter Ref. No: 1345/2021/DRAP-AD-VI (I&E) dated 08-05-2020 is submitted wherein the permission to import different APIs including Metformin Hcl & Sitagliptin for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Did not provided the data.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Sr No.	**Short-Comings**	**Reply from the Firm**
a.	Valid GMP/DML of API manufacturers are required.	
b.	In EMA public assessment report, limits for the assay test for drug product are 95% - 105% while the specification of the drug product provided by the drug product manufacturer is 90% - 110%. Clarification is required.	
c.	3.2.S.4 Control of Drug Substance :- A discussion and justification should be	

	provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification.	
d.	3.2.P.5 Control of Drug Product: - You have prepared batches without considering the equivalency factor of Sitagliptin in master formulation. Clarification is needed	
Remarks of the Evaluator:		
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		

411.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,**
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23876 dated 01-09-2021
	Details of fee submitted	PKR 30,000/-: dated 01-09-2021
	The proposed proprietary name / brand name	Mfor-Sita Tablets JPL 50mg/500mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Metformin HCL … 500mg Sitagliptin as phosphate …50mg
	Pharmaceutical form of applied drug	Green, oblong shaped, film coated tablet, embossed "Jawa" on one side-
	Pharmacotherapeutic Group of (API)	Sitagliptin belongs to a class of medicines called DPP-4 inhibitors (dipeptidyl peptidase-4 inhibitors) Metformin belongs to a class of medicines called biguanides.
	Reference to Finished product specifications	In-House
	Proposed Pack size	2 x 7's
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Janumet Tablet by Merck Sharp & Dohme
	For generic drugs (me-too status)	Janumet Tablet by OBS Pharma
	GMP status of the Finished product manufacturer	New license granted on 04-03-2020
	Name and address of API manufacturer.	Metformin HCL: M/s IPCA Laboratories Limited, H-4, M.I.D.C., Waluj Aurangabad (Maharashtra) Pin : 431136, India Sitagliptin as phosphate: M/s Zhejiang Yougtai Pharmaceuticals Co., Ltd, No,1,4th Doughi Zhejiang Provincial and Chemical and Medical Raw Material Base Linhai Zone, Linhai City, Zhejiang Province, 317016, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Metformin Hcl & Sitagliptin as phosphate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, , container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (Trial 1, Trial 2, Trial 3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the Janumet Tablet by Merck Sharp & Dohme B.V., Waarderweg 39, 2031 BN Haarlem, The Netherlands

		EU/1/08/455/008
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Metformin HCL: M/s IPCA Laboratories Limited, H-4, M.I.D.C., Waluj Aurangabad (Maharashtra) Pin : 431136, India Sitagliptin as phosphate: M/s Zhejiang Yougtai Pharmaceuticals Co., Ltd, No,1,4th Doughi Zhejiang Provincial and Chemical and Medical Raw Material Base Linhai Zone, Linhai City, Zhejiang Province, 317016, China.		
API Lot No.	Metformin HCL:20549ML2ARMI Sitagliptin as phosphate: 2036-0001-20196		
Description of Pack (Container closure system)	Mfro-Sita tablet supplied Alu alu/aluminum foil blister packs as 2 x 7`s.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 1	Trial 2	Trail 3
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	21-09-2020	25-09-2020	28-09-2020
Date of Initiation	29-09-2020	29-09-2020	29-09-2020
No. of Batches	03		

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Submitted
9.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter Ref. No: 1345/2021/DRAP-AD-VI (I&E) dated 08-05-2020 is submitted wherein the permission to import different APIs including Metformin Hcl & Sitagliptin for the purpose of test/analysis and stability studies is granted.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Did not provided the data.
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks of the Evaluator:		
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		
412.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,**
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24077 dated 01-09-2021
	Details of fee submitted	PKR 30,000/-: dated 07-06-2021
	The proposed proprietary name / brand name	J-Pride Tablet 2mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Glimepride … 2mg
	Pharmaceutical form of applied drug	White colored round, uncoated tablet with score line on one side & plain on other side
	Pharmacotherapeutic Group of (API)	Glimepiride belongs to a group called sulfonylurea works as Inhibition of ATP-dependent potassium channels treatment of diabetes mellitus.
	Reference to Finished product specifications	In-House
	Proposed Pack size	2 x 10’s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glimepiride Tablet by Accord Healthcare Limited, MHRA

	For generic drugs (me-too status)	Amaryl 2mg Tablet by Sanofi-Aventis Reg No: 019568
	GMP status of the Finished product manufacturer	New license granted on 04-03-2020 Tablets (general) section approved
	Name and address of API manufacturer.	M/s Indico Remedies Ltd R-104, M.I.D.C., T.T.C. Area, Thane Belapur Road, Rabale, Navi Mumbai — 400 701, Maharashtra, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Glimepiride is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (Trial 1, Trial 2, Trial 3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the Amaryl 2mg Tablet by Sanofi-Aventis.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity
STABILITY STUDY DATA		

Manufacturer of API	M/s Indico Remedies Ltd R-104, M.I.D.C., T.T.C. Area, Thane Belapur Road, Rabale, Navi Mumbai — 400 701, Maharashtra, India.		
API Lot No.	GLM19012R		
Description of Pack (Container closure system)	J-Pride tablet supplied PVC/aluminum foil blister packs - pack sizes of 2 x 10`s.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 1	Trial 2	Trail 3
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	16-09-2020	19-09-2020	23-09-2020
Date of Initiation	24-09-2020	24-09-2020	24-09-2020
No. of Batches	03		

Administrative Portion		
13.	Reference of previous approval of applications with stability study data of the firm (if any)	
14.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate valid till 07-04-2023 provided
15.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter Ref. No: 1345/2021/DRAP-AD-VI (I&E) dated 08-05-2020 is submitted wherein the permission to import different APIs including Paroxetine HCl for the purpose of test/analysis and stability studies is granted.
16.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
17.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Did not provided the data
18.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Sr No.	**Short-Comings**	**Reply from the Firm**
e.	Valid GMP/DML of API manufacturers are required.	

f.	3.2.S.4 Control of Drug Substance :- A discussion and justification should be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification.	
g.	Justify the dissolution conditions and criteria of NLT 85% in 15minutes for the drug product.	
h.	3.2.P.5.3:- Specificity parameter has been performed by injecting the blank, and standard solution. Whereas USP chapter <1225> & ICH Q2 (R1) guidelines suggests spiking the drug substance with appropriate levels of impurities. Justification shall be submitted for this variation	
i.	Reference of previous approval of applications with stability study data of the firm (if any	
j.	Documents for the procurement of API with approval from DRAP (in case of import).	
k.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	
Remarks of the Evaluator:		
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		

413.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jawa Pharmaceuticals Private Limited** **112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,**
	Name, address of Manufacturing site.	M/s Jawa Pharmaceuticals Private Limited 112/10 Quaid-e-Azam Industrial Area Kot Lakhpat, Lahore,
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 24078 dated 01-09-2021
	Details of fee submitted	PKR 30,000/-: dated 07-06-2021
	The proposed proprietary name / brand name	J-Pride Tablet 4mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Glimepride … 4mg
	Pharmaceutical form of applied drug	White colored round, uncoated tablet with score line on one side & plain on other side
	Pharmacotherapeutic Group of (API)	Glimepiride belongs to a group called sulfonylurea works as Inhibition of ATP-dependent potassium channels treatment of diabetes mellitus.
	Reference to Finished product specifications	In-House
	Proposed Pack size	2 x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Glimepiride Tablet by Accord Healthcare Limited, MHRA
	For generic drugs (me-too status)	Amaryl 4mg Tablet by Sanofi-Aventis
	GMP status of the Finished product manufacturer	New license granted on 04-03-2020 Tablets (general) section approved
	Name and address of API manufacturer.	M/s Indico Remedies Ltd R-104, M.I.D.C., T.T.C. Area, Thane Belapur Road, Rabale, Navi Mumbai — 400 701, Maharashtra, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Glimepiride is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions:

		Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (Trial 1, Trial 2, Trial 3)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the Amaryl 4mg Tablet by Sanofi-Aventis.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity

STABILITY STUDY DATA

Manufacturer of API	M/s Indico Remedies Ltd R-104, M.I.D.C., T.T.C. Area, Thane Belapur Road, Rabale, Navi Mumbai — 400 701, Maharashtra, India.		
API Lot No.	GLM19012R		
Description of Pack (Container closure system)	J-Pride tablet supplied PVC/aluminum foil blister packs - pack sizes of 2 x 10`s.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 1	Trial 2	Trail 3
Batch Size	5000 tablets	5000 tablets	5000 tablets
Manufacturing Date	16-09-2020	19-09-2020	23-09-2020
Date of Initiation	24-09-2020	24-09-2020	24-09-2020
No. of Batches	03		

Administrative Portion

19.	Reference of previous approval of applications with stability study data of the firm (if any)	
20.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate valid till 07-04-2023 provided

21.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter Ref. No: 1345/2021/DRAP-AD-VI (I&E) dated 08-05-2020 is submitted wherein the permission to import different APIs including Paroxetine HCl for the purpose of test/analysis and stability studies is granted.
22.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
23.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Did not provided the data
24.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Sr No.	**Short-Comings**	**Reply from the Firm**
a.	Valid GMP/DML of API manufacturers are required.	
b.	3.2.S.4 Control of Drug Substance :- A discussion and justification should be provided for any incomplete analyses of the drug substance / API by Drug Product manufacturer (e.g. results not tested according to the proposed specification.	
c.	Justify the dissolution conditions and criteria of NLT 85% in 15minutes for the drug product.	
d.	3.2.P.5.3:- Specificity parameter has been performed by injecting the blank, and standard solution. Whereas USP chapter <1225> & ICH Q2 (R1) guidelines suggests spiking the drug substance with appropriate levels of impurities. Justification shall be submitted for this variation	
e.	Reference of previous approval of applications with stability study data of the firm (if any	
f.	Documents for the procurement of API with approval from DRAP (in case of import).	

g.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	
Remarks of the Evaluator:		
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		
414.	Name, address of Applicant / Marketing Authorization Holder	M/s W.Woodward Pakistan Private Limited Karachi, Pakistan
	Name, address of Manufacturing site.	M/s W.Woodward Pakistan Private Limited, F-275, S.I.T.E. Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy.No 19877 dated 15-07-2021
	Details of fee submitted	Rs.20,000/- dated 14-06-2021 & Rs.10,000/- dated 10-06-2021
	The proposed proprietary name / brand name	Lifo Tablet 5 mg/850mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Dapagliflozin propanediol monohydrate…5mg Metformin HCl……..850mg
	Pharmaceutical form of applied drug	Off-white oblong shaped biconvex film coated tablet
	Pharmacotherapeutic Group of (API)	Anti-hyperglycemia
	Reference to Finished product specifications	Manufacturer's Specifications
	Proposed Pack size	14's Tablets
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Xingduo tablet by M/s Astra Zeneca ABSF-15185 sodertalji Sweden , MHRA
	For generic drugs (me-too status)	Dapamet Tablet by M/s Hilton Pharma, Reg. No. 093071
	GMP status of the Finished product manufacturer	Last GMP Inspection dated on 14-03-2022 concludes that M/s W.Woodward Pakistan (Pvt) Ltd is considered to be compliance of good level of GMP .

	Name and address of API manufacturer.	**Dapagliflozin propandiol monohydrate:-** M/s Fuxin Long Rul Pharmaceutical Co. Ltd. Fluorida Industrial Park, Fumwng Country (YiMaTu). Fuxin City, Liaoning Province 123000, China. **Metformin Hydrochloride :-**M/s IPCA Laboratories Ltd, 48, Kandivali Industrial Estate, Kandivali (West) 400067 Mumbai Maharashtra India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Dapagliflozin Propandiol monohydrate is a manufacturer's specification. The firm submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance Official monograph of Metformin hydrochloride is a USP specification. The firm submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (PD-161,PD-162,PD-163)
	Module-III (Drug Product):	The firm has submitted detail of drug Product including its description, composition, pharmaceutical development, manufacture,

		manufacturing process and process control, process validation protocols, control of excipients , control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Dapamet 5mg/850mg Tablet Hilton Pharma by performing quality tests (Description, Dissolution, and, Assay,). CDP has been performed against the same brand that is brand leader that is Dapamet 5mg/850mg Tablet Hilton Pharma in 0.1N HCl, Acetate buffer pH 4.5, Phosphate Buffer pH 6.8 and Phosphate buffer pH 7.2. The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Fuxin Long Rul Pharmaceutical Co. Ltd. Fluorida Industrial Park, Fumwng Country (YiMaTu). Fuxin City, Liaoning Province 123000, China. M/sIPCA Laboratories Ltd, 48, Kandivali Industrial Estate, Kandivali (West) 400067 Mumbai Maharashtra India.		
API Lot No.			
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton with leaflet (14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	PD-161	PD-162	PD-163
Batch Size	1000 tab	1500 tab	1500 tab
Manufacturing Date	14-02-2020	14-02-2020	14-02-2020
Date of Initiation	15-02-2020	15-02-2020	15-02-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Information by the firm did not provided.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of letter from M/s Biofar Chemicals in name of M/s Woodward Pakistan, for provision of 15gm of Dapagliflozin propanediol monohydrate.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Did not provide.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.
Remarks of Evaluator:		
Decision: Deferred for submission of documents for the procurement of APIs with approval from DRAP I&E office & compliance record of HPLC software 21CFR & audit trail reports on product testing		

415.	Name, address of Applicant / Marketing Authorization Holder	M/s CITY PHARMACEUTICALS LABORATORIES PLOT # 12-A, I-5 SECTOR 5, NEW SURVEY No. 276, KORANGI INDUSTRIAL AREA KARACHI PAKISTAN
	Name, address of Manufacturing site.	M/s **CITY PHARMACEUTICALS LABORATORIES** PLOT # 12-A, I-5 SECTOR 5, NEW SURVEY No. 276, KORANGI INDUSTRIAL AREA KARACHI PAKISTAN
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales

	Dy. No. and date of submission	Dy.No 26929 dated 29-09-2021
	Details of fee submitted	Rs.30,000/- dated 15-09-2021
	The proposed proprietary name / brand name	EXIT 2 gm powder for solution for injection / infusion
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	**Each Vial contains:** Ceftriaxone sodium Sterile Powder for solution for injection eq. to Ceftriaxone ……. 2 gm
	Pharmaceutical form of applied drug	Lyophilized powder for solution for IV injection or Infusion
	Pharmacotherapeutic Group of (API)	Cephalosporin antibiotic
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	A Ceftriaxone 2 g Powder for Solution for Injection or Inf by M/s MIP Pharma GmbH Kirkeler Str. 41 66440 Blieskastel Germany, MHRA Approved.
	For generic drugs (me-too status)	INOCEF 2gm Injection by M/s Barrett Hodgson, Reg. No. 032582
	GMP status of the Finished product manufacturer	DML granted on 15/06/2016
	Name and address of API manufacturer.	**Henan Kangda Pharmaceutical Co., Ltd**. No.66 Jingwu Road, Xiangcheng city, Henan Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of *Ceftriaxone Sodium* is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug

		substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the INOCEF 2gm IV by BARRET HODGSON PAKISTAN by performing quality tests (Identification, Assay, pH).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA			
Manufacturer of API	**Henan Kangda Pharmaceutical Co., Ltd**. No.66 Jingwu Road, Xiangcheng city, Henan Province, China.		
API Lot No.	2022005028		
Description of Pack (Container closure system)	30ml round neck Type 3 glass vial with dark grey rubber stopper and Aluminium seal (1's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	750 Vials	750 Vials	750 Vials
Manufacturing Date	02-2021	02-2021	02-2021
Date of Initiation	25-02-2021	25-02-2021	25-02-2021
No. of Batches	03		

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.

8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. HA20170010 issued by China FDA valid till 02-16-2022.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	• Invoice # YK21063022, Dated 05-12-2020 is submitted with ADC approval date 18-12-2020
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc. is Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	We have maintained manual logs of all tests.
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted

Sr No.	**Short-Comings**	**Reply from the Firm**
h.	**3.2.S.4.3** Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted.	Submitted by M/s City Pharmaceuticals Laboratories.
i.	**3.2.S.7** Submit sterility testing reports.	Firm has submitted reports for bacterial Endotoxin Test for drug substance.
j.	**3.2.P.1** Justify the equivalency factor of Ceftriaxone sodium for Ceftriaxone.	Firm has submitted calculations declaring the theoretical factor for the sodium salt.
k.	3.2.P.2 Compatibility studies for the dry powder for injections should be performed as per the instructions provided in individual label of the drug product.	Submitted.
l.	**3.2. P.8**Microbiological analysis record for the performance of sterility test & Bacterial Endotoxin test shall be submitted..	Submitted.
m.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	--
Remarks of the Evaluator:		
Decision: Approved. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**		

Item no 3. Stability studies cases on Form 5 D		
416.	**Name and address of manufacturer / Applicant**	**M/s Neutro Pharma (Pvt) Ltd. 9.5 km, Sheikhupura Road,Lahore**
	Brand Name +Dosage Form + Strength	Etoricoxib 120mg Tablet
	Composition	Each Film Coated Tablet Contains: Etoricoxib…….120mg
	Diary No. Date of R& I & fee	Dy.No 41592 dated 07-12-2018 Rs.50,000/- Dated 07-12-2018
	Pharmacological Group	(NSAIDs)
	Type of Form	Form 5D
	Finished product Specifications	Manufacturer's Specifications
	Pack size & Demanded Price	10's, 14's, 20's, 28's, 30's, (4×7's); As per SRO
	Approval status of product in Reference Regulator Authorities	Etoricoxib 120mg film coated tablet (USFDA Approved)
	Me-too status	
	GMP status	The last inspection conducted on 18-07-2017 concluding that the firm maintained a fair level of GMP compliance
	Remarks of the Evaluator	Stability data is not provided

Decision of 295th: Deferred for submission of stability studies of 3 batches according to the conditions of zone IV-A as per the directions given in 278th meeting of Registration Board.

STABILITY STUDY DATA

Remarks of the Evaluator:- Firm was asked to provide the stability data on 14points as per the decision of the registration Board in its 293rd meeting.

Manufacturer of API	M/s AURORE LIFE SCIENCES PVT LTD. Plot # 68, 69, 2nd Floor, Jubilee Heights, beside Shiplaramam, Madhapur, Hyderabad, Telangana 50008, India.		
API Lot No.	ETX-60010119		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	**Real time**: 30°C ± 2° C / 65% ± 5% **Accelerated**: 40 °C ± 2 °C / 75% ± 5%		
Time Period	**Real time**: 6th months **Accelerated**: 6th months		
Frequency	**Accelerated**: initial, 3rd , 6th (months) **Real Time**: initial, 3rd , 6th (months)		
Batch No.	**ETC-FC-120-001-19**	**ETC-FC-120-002-19**	**ETC-FC-120-003-19**
Batch Size	1200 tablets	1200 tablets	1200 tablets
Manufacturing Date	09-2019	09-2019	09-2019

Date of Initiation	17-09-2019	17-09-2019	17-09-2019
No. of Batches	03		
Date of Submission	07-09-2022		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT			
Sr. No.	**Documents to Be Provided**	**Status**	
15.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection for authenticity of stability data of their products conducted by the panel, on the basis of which Registration Board approved Neutro pharma "Dexlanzoprazol products" •	
16.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Copies of API (Etoricoxib) COA's (Batch# ETX-60010119) from AURORE LIFE SCIENCES PVT LTD. Plot # 68, 69, 2nd Floor, Jubilee Heights, beside Shilparamam, Madhapur, Hyderabad, Telangana 50008, India and M/s Neutro Pharmaceuticals (Pvt.) Ltd are submitted.	
17.	Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer	Methods used for analysis of API from both API Manufacturers and Finished Product Manufacturer is provided by the firm.	
18.	Stability study data of API from API manufacturer	Firm has submitted stability study data of API as per zone IV-A. Stability study is conducted at **Real time**:- Temp 30°C ± 2°C / 65% ± 5%RH **Accelerated**:- Temp 40°C ± 2°C / 75% ± 5%RH **Batches #**: (50011115, 50021115 ,50031115)	
19.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of valid GMP certificate in the name of M/s AURORE LIFE SCIENCES PVT LTD. Plot # 68, 69, 2nd Floor, Jubilee Heights, beside Shiplaramam, Madhapur, Hyderabad, Telangana 50008, India.	
20.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of ADC attested invoice No. 154 dated 25-02-2019 from exporter M/s AURORE LIFE SCIENCES PVT LTD. Plot # 68, 69, 2nd Floor, Jubilee Heights, beside Shilparamam, Madhapur, Hyderabad, Telangana 50008, India. For import of 6.0 Kg of Etoricoxib (Batch No. ETX-60010119) in name of M/s Neutro Pharmaceuticals (Pvt.) Ltd. Lahore attested by AD (I&E) DRAP Lahore dated 29-04-2019.	
21.	Protocols followed for conduction of stability study	Protocols followed for conduction of stability study is submitted	
22.	Method used for analysis of FPP	Method for Finished product analysis has been submitted	

<table>
<tr><td>23.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Drug excipients compatibility study performed.</td></tr>
<tr><td>24.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted Batch Manufacturing record of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>ETC-FC-120-001-19</td><td>1200 tablets</td><td>09-2019</td></tr>
<tr><td>ETC-FC-120-002-19</td><td>1200 tablets</td><td>09-2019</td></tr>
<tr><td>ETC-FC-120-003-19</td><td>1200 tablets</td><td>09-2019</td></tr>
</table></td></tr>
<tr><td>25.</td><td>Record of comparative dissolution data (where applicable)</td><td>Comparative dissolution was performed against Arcoxia 120mg Tablet Batch # M045935 in HCl buffer (pH 1.2), Acetate buffer (pH 4.5) & Phosphate buffer (pH 6.8).</td></tr>
<tr><td>26.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td>Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc. is submitted</td></tr>
<tr><td>27.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing.</td><td>Submitted</td></tr>
<tr><td>28.</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)</td><td>Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted</td></tr>
<tr><td colspan="3">REMARKS OF EVALUATOR</td></tr>
<tr><td colspan="3">Decision: Approved with Innovator’s specifications.
• Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.
• Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.
• The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.</td></tr>
<tr><td>417.</td><td>Name and address of manufacturer / Applicant</td><td>M/s Neutro Pharma (Pvt) Ltd. 9.5 km, Sheikhupura Road,Lahore</td></tr>
<tr><td></td><td>Brand Name +Dosage Form + Strength</td><td>Etoricoxib 90mg Tablet</td></tr>
<tr><td></td><td>Composition</td><td>Each Film Coated Tablet Contains:
Etoricoxib…….90mg</td></tr>
<tr><td></td><td>Diary No. Date of R& I & fee</td><td>Dy.No 41296 dated 07-12-2018 Rs.50,000/- Dated 07-12-2018</td></tr>
<tr><td></td><td>Pharmacological Group</td><td>(NSAIDs)</td></tr>
<tr><td></td><td>Type of Form</td><td>Form 5D</td></tr>
<tr><td></td><td>Finished product Specifications</td><td>Manufacturer’s Specifications</td></tr>
<tr><td></td><td>Pack size & Demanded Price</td><td>As per SRO</td></tr>
</table>

	Approval status of product in Reference Regulator Authorities	ARCOXIA (30mg, 60mg, 90mg,120mg) film coated tablet by M/s MSD, MHRA Approved.
	Me-too status	
	GMP status	The last inspection conducted on 18-07-2017 concluding that the firm maintained a fair level of GMP compliance.
	Remarks of the Evaluator	Stability data is not provided

Decision of 295th: Deferred for submission of stability studies of 3 batches according to the conditions of zone IV-A as per the directions given in 278th meeting of Registration Board.

STABILITY STUDY DATA

Remarks of the Evaluator:- Firm was asked to provide the stability data as per the decision of the registration Board in its 293rd meeting.

Manufacturer of API	M/s_ AURORE LIFE SCIENCES PVT LTD. Plot # 68, 69, 2nd Floor, Jubilee Heights, beside Shiplaramam, Madhapur, Hyderabad, Telangana 50008, India.		
API Lot No.	ETX-60010119		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton		
Stability Storage Condition	**Real time**: 30°C ± 2° C / 65% ± 5% **Accelerated**: 40 °C ± 2 °C / 75% ± 5%		
Time Period	**Real time**: 6th months **Accelerated**: 6th months		
Frequency	**Accelerated**: initial, 3rd , 6th (months) **Real Time**: initial, 3rd , 6th (months)		
Batch No.	**ETC-FC-90-001-19**	**ETC-FC-90-002-19**	**ETC-FC-90-003-19**
Batch Size	1200 tablets	1200 tablets	1200 tablets
Manufacturing Date	08-2019	08-2019	08-2019
Date of Initiation	15-08-2019	15-08-2019	15-08-2019
No. of Batches	03		
Date of Submission	17-09-2022		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

Sr. No.	Documents to Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	The firm has referred to previous inspection for authenticity of stability data of their products conducted by the panel, on the basis of which Registration Board approved Neutro pharma "Dexlansoprazol products" •
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Copies of API (Etoricoxib) COA's (Batch# ETX-60010119) from AURORE LIFE SCIENCES PVT LTD. Plot # 68, 69, 2nd Floor, Jubilee Heights, beside Shilparamam, Madhapur, Hyderabad, Telangana 50008,

<table>
<tr><td></td><td></td><td>India and M/s Neutro Pharmaceuticals (Pvt.) Ltd are submitted.</td></tr>
<tr><td>3.</td><td>Method used for analysis of API from both API Manufacturer and Finished Product Manufacturer</td><td>Methods used for analysis of API from both API Manufacturers and Finished Product Manufacturer is provided by the firm.</td></tr>
<tr><td>4.</td><td>Stability study data of API from API manufacturer</td><td>Firm has submitted stability study data of API as per zone IV-A. Stability study is conducted at Real time:- Temp 30˚C ± 2˚C / 65% ± 5%RH Accelerated:- Temp 40˚C ± 2˚C / 75% ± 5%RH
Batches #: (50011115, 50021115 ,50031115)</td></tr>
<tr><td>5.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td>Firm has submitted copy of valid GMP certificate in the name of M/s AURORE LIFE SCIENCES PVT LTD. Plot # 68, 69, 2nd Floor, Jubilee Heights, beside Shiplaramam, Madhapur, Hyderabad, Telangana 50008, India.</td></tr>
<tr><td>6.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td>The firm has submitted copy of ADC attested invoice No. 154 dated 25-02-2019 from exporter M/s AURORE LIFE SCIENCES PVT LTD. Plot # 68, 69, 2nd Floor, Jubilee Heights, beside Shilparamam, Madhapur, Hyderabad, Telangana 50008, India. For import of 6.0 Kg of Etoricoxib (Batch No. ETX-60010119) in name of M/s Neutro Pharmaceuticals (Pvt.) Ltd. Lahore attested by AD (I&E) DRAP Lahore dated 29-04-2019.</td></tr>
<tr><td>7.</td><td>Protocols followed for conduction of stability study</td><td>Protocols followed for conduction of stability study is submitted</td></tr>
<tr><td>8.</td><td>Method used for analysis of FPP</td><td>Method for Finished product analysis has been submitted</td></tr>
<tr><td>9.</td><td>Drug-excipients compatibility studies (where applicable)</td><td>Drug excipients compatibility study performed.</td></tr>
<tr><td>10.</td><td>Complete batch manufacturing record of three stability batches.</td><td>The firm has submitted Batch Manufacturing record of following 03 Batches:
<table>
<tr><th>Batch No.</th><th>Batch Size</th><th>Mfg. Date</th></tr>
<tr><td>ETC-FC-90-001-19</td><td>1200 tablets</td><td>08-2019</td></tr>
<tr><td>ETC-FC-90-002-19</td><td>1200 tablets</td><td>08-2019</td></tr>
<tr><td>ETC-FC-90-003-19</td><td>1200 tablets</td><td>08-2019</td></tr>
</table></td></tr>
<tr><td>11.</td><td>Record of comparative dissolution data (where applicable)</td><td>Comparative dissolution was performed against Arcoxia 90mg Tablet Batch # M022039 in HCl buffer (pH 1.2), Acetate buffer (pH 4.5) & Phosphate buffer (pH 6.8).</td></tr>
</table>

12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc. is submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) is submitted
REMARKS OF EVALUATOR		
Decision: Approved with Innovator's specifications. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**		

1. For Stability Panel

418.	Name and address of manufacturer / Applicant	**M/s. NEXT Pharmaceutical Products Pvt. Ltd. Plot# 44 A-B, Sundar Industrial Estate Lahore.**
	Brand Name +Dosage Form + Strength	Empaglif 10mg Tablets
	Composition	Each film coated tablet contains: Empagliflozin……..10 mg
	Diary No. Date of R& I & fee	Dy. No. 41051 dated 06-12-2018 Rs. 20,000 Dated 06-12-2018
	Pharmacological Group	Anti-Diabetic
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	14, 28, 30 & As per SRO
	Approval status of product in Reference Regulatory Authorities	MHRA Approved
	Me-too status	XENGLU 10mg by Hilton Pharma Karachi (reg # 093065)
	GMP status	28-05-2022 Satisfactory level of GMP compliance.
	Remarks of the Evaluator	

STABILITY STUDY DATA	
Drug	Empaglif 10mg
Name of Manufacturer	M/s. NEXT Pharmaceutical Products Pvt. Ltd. Plot# 44 A-B, Sundar Industrial Estate Lahore
Manufacturer of API	M/s Jiangsu Yongan Pharmaceutical Co. Ltd China
API Lot No.	4500-201909001
Description of Pack (Container closure system)	Alu-Alu blister
Stability Storage Condition	Real Time: 30^{o}C ± 2^{o}C / 65% ± 5%RH

	Accelerated:40°C ±2°C / 75% ± 5%RH		
Time Period	Real Time: 06 Months Accelerated:06Months		
Frequency	Real Time: 0,1,3,6 Accelerated: 0,1,3,6 Months		
Batch No.	T-0001 TAA	T-0002 TAA	T-0003 TAA
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	01-2020	02-2020	02-2020
Date of Initiation	07-2020	07-2020	07-2020
No. of Batches	03		
Date of Submission			

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

1.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	The firm has provided copy of GMP certificate (Certificate# JS 2020921) issued by Jiansu Drug Administration for M/s Jiangu Yongan Pharmaceutical Co., Ltd. Valid Up to 14-03-2023
2.	Protocols followed for conduction of stability study and details of tests..	The firm has submitted complete protocol for conduction of stability study and details of tests.
3.	Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc	The firm has provided data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets
4.	Documents confirming import of API etc.	Copy of invoice (Invoice No. ZY 19101701G/W) for 0.5 Kg of Empagliflozin has been submitted attested by Assistant Director DRAP, Lahore dated 24-10-2019.
5.	All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents.	Submitted
6.	Commitment to continue real time stability study till assigned shelf life of the product.	Submitted
Commitment to follow Drug Specification Rules, 1978.		Submitted

419.	Name and address of manufacturer / Applicant	**M/s. NEXT Pharmaceutical Products Pvt. Ltd. Plot# 44 A-B, Sundar Industrial Estate Lahore.**
	Brand Name +Dosage Form + Strength	DAPGLIF 5mg Tablets
	Composition	Each Film Coated Tablet Contains: Dapagliflozin as Propanediol Monohydrate…5mg
	Diary No. Date of R& I & fee	Dy. No. 41345 dated 07-12-2018 Rs. 20,000 Dated 07-12-2018
	Pharmacological Group	Anti-Diabetic
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	14, 28, 30 & As per SRO
	Approval status of product in Reference Regulatory Authorities	MHRA Approved
	Me-too status	DAPA 5mg by Hilton Pharma Karachi (reg # 089367)
	GMP status	28-05-2022 Satisfactory level of GMP compliance.

	Remarks of the Evaluator	

STABILITY STUDY DATA			
Drug	Dapaglif 5mg		
Name of Manufacturer	M/s. NEXT Pharmaceutical Products Pvt. Ltd. Plot# 44 A-B, Sundar Industrial Estate Lahore		
Manufacturer of API	M/s Jiangsu Yongan Pharmaceutical Co. Ltd China		
API Lot No.	7100-201910001		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real Time: 30°C ± 2°C / 65% ± 5%RH Accelerated:40°C ±2°C / 75% ± 5%RH		
Time Period	Real Time: 06 Months Accelerated:06Months		
Frequency	Real Time: 0,1,3,6 Accelerated: 0,1,3,6 Months		
Batch No.	T-0001 TAE	T-0002 TAE	T-0003 TAE
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	01-2020	02-2020	02-2020
Date of Initiation	07-2020	07-2020	07-2020
No. of Batches	03		
Date of Submission			

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
1.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	The firm has provided copy of GMP certificate (Certificate# JS 2020921) issued by Jiansu Drug Administration for M/s Jiangu Yongan Pharmaceutical Co., Ltd. Valid Up to 14-03-2023
2.	Protocols followed for conduction of stability study and details of tests..	The firm has submitted complete protocol for conduction of stability study and details of tests.
3.	Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc	The firm has provided data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets
4.	Documents confirming import of API etc.	Copy of invoice (Invoice No. ZY 19101701G/W) for 0.5 Kg of Dapagliflozin Propanediol Monohydrate has been submitted attested by Assistant Director DRAP, Lahore dated 24-10-2019.
5.	All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents.	Submitted
6.	Commitment to continue real time stability study till assigned shelf life of the product.	Submitted
Commitment to follow Drug Specification Rules, 1978.		Submitted

420.	Name and address of manufacturer / Applicant	**M/s. NEXT Pharmaceutical Products Pvt. Ltd. Plot# 44 A-B, Sundar Industrial Estate Lahore.**

	Brand Name +Dosage Form + Strength	DAPGLIF 10mg Tablets
	Composition	Each Film Coated Tablet Contains: Dapagliflozin as Propanediol Monohydrate…10mg
	Diary No. Date of R& I & fee	Dy. No. 41348 dated 07-12-2018 Rs. 20,000 Dated 07-12-2018
	Pharmacological Group	Anti-Diabetic
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	14, 28, 30 & As per SRO
	Approval status of product in Reference Regulatory Authorities	MHRA Approved
	Me-too status	DAPA 10mg by Hilton Pharma Karachi (reg # 089368)
	GMP status	28-05-2022 Satisfactory level of GMP compliance.
	Remarks of the Evaluator	

STABILITY STUDY DATA

Drug	Dapaglif 10mg		
Name of Manufacturer	M/s. NEXT Pharmaceutical Products Pvt. Ltd. Plot# 44 A-B, Sundar Industrial Estate Lahore		
Manufacturer of API	M/s Jiangsu Yongan Pharmaceutical Co. Ltd China		
API Lot No.	7100-201910001		
Description of Pack (Container closure system)	Alu-Alu blister		
Stability Storage Condition	Real Time: 30°C ± 2°C / 65% ± 5%RH Accelerated:40°C ±2°C / 75% ± 5%RH		
Time Period	Real Time: 06 Months Accelerated:06Months		
Frequency	Real Time: 0,1,3,6 Accelerated: 0,1,3,6 Months		
Batch No.	T-0001 TAF	T-0002 TAF	T-0003 TAF
Batch Size	2500 Tablets	2500 Tablets	2500 Tablets
Manufacturing Date	01-2020	02-2020	02-2020
Date of Initiation	07-2020	07-2020	07-2020
No. of Batches	03		
Date of Submission			

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

1.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	The firm has provided copy of GMP certificate (Certificate# JS 2020921) issued by Jiansu Drug Administration for M/s Jiangu Yongan Pharmaceutical Co., Ltd. Valid Up to 14-03-2023
2.	Protocols followed for conduction of stability study and details of tests..	The firm has submitted complete protocol for conduction of stability study and details of tests.
3.	Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc	The firm has provided data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets

4.	Documents confirming import of API etc.	Copy of invoice (Invoice No. ZY 19101701G/W) for 0.5 Kg of Dapagliflozin Propanediol Monohydrate has been submitted attested by Assistant Director DRAP, Lahore dated 24-10-2019.
5.	All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents.	Submitted
6.	Commitment to continue real time stability study till assigned shelf life of the product.	Submitted
Commitment to follow Drug Specification Rules, 1978.		Submitted

Inspection Report

1.1 General Information.

Name of Manufacturer	M/s Next Pharmaceuticals (Pvt.) Ltd.
Physical Address	Plot No. 44 A-B, Sundar Industrial Estate, Lahore.
Drug Manufacturing License No. and validity	000 by way of formulation Valid till .
Contact Address	Plot No. 44 A-B, Sundar Industrial Estate, Lahore.
Date of Inspection.	14-06-2021
Purpose of Inspection	Verification of Authenticity of Stability Data for Purpose of Registration of Drugs with reference DRAP's letter No. F.15-1/2022-PEC(AD-PEC-VI) dated 16th August, 2022.
Name of Inspector	01 Mr. Iftikhar Chaudhry, Member, Registration Board. 03. Ms. Ufaq Tanveer AD, DRAP, Lahore
Name of firm Representatives	

1.2 Focus of Inspection:

The inspection was focused on a thorough evaluation of data for stability studies of following products namely:

Sr. No.	Name / Composition of Drugs
01	Empaglif 10mg Tablets Each Film Coated tablet contains: Empagliflozin….. 10mg
02	Dapaglif 10mg Tablet Each film coated tablet contains: Dapagliflozin……10mg
03	Dapaglif 5mg Tablet Each film coated tablet contains: Dapagliflozin……5mg

Detail of investigation:

Q.no.	Questions	Observation by Panel
1.	Do you have documents confirming the import Dapagliflozin and Empagliflozin API including approval from DRAP?	The firm has imported Dapagliflozin and Empagliflozin from Jiangsu Yongan Pharmaceutical Co. Ltd. China, Supplier Suzhou Zhiyu Biotechnology Co. Ltd. China. Invoice No. ZY19101701G/W dated 17-10-2019. Batch # 7100-201910001 and 4500-201909001. The total quantity purchased was 500 g each. the approval from DRAP is available vide letter no. 10998/2019/DRAP-AD-CD(I&E).
2.	What was the rationale behind selecting the particular manufacturer of API?	Rationale behind selecting the particular manufacturer of API as informed by the firm is that the manufacturer is GMP complaint and vendor evaluation had been done.
3.	Do you have documents confirming the import of Dapagliflozin and Empagliflozin reference standard and impurity standards?	The working standard was imported through Jiangsu Yongan Pharmaceutical Co. Ltd. China. Batch # 7100-201901001(ws) for Dapagliflozin and Batch No. 4500-201901001 (WS) for Empagliflozin with quantity 100mg each.
4.	Do you have certificate of Analysis of the API, reference standards and impurity standards?	The firm has COAs for API and Working Standard.
5.	Do you have GMP certificate of API manufacturer issued by regulatory authority of country of origin?	The firm has GMP certificate of API manufacturer issued by Jiangsu Food and Drug Administration China. Certificate No. JS20160548 dated. 4-3-2016.
6.	Do you use API manufacturer method of testing for testing API?	The firm had used manufacturer's method for testing the API.
7.	Do you have stability studies reports on API?	The firm had manufacturer's stability study reports of the API.
8.	If yes, whether the stability testing has been performed as per SIM method and degradation products have been quantified?	Yes, stability had been performed as per SIM Method and Degradation products had been quantified by API manufacturer.
9.	Do you have method for quantifying the impurities in the API?	The Firm had not performed quantification of the impurities.
10.	Do you have some remaining quantities of the API, its reference standard and impurities standards?	The Firm had some remaining quantities of API and Working Standard for reference.
11.	Have you used pharmaceutical grade excipients?	The firm had used pharmaceutical grade excipients as per available documents.
12.	Do you have documents confirming the import of the used excipients?	The firm had necessary documents confirming the import of excipients.
13.	Do you have test reports and other records on the excipients used?	The firm had certificates of analysis and other record of excipients used.

<table>
<tr><td>14.</td><td>Do you have written and authorized protocols for the development of Dapagliflozin and Empagliflozin as Tablet?</td><td>The firm had written protocol for the development of Dapagliflozin 10mg Tablet, Dapagliflozin 5mg and Empagliflozin 10mg Tablets.</td></tr>
<tr><td>15.</td><td>Have you performed Drug-excipients compatibility studies?</td><td>The firm had not performed compatibility studies because the composition of their product is similar to that of the innovator’s product (Forxiga Tablet for Dapagliflozin and Jardiance 10mg Tablets for Empagliflozin) as informed by the firm.</td></tr>
<tr><td>16.</td><td>Have you performed comparative dissolution studies?</td><td>Yes. The firm had performed comparative dissolution studies.</td></tr>
<tr><td>17.</td><td>Do you have product development (R&D) section?</td><td>The firm had separate product development (R&D) section.</td></tr>
<tr><td>18.</td><td>Do you have necessary equipment’s available in product development section for development of Dapagliflozin and Empagliflozin tablet?</td><td>The firm had all necessary equipment in Product development section for the development of Dapagliflozin 10mg and 5mg Tablet and Empagliflozin 10mg Tablet. However, the compression machine was not available in this section. So the compression was performed in Tablet Section of Production area.</td></tr>
<tr><td>19.</td><td>Are the equipment’s in product development section qualified?</td><td>All the equipment’s in Product Development Section was qualified.</td></tr>
<tr><td>20.</td><td>Do you have proper maintenance / calibration / requalification program for the equipment used in PD section?</td><td>The firm had proper maintenance and calibration for the equipment’s used in product development section.</td></tr>
<tr><td>21.</td><td>Do you have qualified staff in product development section with proper knowledge and training in product development?</td><td>The firm had qualified staff for the development of product in product development Section.</td></tr>
<tr><td>22.</td><td colspan="2">Have you manufactured three stability batches for the stability studies of Dapagliflozin and Empagliflozin tablet as required?</td></tr>
<tr><td></td><td>The firm had manufactured three stability batches of Dapagliflozin 5mg & 10mg Tablet and three stability batches of Empagliflozin 10mg Tablet.</td><td>Dapagliflozin 10mg
<table>
<tr><th>Batch #</th><th>Mfg. Date</th><th>Exp. Date</th></tr>
<tr><td>T-0001TAF</td><td>22-01-2020</td><td>21-01-2022</td></tr>
<tr><td>T-0002TAF</td><td>11-02-2020</td><td>10-02-2022</td></tr>
<tr><td>T-0003TAF</td><td>11-02-2020</td><td>10-02-2022</td></tr>
</table>
Dapahgliflozin 5mg
<table>
<tr><th>Batch #</th><th>Mfg. Date</th><th>Exp. Date</th></tr>
<tr><td>T-0001TAE</td><td>21-01-2020</td><td>20-01-2022</td></tr>
<tr><td>T-0002TAE</td><td>17-02-2020</td><td>16-02-2022</td></tr>
<tr><td>T-0003TAE</td><td>17-02-2020</td><td>16-02-2022</td></tr>
</table>
Empagliflozin 10mg</td></tr>
</table>

		<table><tr><td>Batch #</td><td>Mfg. Date</td><td>Exp. Date</td></tr><tr><td>T-0001TAA</td><td>17-01-2020</td><td>16-01-2022</td></tr><tr><td>T-0002TAA</td><td>11-02-2020</td><td>10-02-2022</td></tr><tr><td>T-0003TAA</td><td>11-02-2020</td><td>10-02-2022</td></tr></table>
23.	Do you have any criteria for fixing the batch size of stability batches?	The firm had written sop for fixing the stability batch size as per number of testing.
24.	Do you have complete record of production of stability batches?	The firm had complete record of production of stability batches. All the BPR's and log books were properly maintained and reviewed at the time of inspection.
25.	Do you have protocols for stability testing of stability batches?	The firm had protocols for testing of stability batches.
26.	Do you have developed and validated the method for testing of stability batches?	Yes, the firm had developed and validated the method for testing of stability batches.
27.	Do you have method transfer studies in case when the method of testing being used by your firm is given by any other lab?	Method transfer studies was not performed, as the firm had developed In-House Method of testing and validation
28.	Do you have documents confirming the qualification of equipment's / instruments being used in the test and analysis of Dapagliflozin and Empagliflozin API and the finished drug?	Yes, the firm has proper documents confirming the qualification of equipment and instruments being used in the test and analysis of API and Finished Product.
29.	Does your method of analysis stability indicate?	Yes, the method of analysis is stability indicating.
30.	Do your HPLC software 21CFR Compliant?	Yes, the HPLC software is 21CFR compliant.
31.	Can you show Audit trail reports on Dapagliflozin and Empagliflozin testing?	The firm showed the audit trail reports on API testing and finished product testing.
32.	Do you have some remaining quantities of degradation products and stability batches?	The firm had remaining quantities of stability batches.
33.	Do you have stability batches kept on stability testing?	Yes, the firm have few packs available, however stability study had been completed for 24 months.
34.	Do you have valid calibration status for the equipment's used in Dapagliflozin and Empagliflozin tablet production and analysis?	Yes, the firm has valid calibration status for the equipment used in production and analysis of Dapagliflozin 5mg and 10mg Tablets and Empagliflozin 10mg Tablets.
35.	Do proper and continuous monitoring and control are available for stability chamber?	Continuous monitoring and controls were available for stability chambers.
36.	Do related manufacturing area, equipment, personnel and utilities be rated as GMP compliant?	GMP certificate issued by DRAP was available with validity.

CONCLUSION:

Based on the documents reviewed, areas inspected and technical personnel met, and considering the findings of the inspection, the panel is of the view that stability studies were conducted by the firm M/S Next Pharmaceuticals (Pvt.) Ltd, Lahore for Dapa 10mg, Dapa 5mg and Empa 10mg Tablets.

Decision of 322nd meeting:

- **Registration Board decided to approve the applications of Empaglif 10mg Tablets, Dapglif 5mg Tablets & Dapglif 10mg Tablets with Innovator' specifications.**
- **The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications for each product as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**
- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months.**

Item No. XII: Agenda of Assistant Director PE&R (Mr. Muhammad Zubair)

421.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Winbrains Research Laboratories Plot No.69/1 Block B, Phase I-II, Industrial Estate, Hattar Pakistan**
	Name, address of Manufacturing site.	M/s Winbrains Research Laboratories Plot No.69/1 Block B, Phase I-II, Industrial Estate, Hattar Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 1739 dated 02/06/2021
	Details of fee submitted	PKR 20,000/-: dated 02/03/2021
	The proposed proprietary name / brand name	Lunaz 1% Cream
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Gm Contains: Luliconazole (In-House)…10 mg (Product complies Innovator's Specs)
	Pharmaceutical form of applied drug	Off white to light yellow cream
	Pharmacotherapeutic Group of (API)	SSRI (Anti-depressant)
	Reference to Finished product specifications	Innovator Specification
	Proposed Pack size	1 ×1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Luzu 1% Japan
	For generic drugs (me-too status)	Not Available
	GMP status of the Finished product manufacturer	Copy of GMP Certificate No. F. 3-20/2019-DRAP-40 dated 03-06-2019
	Name and address of API manufacturer.	FLAX LABORATORIES B-29/1, MIDC MAHAD, BIRVADI VILLAGE, DIST-RAIGAD, MAHARASHTRA, INDIA.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to

		nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Paroxetine Hydrochloride is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (T-09, T-10, T-11)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Not Applicable
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	FLAX LABORATORIES B-29/1, MIDC MAHAD, BIRVADI VILLAGE, DIST-RAIGAD, MAHARASHTRA, INDIA.
API Lot No.	5301-20-029
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×1's)
Stability storage condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months

	Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 24 (Months)		
Batch No.	T-09	T-10	T-11
Batch Size	500 Tube	500 Tube	500 Tube
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	02-04-2021	02-04-2021	02-04-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Provided
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.17133/2019/DRAP-AD-CD(I&E) dated 26/12/2019 is submitted wherein the permission to import different APIs including Paroxetine HCl for the purpose of test/analysis and stability studies is granted. • DHL No.XMLPI6.2/90-1504 dated 22/07/2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Observations	Response of Firm
Submit valid GMP certificate as provided is expired.	**Not Submitted**
Clarification regarding mentioning Route of administration as oral instead of topical.	**Corrected as Topical**
Approval/ GMP Certificate of API manufacturing facility issued by relevant regulatory authority.	**Not Submitted**
Reference of public assessment report is not provided while it is mandatory for non-pharmacopoeial products.	**Not Submitted**
API specifications provided by drug substance manufacturer are not readable.	**Provided**
Summary of verification of analytical procedures for drug substance is not provided.	**Provided**
Container closure system is indicating 15 g Cream while applied product is 60g cream.	**Corrected**
Section 1.5.10 indicates pre-printed Aluminum tube while container closure system in 3.2.P.1 (d) indicates polypropylene dispenser tube.	**Pre-printed Aluminium Tube is confirmed.**

Cetyl Alcohol, All-rac-α-tocopherol, liquid paraffin, White soft paraffin and Potassium Sorbate are indicated as excipients while these excipients are not mentioned in 2.3.P.1(b).	**Corrected as Typo error**
Formulation Development is not provided.	**Formulation development is not provided.**
Maximum holding time of bulk before final packing is not submitted	**Not Provided.**
In process validation protocol, Appearance is mentioned as Off white to light yellow cream while in product specification appearance is as Clear Colourless cream.	**Not Provided.**
Test to check the amount of S enantiomer is not included in drug product specifications while it is being performed by the Innovator.	**Not Performed.**
Justification of non-applicability of Characterization of Impurities.	**Not Provided.**
Justification of specifications is not provided.	**Not Provided.**
Calrification of different Drug substance manufacturer in Module-II & Module-III.	**Corrected**
COA of drug substance from drug substance manufacturer is not provided.	**Provided report indicates results from both API manufacturer & FPP manufacturer.**
Stability data of drug substance is not readable.	**Provided.**
pH, Viscosity and Particulate Matter is not tested during Pharmaceutical Equivalence.	**pH & Viscosity tests are provided.**
Provided data is for oral dosage form instead of topical dosage form.	**Provided**
Information regarding Physicochemical and Biological properties is not provided	**Not Provided**
Justification of critical steps of manufacturing process is not provided.	**Provided**
Process Validation protocol indicates Sifting, Melting, Milling, Congealing & Cooling as processing steps while these steps are not indicated in description of manufacturing process & flow diagram.	**Not Provided**
Justification of not performing Identification & Particulate matter tests during stability studies. Compliance record of HPLC software 21CFR & audit trail reports on product testing. Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated). Clarification of 24 months demanded shelf life while Innovator has shelf life of 18 months.	**The firm submitted that HPLC is not 21CFR compliant. Rest are not provided.**

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings which have not been replied earlier, within six months.

422.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Jaskan Pharmaceutical (Pvt.) Ltd., Plot No. 50, Sunder Industrial Estate, Lahore**
	Name, address of Manufacturing site.	M/s Jaskan Pharmaceutical (Pvt.) Ltd., Plot No. 50, Sunder Industrial Estate, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale

		☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 29542 dated 29/10/2021
	Details of fee submitted	PKR 30,000/-: dated 18-06-2021
	The proposed proprietary name / brand name	Clarkan 500mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated Tablet Contain: Clarithromycin..…….500mg
	Pharmaceutical form of applied drug	Tablet Oral
	Pharmacotherapeutic Group of (API)	Macrolide Antibiotics
	Reference to Finished product specifications	USP (United States Pharmacopoeia)
	Proposed Pack size	1x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Clarithromycin 500mg film-coated tablets of M/s Red Knights Pharma Ltd., UK
	For generic drugs (me-too status)	Macrocid 500mg Tablet of M/s Don Valley Pharmaceuticals (Pvt.) Ltd., Lahore Reg. No. 101872
	GMP status of the Finished product manufacturer	cGMP No. 10/2021-DRAP (FID-797667-1346) dated 18-02-2021 issued by DRAP. DML renewal granted by Licensing Division w.e.f. 26-03-2019.
	Name and address of API manufacturer.	M/s Nexchem Pharmaceutical Co., Ltd. No. 1318 Jinsha street, Linjiang industrial zone, Wucheng Area, Jinhua city, Zhejiang Province, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Clarithromycin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30˚C ± 2˚C / 75% ± 5%RH for 60

		months Batches: (1304-509-FP018, 1304-509-FP020, 1304-509-FP022) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (1105-509-FP006, 1105-509-FP007, 1105-509-FP008)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence established vis-à-vis the brand leader, KLARICID Tablet 500mg by M/s Abbott Laboratories (Pakistan) Ltd by performing quality tests the results of all the tests of both products fall within the specifications and are comparable. The firm has performed comparative analyses with innovator's product. The studies demonstrate comparable results with the innovator product. Jaskan Pharmaceuticals has been performed against the same brand that is KLARICID Tablet 500mg by Abbott Laboratories (Pakistan) Ltd in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted reports of verification studies of analytical method for the drug substance. Firm has also submitted reports of validation of analytical method for the drug product.

STABILITY STUDY DATA

Manufacturer of API	M/s Nexchem Pharmaceutical Co., Ltd. No. 1318 Jinsha street, Linjiang industrial zone, Wucheng Area, Jinhua city, Zhejiang Province, China.		
API Lot No.	2006-5091-ws03		
Description of Pack (Container closure system)	Blister Pack of PVC and Aluminum print Foil.		
Stability Storage Condition	Real time: 30°C ± 2°C / 60% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 3 months Accelerated: 3 months		
Frequency	Accelerated: 0, 1, 2, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.	CL 01	CL 02	CL 03

Batch Size	1666 Tablets	1666 Tablets	1666 Tablets
Manufacturing Date	12-2020	12-2020	12-2020
Date of Initiation	16-12-2020	16-12-2020	16-12-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not Submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. ZJ20160068 dated 06-07-2016 issued China Food And Drug Administration valid till 06-06-2021.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not Submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

i. 1.5.4 Submit proposed pack size.
ii. 1.5.20 (a) & (b) Submit the undertakings.
iii. 1.6.5 Submit valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin as submitted is expired.
iv. 3.2.S.1.3 Submit clarification of difference in pH from pharmacopoeia monograph.
v. 3.2.P.2 Submit justification of non-applicability of compatibility studies of drug substance with excipients.
vi. 3.2.P.2 Submit information regarding key physicochemical characteristics of drug substance that can influence the performance of drug product.
vii. 3.2.P.2 Submit brief about choice of excipients, their concentrations and characteristics that can influence drug product performance.
viii. 3.2.P.2 Submit clarification of not performing Loss on Drying (LOD) test during Pharmaceutical Equivalence study.
ix. 3.2.P.2 Submit the Comparative dissolution profile (CDP) conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 as submitted CDP is in only one media.
x. 3.2.P.5 Submit clarification regarding not including Loss on Drying (LOD) test in finished product specification while it is included in pharmacopoeia monograph.
xi. 3.2.P.5 Submit detailed analytical procedures used for testing the drug product.
xii. 3.2.P.6 Submit COA of primary / secondary reference standard.
xiii. 3.2.P.8 Submit clarification of different lot no. in COA & stability data sheet.
xiv. 3.2.P.8 Submit clarification of Relative Humidity (RH) condition of 60%±5% instead of 65%±5%
xv. 3.2.P.8 Submit results of accelerated & real time stability data of 03 batches of the products for 06 months.
xvi. 3.2.P.8 Submit justification of batch size of 1666 tablets for stability studies.
xvii. Submit documents for the procurement of API with approval from DRAP (in case of import).

xviii. Submit compliance record of HPLC software 21CFR & audit trail reports on product testing. xix. Submit clarification as Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) indicates that temperature of the chamber got out of the limit of 30°C ± 2°C at multiple points.		
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		
423.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Honig Pharmaceutical Laboratories, Rawalpindi.**
	Name, address of Manufacturing site.	M/s Honig Pharmaceutical Laboratories, 14 km Adyala Road, Rawalpindi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 27301 dated 04-10-2021
	Details of fee submitted	PKR 20,000/-: dated 29/12/2020
	The proposed proprietary name / brand name	Faximin 550 mg tablets.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film coated tablet contains. Rifaximin……..550mg
	Pharmaceutical form of applied drug	Oral solid dosage form
	Pharmacotherapeutic Group of (API)	Rifaximin is a structural analog of rifampin and a non-systemic, gastrointestinal site-specific antibiotic
	Reference to Finished product specifications	BP Spec's
	Proposed Pack size	1X10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	MHRA Approved, Targaxan 550 mg tablet by NORGINE, Norgine House, Widewater Place, Moorhall Road, Harefield, Middlesex, UB9 6NS.
	For generic drugs (me-too status)	**Rifaxa** (Rifaximin... 550 mg) FEROZSONS Laboratories limited XIFAXA 550 mg TABLETS (Rifaximin... 550 mg) BROOKS. Pharma
	GMP status of the Finished product manufacturer	Not Provided.

	Name and address of API manufacturer.	AURORE Life sciences (Pvt) Ltd., Jubilee Enclave, HITEC City, Hyderabad, Telangana 500081, India.
	Module-II (Quality Overall Summary)	Firm has not completely filled QOS as per WHO QOS-PD template.
	Module III (Drug Substance)	Official monograph of Rifaximin 550 mg tablets is present in BP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, specifications, batch analysis and justification of specification, container closure system and stability studies of drug substance
	Stability studies (Drug Substance)	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: Accelerated (RMC0010718, RMC0010720, RMC0010719) Real time (RMC0010718, RMC0010716, RMC0010719)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including BET, testing) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the FOXAMINE tablet by CCL Pharma by performing quality tests (Identification, Assay, pH, Sterility, BET, Uniformity of dosage form, and Clarity of product). The results of Products are found equivalent to that of results of competitor product as well as with limit found in official pharmacopeia.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	AURORE Life sciences
API Lot No.	RMC0010718
Description of Pack (Container closure system)	ALU ALU BLISTER PACK OF 10 TABLETS.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 80°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months)

	Real Time: 0, 3, 6, 9, 12, 18 and 24 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	5000 Packs	5000 Packs	5000 Packs
Manufacturing Date	09-2018	09-2018	09-2018
Date of Initiation	25-08-2020	25-08-2020	25-08-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. IMC 20190118 issued by CFDA valid till 14/21/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Sample Invoice No JTRF210604-MQ dated June 8 2018, DRA letter 1824 Dated 22.06.18, Form 5 No 1042 Dated 22.06.18
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Stability supporting Data documents including chromatograms, Raw data sheets, COA, summary data sheets Submitted.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	21 CFR Compliance Certificate for Lab Solution-Shimadzu Submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Real and Accelerated Data Logger Record Submitted.

Remarks of Evaluator:

i. 1.3.4 Submit copy of valid DML
ii. 1.3.5 Submit GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years.
iii. 1.5.20 submit the commitment/ undertaking.
iv. 1.6.5 Information is not submitted.
v. QOS on WHO Template or template approved in 293rd meeting having data in light of Guidance document for submission of application on Form 5-F (CTD) for registration of pharmaceutical Drug products for human use.
vi. 3.2.S.3 Submit list of API related & process related impurities with their acceptance limit.
vii. 3.2.S.4.1 Description & Color of powder is different from official Pharmacopoeia monograph.
viii. 3.2.S.4.1 Solubility in methanol is not included in specifications while it is mentioned in BP monograph.
ix. 3.2.S.4.1 Assay limit is mentioned as Min. 99.91% while in BP monograph it is 97%-102%.
x. 3.2.S.4.2 Submit detailed analytical procedures for the testing of drug substance.
xi. 3.2.S.4.3 Submit Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer.
xii. 3.2.S.4.4 Batch size is different in COA of drug product manufacturer than from Batch Size in COA of API Manufacturer.
xiii. 3.2.S.5 Submit COA of reference standard.
xiv. 3.2.S.7.3 Submit reason of not performing related substance test during stability studies.
xv. 3.2.S.7.3 Submit clarification of similar results of all the tests performed during accelerated stability studies for all the batches at all time points.

xvi.	3.2.S.7.3 Submit clarification of different batches in real time & accelerated stability studies.
xvii.	3.2.P.1 Submit the description of dosage form as per CTD guidance document.
xviii.	3.2.P.2 Submit Brief on Pharmaceutical Development including discussion on Critical Quality Attributes (CQAs) & Critical Process Parameters (CPPs)
xix.	3.2.P.2 Maximum holding time of bulk before final packing is not submitted
xx.	3.2.P.2 Submit compatibility studies of drug substance with excipients which are not similar to Innovator product.
xxi.	Submit clarification of indicating different Pharmacopoeia references in different sections of dossier.
xxii.	3.2.P.2 Submit USP monograph of Rifaximin Tablet.
xxiii.	3.2.P.2 Submit clarification of not performing comparative dissolution profile (CDP) with Innovator product.
xxiv.	3.2.P.2 Clarification of using 75RPM speed in CDP while as per BP monograph it should be 50RPM.
xxv.	3.2.P.2 Clarification is required as value of similarity factor f2 is less than 50 in phosphate buffer pH 4.5 media.
xxvi.	3.2.P.2 Submit clarification of similar results of dissolution profile for all the batches at all time points.
xxvii.	3.2.P.3 Submit clarification as manufacturing process flow chart in process validation protocol is for capsule while instant application is of Tablet.
xxviii.	3.2.P.3 Justification of submitting only Compression process validation protocol while other steps are also involved in manufacturing process.
xxix.	3.2.P.3 Submit clarification as Compression process validation protocol does not specify the speed for which validation is done.
xxx.	3.2.P.5 Clarification of different specifications of the product from official pharmacopoeia monograph.
xxxi.	3.2.P.6 Submit COA of reference standard.
xxxii.	3.2.P.8 Testing frequency is not correct in post-approval stability protocol.
xxxiii.	3.2.P.8 Submit results of accelerated & real time stability data of 03 batches of the products as per CTD guidance document.
xxxiv.	Approval of API manufacturing facility by regulatory authority of country of origin
xxxv.	Documents for the procurement of API with approval from DRAP (in case of import).
xxxvi.	Compliance record of HPLC software 21CFR & audit trail reports on product testing.
xxxvii.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	

424.	**Name, address of Applicant / Marketing Authorization Holder**	**M/s Ophth Pharma (Pvt) Ltd, Plot No. 241, Sector 24, Korangi Industrial Area,Karachi.**
	Name, address of Manufacturing site.	M/s Ophth Pharma (Pvt) Ltd, Plot No. 241, Sector 24, Korangi Industrial Area,Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 30258 dated 05-11-2021
	Details of fee submitted	PKR 50,000/- dated 19-01-2021
	The proposed proprietary name / brand name	**Mydraine Intracameral Injection**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each ml contains: Tropicamide……..0.2mg Phenylephrine HCl…….3.1mg Lidocaine HCl……..10mg
	Pharmaceutical form of applied drug	Clear, Colorless Aqueous Solution
	Pharmacotherapeutic Group of (API)	Anticholinergic
	Reference to Finished product specifications	Manufacturer's Specifications
	Proposed Pack size	20 x 0.6ml
	Proposed unit price	Not Provided.
	The status in reference regulatory authorities	Mydrane 0.2 mg/ml + 3.1 mg/ml + 10 mg/ml solution for injection by M/s Laboratoires Thea, France MHRA Approved. Also approved in France & Germany.
	For generic drugs (me-too status)	Not Provided.
	GMP status of the Finished product manufacturer	M/s Ophth Pharma (Pvt.) Ltd., Copy of GMP certificate No. 121/2020-DRAP(K) dated 02-10-2020 issued on the basis of inspection conducted on 27-09-2019
	Name and address of API manufacturer.	**Tropicamide** M/s Medigraph Pharmaceuticals Pvt. Ltd., Plot No. J-46/57, M.I.D.C., Taloja Dist. Raigad, Maharashtra 410208, India. **Phenylephrine HCL:** M/s Aarti Industries Limited, Unit-IV, Plot No. E-50, MIDC, Tarapur, Taluka & District- Palghar, Pin-401506, Maharashtra, India. **Lidocaine HCl:** M/s Gufic Bioscience Limited, National Highway No. 8, Noor Grid, Al Post Kabilpore-396 242, Dist Navsan (Gujarat), India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, specifications, batch analysis and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, specifications, batch analysis and stability studies of drug substance
	Stability studies	Stability study conditions: **Tropicamide:**

		Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: PB/TD/007/07/10, PB/TD/008/07/10, PB/TD/009/07/10. **Phenylephrine HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: PEP(U)/II/1107/51/055, PEP(U)/II/1107/51/056, PEP(U)/II/1107/51/057. **Lidocaine HCl:** Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: 1159, 1160, 1161.
	Module-III (Drug Product):	The firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, control of excipients, control of drug product. Specifications, analytical procedures, verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for their product against the Mydrane 0.2 mg/ml + 3.1 mg/ml + 10 mg/ml solution for injection by M/s Laboratoires Thea, France. The results of all the tests of both products falls within the specifications and are comparable.
	Analytical method validation/verification of product	Method verification studies have been submitted including accuracy, precision, specificity, repeatability, linearity.

STABILITY STUDY DATA	
Manufacturer of API	**Tropicamide** M/s Medigraph Pharmaceuticals Pvt. Ltd., Plot No. J-46/57, M.I.D.C., Taloja Dist. Raigad, Maharashtra 410208, India. **Phenylephrine HCL:** M/s Aarti Industries Limited, Unit-IV, Plot No. E-50, MIDC, Tarapur, Taluka & District- Palghar, Pin-401506, Maharashtra, India. **Lidocaine HCl:** M/s Gufic Bioscience Limited, National Highway No. 8, Noor Grid, Al Post Kabilpore-396 242, Dist Navsan (Gujarat), India.
API Lot No.	
Description of Pack (Container closure system)	Glass Ampoule
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months

Frequency	Accelerated: 0,3,6 months Real Time: 0,3,6 months		
Batch No.	TB-101	TB-102	TB-103
Batch Size	1666 Ampoules	1666 Ampoules	1666 Ampoules
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	03-06-2020	09-06-2020	25-06-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not Provided
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not Submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not Submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted.

Remarks OF Evaluator:

i. Fee as per relevant SRO is required.
ii. 1.5.1 Submit information as per CTD guidance document.
iii. 1.5.2 Submit information as per CTD guidance document.
iv. 1.5.4 Submit proposed MRP
v. 1.5.5 Submit Pharmacotherapeutic groups of APIs.
vi. 1.5.6 Submit Pharmacopoeial Reference of applied formulation
vii. 1.5.8 Submit information as per CTD guidance document.
viii. 1.5.10 Submit information as per CTD guidance document.
ix. 1.5.20 Submit the undertakings.
x. 2.3.S Submit QOS for all the APIs as per CTD guidance document.
xi. 3.2.S.3 Submit information as per CTD guidance document for all the APIs.
xii. 3.2.S.4 Submit clarification as melting point mentioned in physicochemical properties is 96^0C -100^0C which is different from BP monograph.
xiii. 3.2.S.4 Submit clarification as solubility mentioned in physicochemical properties is different from BP monograph.
xiv. 3.2.S.4 Submit detailed analytical procedures for the testing of all the APIs.
xv. 3.2.S.4 Submit Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for all the APIs.

xvi.	3.2.S.4 Submit clarification as batch no. is not indicated in COAs of all the APIs of drug product manufacturer.
xvii.	3.2.S.4 Submit clarification of difference in limit of optical rotation in batch analysis (-42.0^{o} to -47.5^{o}) and in USP monograph (-43.0^{o} to -47^{o}) of Phenylephrine HCL.
xviii.	3.2.S.4 Submit clarification of difference in limit of Assay in batch analysis & stability studies (97.5% to 102.5%) from USP monograph (98%-102%) of Phenylephrine HCL.
xix.	3.2.S.4 Submit clarification of difference in limit of Impurities in batch analysis and in USP monograph of Phenylephrine HCL.
xx.	3.2.S.5 Submit COA of primary / secondary reference standard including source and lot number for all the APIs.
xxi.	3.2.S.6 Submit Description of the container closure system(s) for the shipment and storage of all the APIs including materials of construction of each primary packaging component.
xxii.	3.2.S.7 Submit clarification of difference in limit of Impurity A in batch analysis (NMT 0.15%) and in stability study of Tropicamide (NMT 0.2%)
xxiii.	3.2.P.2 Submit clarification as in excipient compatibility studies, the theoretical contents of Tropicamide are mentioned as 0.1mg/ml while as per composition, it is 0.2mg/ml.
xxiv.	3.2.P.2 Submit clarification that how %age recovery of Lidocaine HCl in excipient compatibility studies is 100.2%, 99.8% & 101.0% while the theoretical contents of Tropicamide are mentioned as 10mg/ml and actual contents are mentioned as 5.01, 4.99 & 5.05.
xxv.	3.2.P.2 Submit brief discussion for the key physicochemical characteristics (e.g. water content, solubility, particle size distribution, polymorphic or solid state form) of the APIs that can influence the performance of the Drug Product.
xxvi.	3.2.P.2 Submit detailed procedure used to test assay equivalence and release equivalence in Pharmaceutical Equivalence Studies.
xxvii.	3.2.P.3 Submit detailed manufacturing process indicating step numbers.
xxviii.	3.2.P.3 Submit the details of critical steps and points at which process controls, intermediate tests or final product controls are conducted along with tests and acceptance criteria (with justification, including experimental data).
xxix.	3.2.P.3 Submit a brief description of process validation including the proposed protocolalong with commitment to perform process validation on first three consecutive batches of commercial scale.
xxx.	3.2.P.5 Submit clarification of using spectrophotometry for assay of Phenylephrine instead of HPLC.
xxxi.	3.2.P.5 Submit Batch Analysis of two locally manufactured batches.
xxxii.	3.2.P.5 Submit detail of impurities that are degradation products.
xxxiii.	3.2.P.5 Submit justification of specifications of finished drug.
xxxiv.	3.2.P.6 Submit COAs of reference standards.
xxxv.	3.2.P.7 Submit complete description of container closure system along with capacity & construct of ampoule.
xxxvi.	3.2.P.8 Submit scientific rational of batch size selected for stability studies.
xxxvii.	Approval of APIs manufacturing facilities by regulatory authority of country of origin
xxviii.	Documents for the procurement of APIs with approval from DRAP.
xxxix.	Compliance record of HPLC software 21CFR & audit trail reports on product testing.
xl.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

Item No. XIII: Agenda of Evaluator-XIII (Mr. Shahid Nawaz)

Case 01; Export Facilitation:

a. Registration applications of locally manufactured Human Drugs of Export Facilitation on form 5F.

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the *pharmaceutical* i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year.
In compliance to the aforementioned decision of the Board, Assistant Director (PR-I/EFD) vide letter No. F.1-6/2019-PR-I (EFD) dated 06th October, 2022 has informed that **M/s Surge Laboratories (Pvt.) Ltd, Sheikhupura** has achieved the benchmark of more than **100,000 USD (790529.78 USD)** during the fiscal Year 2019-2020 and submitted their applications for priority consideration/ evaluation.
Following products are presented before the Board in light of the decision of the 133rd meeting of DRAP Authority held on 13th April 2022 for consideration.

425.	Name, address of Applicant / Marketing Authorization Holder	M/s. Surge Laboratories (Pvt.) Ltd., 10th Km, Faisalabad road, Bikhi, District Sheikhupura.
	Name, address of Manufacturing site.	M/s Nabi Qasim Industries Private Limited, 17 / 24, Korangi Industrial Area, Karachi.
	Status of the applicant	☐Manufacturer ☐ Importer ☒Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 4646 dated 18-02-2022.
	Details of fee submitted	PKR 30,000/- vide slip No.9509332184 dated 12/01/2022. PKR 45,000/- vide slip No.65562075 dated 08/02/2022.
	The proposed proprietary name / brand name	Prexa Tablets 5mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Escitalopram as Oxalate …….. ……..5mg
	Pharmaceutical form of applied drug	A Light yellow colored, Square shape film coated tablet, one side Plain while other side engraved by (+) sign.
	Pharmacotherapeutic Group of (API)	Selective Serotonin Reuptake Inhibitor (SSRI), Anti-Depressant (N06AB)
	Reference to Finished product specifications	USP Specifications.

	Proposed Pack size	1×14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cipralex 5mg film coated Tablets, (Escitalopram as oxalate) MHRA approved.
	For generic drugs (me-too status)	Citanew Tablets 5mg by M/s Hilton Pharma (Pvt.) Ltd., Reg. No. 037707
	GMP status of the Finished product manufacturer	**M/s Nabi Qasim Industries Private Limited,** Copy of GMP certificate No.63/2022-DRAP (K) dated 28-05-2022 on the basis of inspection conducted on 27-05-2022 is submitted. **M/s. Surge Laboratories (Pvt.) Ltd.,** Not submitted.
	Evidence of section approval.	Tablet general section approved vide letter No. F.2-20/85-Lic. (Vol-V) dated 27-04-2020.
	Name and address of API manufacturer.	M/s**.** Alcon Biosciences Private Limited, Plot No. A-I/2014, phase III, G.I.D.C. Vapi -396 195, Dist. – Valsad, Gujrat –India. Copy of GMP certificate No. S-GMP/20102297 in the name of M/s**.** Alcon Biosciences Private Limited, issued by Food & Drug Control Administration Gandhinagar, Gujrat, India valid till 21-10-2022 is submitted.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (5-Dimethylamino butyrylcitalopram, Citalopram related compound A, Citalopram related compound B (3- hydroxyl citalopram) , Citalopram related compound C (3– oxocitalopram), Citalopram related compound D (desmethyl citalopram), Citalopram related compound E (citalopram N-Oxide) , Any other Individual unspecified impurity, Total Impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 36 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months

		Batches: (ALC/ESO/180703, ALC/ESO/180704, ALC/ESO/180705)
	Module-III (Drug Product):	The firm has submitted detail of the description and composition of the drug product, manufacturers, description of manufacturing process and controls, Process validation, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the brand leader that is Citanew Tablet 5mg, Batch No. 138276, Mfg. date March, 2021 manufactured by Hilton Pharma, by performing quality tests (Description, Identification, Dissolution and Assay). Results of both the products are comparable with each other. Comparative Dissolution Profile is also performed against the same brand that is Citanew Tablet 5mg, Batch No. 138276, Mfg. date March, 2021 manufactured by M/s Hilton Pharma (Pvt.) Ltd., in acidic and Buffer mediums i.e. 0.1 N HCL medium pH 1.2, Acetate Buffer medium pH 4.5 & Phosphate Buffer medium pH 6.8). Values of F2 are not calculated as more than 85% release is observed in all the three mediums in 15 minute time point.
	Analytical method validation/verification of product	Method verification studies have submitted including specificity, accuracy (recovery), precision, linearity& range.

STABILITY STUDY DATA			
Manufacturer of API	M/s**.** Alcon Biosciences Private Limited, Plot No. A-I/2014, phase III, G.I.D.C. Vapi -396 195, Dist. – Valsad, Gujrat –India.		
API Lot No.	ESO/FPR/007/20		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (1×14's).		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MA0121.	MA0221	MA0321
Batch Size	3000 tablets.	3000 tablets	3000 tablets
Manufacturing Date	05-2021.	05-2021	05-2021
Date of Initiation	14-05-2021.	14-05-2021	14-05-2021
No. of Batches	03		
Administrative Portion			

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. S-GMP/20102297 in the name of M/s**.** Alcon Biosciences Private Limited, issued by Food & Drug Control Administration Gandhinagar, Gujrat, India valid till 21-10-2022 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice No. AB/V00144/20-21 dated 28-01-2021 mentioning 1kg quantity of Escitalopram Oxalate USP, batch No. ESO/FPR/007/20, Mfg. date December, 2020 duly attested by Assistant Director, DRAP, Karachi on 16-02-2021 is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Section	Observation	Reply by the firm
1.	1.3.4	Valid copy of GMP certificate/last inspection report of the applicant shall be submitted.	Copy of GMP certificate No. 41/202-DRAP(Ad-9978029213) dated 05-04-2022 issued on the basis of inspection conducted on 05-10-2021 is submitted.
2.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer shall be submitted.	Firm has once again submitted copy of GMP certificate No. S-GMP/20102297 in the name of M/s**.** Alcon Biosciences Private Limited, issued by Food & Drug Control Administration Gandhinagar, Gujrat, India valid till 21-10-2022 is submitted. **Not valid.** Firm has also submitted copy of Retention of license issued by Commissioner Food & Drugs Control Administration, Gujrat State of India wherein M/s Alcon Biosciences P Ltd., has been retained from 01-01-2022 to 31-12-2026.
3.	3.2.P.2	Justification for not performing CDP against the innovator product.	Firm has submitted that at the time of development, the innovator product Cipralex 5mg was not available, that's why CDP studies were performed with the comparator product "Citanew tablets

			5mg" as per the guidance document No. PE&R/GL/AF/004 issued by DRAP.
4.	3.2.P.8	Stability study data of commercial batches shall be submitted.	Firm has submitted that in 321st meeting of Registration Board, it was decided that the product development data/stability data of trial batches manufactured by contract manufacturer will also be acceptable.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

426.	Name, address of Applicant / Marketing Authorization Holder	M/s. Surge Laboratories (Pvt.) Ltd., 10th Km, Faisalabad road, Bikhi, District Sheikhupura.
	Name, address of Manufacturing site.	M/s Nabi Qasim Industries Private Limited, 17 / 24, Korangi Industrial Area, Karachi.
	Status of the applicant	☐Manufacturer ☐ Importer ☒Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 4647 dated 18-02-2022.
	Details of fee submitted	PKR 30,000/- vide slip No.73252091018 dated 12/01/2022. PKR 45,000/- vide slip No.9287160241 dated 08/02/2022.
	The proposed proprietary name / brand name	Prexa Tablets 20mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film-coated tablet contains: Escitalopram as Oxalate …….. ……..20mg
	Pharmaceutical form of applied drug	Purple colored, Square shape film coated tablet, one side Plain while other side engraved by (+) sign.
	Pharmacotherapeutic Group of (API)	Selective Serotonin Reuptake Inhibitor (SSRI), Anti-Depressant (N06AB)
	Reference to Finished product specifications	USP Specifications.
	Proposed Pack size	1×14's
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	Cipralex 20mg film coated Tablets, (Escitalopram as oxalate) MHRA approved.

	For generic drugs (me-too status)	Citanew Tablets 20mg by M/s Hilton Pharma (Pvt.) Ltd., Reg. No. 037681.
	GMP status of the Finished product manufacturer	**M/s Nabi Qasim Industries Private Limited,** Copy of GMP certificate No. 124/2020-DRAP (K) dated 06-10-2020 on the basis of inspection conducted on 19-09-2020 is submitted. **M/s. Surge Laboratories (Pvt.) Ltd.,** Not submitted.
	Evidence of section approval.	Tablet general section approved vide letter No. F.2-20/85-Lic. (Vol-V) dated 27-04-2020.
	Name and address of API manufacturer.	M/s**.** Alcon Biosciences Private Limited, Plot No. A-I/2014, phase III, G.I.D.C. Vapi -396 195, Dist. – Valsad, Gujrat –India. Copy of GMP certificate No. S-GMP/20102297 in the name of M/s**.** Alcon Biosciences Private Limited, issued by Food & Drug Control Administration Gandhinagar, Gujrat, India valid till 21-10-2022 is submitted.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification / validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (5-Dimethylamino butyryl citalopram, Citalopram related compound A, Citalopram related compound B (3- hydroxyl citalopram) , Citalopram related compound C (3– oxocitalopram), Citalopram related compound D (desmethyl citalopram), Citalopram related compound E (citalopram N-Oxide) , Any other Individual unspecified impurity, Total Impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 36 months Accelerated: 40˚C ± 2˚C / 75% ± 5%RH for 6 months Batches: (ALC/ESO/180703, ALC/ESO/180704, ALC/ESO/180705)
	Module-III (Drug Product):	The firm has submitted detail of the description and composition of the drug product, manufacturers,

		description of manufacturing process and controls, Process validation, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the brand leader that is Cipralex Tablet 20mg, Batch No. 2689852, Mfg. date March, 2021 registered and being marketed by H. Lundbeck Pakistan by performing quality tests (Description, Identification, Dissolution and Assay). Results of both the products are comparable with each other. Comparative Dissolution Profile is also performed against the same brand that is Cipralex Tablet 20mg, Batch No. 2689852, Mfg. date March, 2021 registered and being marketed by H. Lundbeck Pakistan., in acidic and Buffer mediums i.e. 0.1 N HCL medium pH 1.2, Acetate Buffer medium pH 4.5 & Phosphate Buffer medium pH 6.8). Values of F2 are not calculated as more than 85% release is observed in all the three mediums in 15 minute time point.
	Analytical method validation/verification of product	Method verification studies have submitted including specificity, accuracy (recovery), precision, linearity& range.

STABILITY STUDY DATA			
Manufacturer of API	M/s**.** Alcon Biosciences Private Limited, Plot No. A-I/2014, phase III, G.I.D.C. Vapi -396 195, Dist. – Valsad, Gujrat –India.		
API Lot No.	ESO/FPR/007/20		
Description of Pack (Container closure system)	Alu-PVC blister packed in unit carton (1×14's).		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MA0421.	MA0521	MA0621
Batch Size	3000 tablets.	3000 tablets	3000 tablets
Manufacturing Date	05-2021.	05-2021	05-2021
Date of Initiation	14-05-2021.	14-05-2021	14-05-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. S-GMP/20102297 in the name of M/s**.** Alcon Biosciences Private Limited, issued by Food & Drug Control Administration Gandhinagar, Gujrat, India valid till 21-10-2022 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of commercial invoice No. AB/V00144/20-21 dated 28-01-2021 mentioning 1kg quantity of Escitalopram Oxalate USP, batch No. ESO/FPR/007/20, Mfg. date December, 2020 duly attested by Assistant Director, DRAP, Karachi on 16-02-2021 is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Section	Observation	Reply by the firm
1.	1.3.4	Valid copy of GMP certificate/last inspection report of the applicant shall be submitted.	Copy of GMP certificate No. 41/202-DRAP(Ad-9978029213) dated 05-04-2022 issued on the basis of inspection conducted on 05-10-2021 is submitted.
2.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer shall be submitted.	Firm has once again submitted copy of GMP certificate No. S-GMP/20102297 in the name of M/s**.** Alcon Biosciences Private Limited, issued by Food & Drug Control Administration Gandhinagar, Gujrat, India valid till 21-10-2022 is submitted. **Not valid.** Firm has also submitted copy of Retention of license issued by Commissioner Food & Drugs Control Administration, Gujrat State of India wherein M/s Alcon Biosciences P Ltd., has been retained from 01-01-2022 to 31-12-2026.
3.	3.2.P.8	Stability study data of commercial batches shall be submitted.	Firm has submitted that in 321st meeting of Registration Board, it was decided that the product development data/stability data of trial batches manufactured by contract manufacturer will also be acceptable.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the *pharmaceutical* i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year.

In compliance to the aforementioned decision of the Board, Assistant Director (PR-I/EFD) vide letter No. F.1-6/2019-PR-I (EFD) dated 06th October, 2022 has informed that **M/s Surge Laboratories (Pvt.) Ltd, Sheikhupura** has achieved the benchmark of more than **100,000 USD (793,404.76)** during the fiscal Year 2019-2020 and submitted their applications for priority consideration/ evaluation.

Following products are presented before the Board in light of the decision of the 133rd meeting of DRAP Authority held on 13th April 2022 for consideration.

427.	Name, address of Applicant / Marketing Authorization Holder	M/s Tabros Pharma (Pvt.) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Tabros Pharma (Pvt.) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11094 dated 07-05-2022.
	Details of fee submitted	PKR 75,000/- dated 23-04-2022.
	The proposed proprietary name / brand name	RAST-VT TABLET 10mg/80mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Rosuvastatin Calcium equivalent to Rosuvastatin ……. 10mg Valsartan ……... 80mg
	Pharmaceutical form of applied drug	Light red color, round, biconvex film coated tablets.
	Pharmacotherapeutic Group of (API)	Lipid modifying agents in combination with other drugs (C10BX)
	Reference to Finished product specifications	Tabros Specifications.
	Proposed Pack size	2×14's
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	Rosuvastatin/Valsartan HCS, Marketing Authorization Holder HCS bvba, Germany, (10 mg/80 mg, 20 mg/80 mg, 10 mg/160 mg, 20mg/160 mg) Germany Approved. Belgium approved. VALAROX 10/80mg Tablet by KRKA. d.d., Novomesto, Bulgaria, Latvia Ravalsyo in Slovenia & Hungry.
	For generic drugs (me-too status)	N/A.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conducted on 28-02-2020

	Evidence of section approval.	Tablet section vide letter No. F.2-5/87-Lic. (Vol-III) 30-06-2020.
	Name and address of API manufacturer.	Rosuvastatin Calcium: Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. The firm has submitted copy of GMP certificate No. DE-BE-01-GMP-2019-0042 for M/s Ruyuan HEC Pharm Co. Ltd., wherein the competent authority of Germany has confirmed that the knowledge gained during the inspection of the above said manufacturer, the latest of which was conducted on 29-11-2019, it is considered that it complies with the Good Manufacturing Practice requirements referred to in "the principles of GMP for active substances referred to in" Article 47 of Directive 2001/83/EC. The certificate is valid till 29th 11, 2022. Valsartan: Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China. Copy of GMP certificate No. GD20190988 dated 11-04-2019 in the name of M/s Zhuhai Rundu Pharmaceutical Co., Ltd., valid till 10-04-2024 is submitted.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per template provided in 293rd meeting of Registration Board.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data for rosuvastatin calcium related to general information, nomenclature, structure, general properties, solubility, physical description, manufacturer, Characterization, impurities, Specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Firm has also submitted detailed drug substance data for Valsartan related to general information, nomenclature, structure, general properties, solubility, physical description, manufacturer, Characterization, impurities, Specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies (Drug Substance)	**Rosuvastatin Calcium;** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (RSV-201803001, RSV-201803002 & RSV-201803003). **Valsartan;** Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (64614080101, 64614080102 & 64614080103)
	Module-III (Drug Product):	Firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, control of critical steps and intermediate, process validation protocols , control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the VALAROX 10/80mg Tablet manufactured by KRKA. d.d., Novomesto, Bulgaria by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is VALAROX 10/80mg Tablet manufactured by KRKA. d.d., Novomesto, in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory.
	Analytical method validation /verification of product	Method validation studies for finished product have submitted including following parameters: Linearity & range, Accuracy, Precision, Specificity, Detection limit, Quantitation limit, Robustness, Stability indicating, Solution stability, Analytical method validation for drug substance performed by drug product manufacturer also submitted including following parameters: Linearity & Range, Accuracy, Precision & Specificity.

STABILITY STUDY DATA

Manufacturer of API	**<u>Rosuvastatin Calcium:</u>** Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. **<u>Valsartan:</u>** Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China.		
API Lot No.	Valsartan: 67820030607 Rosuvastatin Calcium: RSV-(RD)202010604(WI)		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TR001-4/RVT	TR002-4/RVT	TR003-4/RVT
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets

Manufacturing Date		09.2021	09-2021	09-2021
Date of Initiation		22.11.2021	22.11.2021	22.11.2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred last onsite panel inspection for instant dosage form conducted during last two years BAXIB (Apixaban) 2.5mg & 5mg Tablets on 5th January, 2021 by following panel: 1. Prof. Dr. Rafeeq Alam Khan, Dean, Faculty of Pharmacy, Zia Uddin University, Karachi. (Member Registration Board). 2. Dr. Saif-ur-Rehman Khattak, Director / FGA, CDL, DRAP, Karachi. • The HPLC software is 21 CFR complaint. • Audit trials on the testing reports of Baxib tablets were available.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Rosuvastatin Calcium:** Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. The firm has submitted copy of GMP certificate No. DE-BE-01-GMP-2019-0042 for M/s Ruyuan HEC Pharm Co. Ltd., wherein the competent authority of Germany has confirmed that the knowledge gained during the inspection of the above said manufacturer, the latest of which was conducted on 29-11-2019, it is considered that it complies with the Good Manufacturing Practice requirements referred to in "the principles of GMP for active substances referred to in" Article 47 of Directive 2001/83/EC. The certificate is valid till 29th 11, 2022. **Valsartan:** Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China. Copy of GMP certificate No. GD20190988 dated 11-04-2019 in the name of M/s Zhuhai Rundu Pharmaceutical Co., Ltd., valid till 10-04-2024 is submitted.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Rosuvastatin Calcium:** Firm has submitted copy of commercial invoice number WIS200291 dated December, mentioning 50Kg quantity of Rosuvastatin Calcium attested by Assistant Director, I & E, DRAP Karachi dated 23-12-2020. ADC signed Form 5 & Invoice are available while Form 3 & Form 7 are also available. **Valsartan:** Firm has submitted copy of commercial invoice No. RD-2020041301-1 dated 16-04-2020 mentioning 650Kg quantity of Valsartan with Batch No. 67820030607, Mfg. date March, 2020 & retest date of		

		February, 2023 attested by Assistant Director I & E, DRAP Karachi dated 27-04-2020. *The utilization is restricted for sampling and for submission & endorsement of certificate of analysis for NDMA & EDMA impurities.* ADC signed Form 5 & Invoice are available while Form 3 & Form 7 are also available.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section No.	Observation	Response by the firm
1.	3.2.S.4.1	• Justification for specification for water determination shall be submitted as the Finished Product manufacturer has provided NMT 6% while drug substance manufacturer has NMT 3.5%. • Assay limit of valsartan is 98% in USP while FPP has mentioned 98.5%. justify.	Firm has submitted that they have followed USP specification for the testing of Rosuvastatin calcium & in USP monograph limit of water content is NMT 6% while drug substance manufacturer has 3.5-4.5% which is in-house. Assay limit of valsartan in USP is 98-102% and we have followed for the same & submitted accordingly.
2.	3.2.S.4.2	Analytical procedures for the drug substance rosuvastatin calcium used by the drug substance manufacturer shall be submitted.	Submitted.
3.	3.2.S.4.4	Certificate of analysis for NDMA and EDMA impurities in the drug substance i.e. valsartan after clearance from DRAP shall be submitted as the utilization was restricted for sampling and for submission & endorsement of certificate of analysis for NDMA & EDMA impurities.	Firm has submitted the same commercial invoice submitted above with following remarks of the Assistant Director, DRAP, Karachi; "COA regarding impurities was checked and utilization allowed." They further referred to a decision of Registration Board in its 312th meeting, wherein in point "a" it is decided by the Board that; *a. The manufacturers of Valsartan API which have valid certificate of suitability as per EDQM or any other Reference Regulatory Authorities (RRAs), as adopted by the Registration Board, are exempted from NDMA/NDEA testing on every consignment.*

			b. Import of Valsartan API by DML holders from manufacturers not covered in point a shall be subject to testing as per decision of 291st meeting of Registration Board. *However, neither any certificates for NDMA and EDMA impurities in the drug substance is provided by the firm nor any valid certificate of suitability as per EDQM or any other Reference Regulatory Authorities (RRAs), as adopted by the Registration Board.*
4.	3.2.P.2.2	Justification for not performing CDP & PE against the Reference Regulatory Authority country product.	Firm has stated that Pharmaceutical equivalence and CDP studies against the reference product of "Valarox Tablets" in three dissolution medium has been submitted with a acceptance level of F2 results. Although the product is available in Germany with the brand name of Rosuvastatin/valsartan HCS film coated tablets which is sufficient reference for RRA country. Furthermore, based on reference regulatory authorities by the DRAP in 275th DRB meeting, in which it has clearly mentioned that at least three EU countries product should be available as reference for consideration of registration board of the product. Reference products are also available more than three EU countries which are as follows: • Bulgaria & Latvia with the brand name of Valarox. • Slovenia & Hungry with the brand name of Ravalsyo.
5.	3.2.P.5.2	Provide scientific rationale for selection of dissolution parameters including type of apparatus, rpm, dissolution medium, sampling time and the analytical method.	The scientific rational for selection of dissolution medium and type of apparatus carried out, based on FPP of Valsartan Tablets in the USP monograph, however, rpm and sample elapsed time set the parameters grounded on practical observation and In-House analytical method was developed, Dissolution method validation is being submitted as per ICH guidelines.
6.	3.2.P.3.3	• Manufacturing process has mentioned bilayer tablets however, label claim has not mentioned. Justification shall be submitted.	Firm has submitted that they have followed same manufacturing procedure as similar as reference product. It is bilayer tablet & finally covered with film coating. Supportive/ Orientation document is attached for your ready reference where it is evidently mentioned film coated tablets, Hence, we are claiming film coated tablets.

		• Evidence of availability of bilayer tablet machine shall be submitted.	Firm has submitted that they are manufacturing the "**Cresar-AM**" bi-layer tablets on commercial scale and marketed accordingly since long time. They further submitted routine GMP inspection report of October, 2018 wherein it is mentioned in the report that the firm has recently purchased Rotary tablet press Machine ZP-31 (for double layer tablet manufacturing).
7.		The chromatograms provided for dissolution studies have run time of 6 minutes and column temperature is mentioned 40ºC. The method validated for assay has a run time of 65 minutes and column temperature is less than 40ºC. It appears as if the HPLC method used in dissolution is not validated. Justify/provide validation studies for HPLC method used in dissolution	Firm has submitted that the assay of SIM method and Dissolution method are developed separately having different chromatographic conditions, hence, both chromatographic conditions are seeming to be different. They further submitted dissolution method validation report which was not submitted in the initial submission.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

428.	Name, address of Applicant / Marketing Authorization Holder	M/s Tabros Pharma (Pvt.) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Tabros Pharma (Pvt.) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11094 dated 07-05-2022.
	Details of fee submitted	PKR 75,000/- dated 23-04-2024.
	The proposed proprietary name / brand name	RAST-VT TABLET 20mg/80mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Rosuvastatin Calcium equivalent to Rosuvastatin ……. 20mg Valsartan ……... 80mg

	Pharmaceutical form of applied drug	Light brown color, oblong, biconvex film coated tablets.
	Pharmacotherapeutic Group of (API)	Lipid modifying agents in combination with other drugs (C10BX)
	Reference to Finished product specifications	Tabros Specifications.
	Proposed Pack size	2×14's
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	Rosuvastatin/Valsartan HCS, Marketing Authorization Holder HCS bvba, Germany, (10 mg/80 mg, 20 mg/80 mg, 10 mg/160 mg, 20mg/160 mg) Germany Approved. VALAROX 20/80mg Tablet by KRKA. d.d., Novomesto, Bulgaria, Latvia Ravalsyo in Slovenia & Hungry.
	For generic drugs (me-too status)	N/A.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conducted on 28-02-2020
	Evidence of section approval.	Tablet section vide letter No. F.2-5/87-Lic. (Vol-III) 30-06-2020.
	Name and address of API manufacturer.	**Rosuvastatin Calcium:** Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. The firm has submitted copy of GMP certificate No. DE-BE-01-GMP-2019-0042 for M/s Ruyuan HEC Pharm Co. Ltd., wherein the competent authority of Germany has confirmed that the knowledge gained during the inspection of the above said manufacturer, the latest of which was conducted on 29-11-2019, it is considered that it complies with the Good Manufacturing Practice requirements referred to in "the principles of GMP for active substances referred to in" Article 47 of Directive 2001/83/EC. The certificate is valid till 29th 11, 2022. **Valsartan:** Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China. Copy of GMP certificate No. GD20190988 dated 11-04-2019 in the name of M/s Zhuhai Rundu Pharmaceutical Co., Ltd., valid till 10-04-2024 is submitted.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per template provided in 293rd meeting of Registration Board.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data for rosuvastatin calcium related to general information, nomenclature, structure, general properties, solubility, physical description, manufacturer, Characterization, impurities, Specifications, analytical procedures and its verification, batch analysis and justification of

		specification, reference standard, container closure system and stability studies of drug substance. Firm has also submitted detailed drug substance data for Valsartan related to general information, nomenclature, structure, general properties, solubility, physical description, manufacturer, Characterization, impurities, Specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies (Drug Substance)	**Rosuvastatin Calcium** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (RSV-201803001, RSV-201803002 & RSV-201803003). **Valsartan** Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (64614080101, 64614080102 & 64614080103)
	Module-III (Drug Product):	Firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, control of critical steps and intermediate, process validation protocols , control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the VALAROX 20/80mg Tablet Batch No. NJ2137 by KRKA. d.d., Novomesto, Bulgaria by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is VALAROX 20/80mg Tablet Batch No. NJ2137 by KRKA. d.d., Novomesto, in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory.
	Analytical method validation /verification of product	Method validation studies for finished product have submitted including following parameters: Linearity & range, Accuracy, Precision, Specificity, Detection limit, Quantitation limit, Robustness, Stability indicating, Solution stability, Analytical method validation for drug substance performed by drug product manufacturer also submitted including following parameters: Linearity & Range, Accuracy, Precision & Specificity.
STABILITY STUDY DATA		
Manufacturer of API	**<u>Rosuvastatin Calcium:</u>** Ruyuan HEC Pharm Co., Ltd.,	

	Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. **Valsartan:** Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China.		
API Lot No.	Valsartan: 67820030607 Rosuvastatin Calcium: RSV-(RD)202010604(WI)		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TR001-3/RVT	TR002-3/RVT	TR003-3/RVT
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	09.2021	09-2021	09-2021
Date of Initiation	22.11.2021	22.11.2021	22.11.2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred last onsite panel inspection for instant dosage form conducted during last two years BAXIB (Apixaban) 2.5mg & 5mg Tablets on 5th January, 2021 by following panel: 1. Prof. Dr. Rafeeq Alam Khan, Dean, Faculty of Pharmacy, Zia Uddin University, Karachi. (Member Registration Board). 2. Dr. Saif-ur-Rehman Khattak, Director / FGA, CDL, DRAP, Karachi. • The HPLC software is 21 CFR complaint. • Audit trials on the testing reports of Baxib tablets were available.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Rosuvastatin Calcium:** Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. The firm has submitted copy of GMP certificate No. DE-BE-01-GMP-2019-0042 for M/s Ruyuan HEC Pharm Co. Ltd., wherein the competent authority of Germany has confirmed that the knowledge gained during the inspection of the above said manufacturer, the latest of which was conducted on 29-11-2019, it is considered that it complies with the Good Manufacturing Practice requirements referred to in "the principles of GMP for active substances referred to in" Article 47 of Directive 2001/83/EC. The certificate is valid till 29th 11, 2022. **Valsartan:** Zhuhai Rundu Pharmaceutical Co., Ltd.,

		No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China. Copy of GMP certificate No. GD20190988 dated 11-04-2019 in the name of M/s Zhuhai Rundu Pharmaceutical Co., Ltd., valid till 10-04-2024 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Rosuvastatin Calcium:** Firm has submitted copy of commercial invoice number WIS200291 dated December, mentioning 50Kg quantity of Rosuvastatin Calcium attested by Assistant Director, I & E, DRAP Karachi dated 23-12-2020. ADC signed Form 5 & Invoice are available while Form 3 & Form 7 are also available. **Valsartan:** Firm has submitted copy of commercial invoice No. RD-2020041301-1 dated 16-04-2020 mentioning 650Kg quantity of Valsartan with Batch No. 67820030607, Mfg. date March, 2020 & retest date of February, 2023 attested by Assistant Director I & E, DRAP Karachi dated 27-04-2020. *The utilization is restricted for sampling and for submission & endorsement of certificate of analysis for NDMA & EDMA impurities.* ADC signed Form 5 & Invoice are available while Form 3 & Form 7 are also available.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Section No.	Observation	Response by the firm
1.	3.2.S.4.1	• Justification for specification for water determination shall be submitted as the Finished Product manufacturer has provided NMT 6% while drug substance manufacturer has NMT 3.5%. • Assay limit of valsartan is 98% in USP while FPP has mentioned 98.5%. justify.	Firm has submitted that they have followed USP specification for the testing of Rosuvastatin calcium & in USP monograph limit of water content is NMT 6% while drug substance manufacturer has 3.5-4.5% which is in-house.

			Assay limit of valsartan in USP is 98-102% and we have followed for the same & submitted accordingly.
2.	3.2.S.4.2	Analytical procedures for the drug substance rosuvastatin calcium used by the drug substance manufacturer shall be submitted.	Submitted.
3.	3.2.S.4.4	Certificate of analysis for NDMA and EDMA impurities in the drug substance i.e. valsartan after clearance from DRAP shall be submitted as the utilization was restricted for sampling and for submission & endorsement of certificate of analysis for NDMA & EDMA impurities.	Firm has submitted the same commercial invoice submitted above with following remarks of the Assistant Director, DRAP, Karachi; "COA regarding impurities was checked and utilization allowed." They further referred to a decision of Registration Board in its 312th meeting, wherein in point "a" it is decided by the Board that; *a. The manufacturers of Valsartan API which have valid certificate of suitability as per EDQM or any other Reference Regulatory Authorities (RRAs), as adopted by the Registration Board, are exempted from NDMA/NDEA testing on every consignment.* *b. Import of Valsartan API by DML holders from manufacturers not covered in point a shall be subject to testing as per decision of 291st meeting of Registration Board.* *However, neither any certificates for NDMA and EDMA impurities in the drug substance is provided by the firm nor any valid certificate of suitability as per EDQM or any other Reference Regulatory Authorities (RRAs), as adopted by the Registration Board.*
4.	3.2.P.2.2	Justification for not performing CDP & PE against the Reference Regulatory Authority country product.	Firm has stated that Pharmaceutical equivalence and CDP studies against the reference product of "Valarox Tablets" in three dissolution medium has been submitted with a acceptance level of F2 results. Although the product is available in Germany with the brand name of Rosuvastatin/valsartan HCS film coated tablets which is sufficient reference for RRA country. Furthermore, based on reference regulatory authorities by the DRAP in 275th DRB meeting, in which it has clearly mentioned that at least three EU countries product should be available as reference for consideration of registration board of the product.

			Reference products are also available more than three EU countries which are as follows: • Bulgaria & Latvia with the brand name of Valarox. Slovenia & Hungry with the brand name of Ravalsyo.
5.	3.2.P.5.2	Provide scientific rationale for selection of dissolution parameters including type of apparatus, rpm, dissolution medium, sampling time and the analytical method.	The scientific rational for selection of dissolution medium and type of apparatus carried out, based on FPP of Valsartan Tablets in the USP monograph, however, rpm and sample elapsed time set the parameters grounded on practical observation and In-House analytical method was developed, Dissolution method validation is being submitted as per ICH guidelines.
6.	3.2.P.3.3	• Manufacturing process has mentioned bilayer tablets however, label claim has not mentioned. Justification shall be submitted. • Evidence of availability of bilayer tablet machine shall be submitted.	Firm has submitted that they have followed same manufacturing procedure as similar as reference product. It is bilayer tablet & finally covered with film coating. Supportive/ Orientation document is attached for your ready reference where it is evidently mentioned film coated tablets, Hence, we are claiming film coated tablets. Firm has submitted that they are manufacturing the "**Cresar-AM**" bi-layer tablets on commercial scale and marketed accordingly since long time. They further submitted routine GMP inspection report of October, 2018 wherein it is mentioned in the report that the firm has recently purchased Rotary tablet press Machine ZP-31 (for double layer tablet manufacturing).
7.	3.2.P.2.2	• The chromatograms provided for dissolution studies have run time of 6 minutes and column temperature is mentioned 40ºC. The method validated for assay has a run time of 65 minutes and column temperature is less than 40ºC. It appears as if the HPLC method used in dissolution is not validated. • Justify/provide validation studies for HPLC method used in dissolution for the applied formulation.	Firm has submitted that the assay of SIM method and Dissolution method are developed separately having different chromatographic conditions, hence, both chromatographic conditions are seeming to be different. They further submitted dissolution method validation report which was not submitted in the initial submission.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**

	• **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
429.	Name, address of Applicant / Marketing Authorization Holder	M/s Tabros Pharma (Pvt.) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Tabros Pharma (Pvt.) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11095 dated 07-05-2022.
	Details of fee submitted	PKR 75,000/- dated 23-04-2022.
	The proposed proprietary name / brand name	RAST-VT TABLET 10mg/160mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Rosuvastatin Calcium equivalent to Rosuvastatin ……. 10mg Valsartan ……... 160mg
	Pharmaceutical form of applied drug	Brown to dark brown color, oblong, biconvex film coated tablets.
	Pharmacotherapeutic Group of (API)	Lipid modifying agents in combination with other drugs (C10BX)
	Reference to Finished product specifications	Tabros Specifications.
	Proposed Pack size	2×14's
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	Rosuvastatin/Valsartan HCS, Marketing Authorization Holder HCS bvba, Germany, (10 mg/80 mg, 20 mg/80 mg, 10 mg/160 mg, 20mg/160 mg) Germany Approved. Belgium approved. VALAROX 10/80mg Tablet by KRKA. d.d., Novomesto, Bulgaria, Latvia Ravalsyo in Slovenia & Hungry.
	For generic drugs (me-too status)	N/A.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conducted on 28-02-2020
	Evidence of section approval.	Tablet section vide letter No. F.2-5/87-Lic. (Vol-III) 30-06-2020.
	Name and address of API manufacturer.	Rosuvastatin Calcium: Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. The firm has submitted copy of GMP certificate No.

		DE-BE-01-GMP-2019-0042 for M/s Ruyuan HEC Pharm Co. Ltd., wherein the competent authority of Germany has confirmed that the knowledge gained during the inspection of the above said manufacturer, the latest of which was conducted on 29-11-2019, it is considered that it complies with the Good Manufacturing Practice requirements referred to in "the principles of GMP for active substances referred to in" Article 47 of Directive 2001/83/EC. The certificate is valid till 29th 11, 2022. Valsartan: Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China. Copy of GMP certificate No. GD20190988 dated 11-04-2019 in the name of M/s Zhuhai Rundu Pharmaceutical Co., Ltd., valid till 10-04-2024 is submitted.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per template provided in 293rd meeting of Registration Board.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data for rosuvastatin calcium related to general information, nomenclature, structure, general properties, solubility, physical description, manufacturer, Characterization, impurities, Specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Firm has also submitted detailed drug substance data for Valsartan related to general information, nomenclature, structure, general properties, solubility, physical description, manufacturer, Characterization, impurities, Specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies (Drug Substance)	**Rosuvastatin Calcium;** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (RSV-201803001, RSV-201803002 & RSV-201803003). **Valsartan;** Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (64614080101, 64614080102 & 64614080103)
	Module-III (Drug Product):	Firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, control of critical steps and intermediate, process validation protocols , control of

		excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the VALAROX 10/160mg Tablet, batch No. NJ8299 manufactured by KRKA. d.d., Novomesto, Bulgaria by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is VALAROX 10/160mg Tablet manufactured by KRKA. d.d., Novomesto, in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory.
	Analytical method validation /verification of product	Method validation studies for finished product have submitted including following parameters: Linearity & range, Accuracy, Precision, Specificity, Detection limit, Quantitation limit, Robustness, Stability indicating, Solution stability, Analytical method validation for drug substance performed by drug product manufacturer also submitted including following parameters: Linearity & Range, Accuracy, Precision & Specificity.

STABILITY STUDY DATA

Manufacturer of API	**<u>Rosuvastatin Calcium:</u>** Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. **<u>Valsartan:</u>** Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China.		
API Lot No.	Valsartan: 67820030607 Rosuvastatin Calcium: RSV-(RD)202010604(WI)		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TR001-2/RVT	TR002-2/RVT	TR003-2/RVT
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	09.2021	09-2021	09-2021
Date of Initiation	22.11.2021	22.11.2021	22.11.2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred last onsite panel inspection for instant dosage form conducted during last two years BAXIB

		(Apixaban) 2.5mg & 5mg Tablets on 5th January, 2021 by following panel: 1. Prof. Dr. Rafeeq Alam Khan, Dean, Faculty of Pharmacy, Zia Uddin University, Karachi. (Member Registration Board). 2. Dr. Saif-ur-Rehman Khattak, Director / FGA, CDL, DRAP, Karachi. • The HPLC software is 21 CFR complaint. • Audit trials on the testing reports of Baxib tablets were available.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Rosuvastatin Calcium:** Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. The firm has submitted copy of GMP certificate No. DE-BE-01-GMP-2019-0042 for M/s Ruyuan HEC Pharm Co. Ltd., wherein the competent authority of Germany has confirmed that the knowledge gained during the inspection of the above said manufacturer, the latest of which was conducted on 29-11-2019, it is considered that it complies with the Good Manufacturing Practice requirements referred to in "the principles of GMP for active substances referred to in" Article 47 of Directive 2001/83/EC. The certificate is valid till 29th 11, 2022. **Valsartan:** Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China. Copy of GMP certificate No. GD20190988 dated 11-04-2019 in the name of M/s Zhuhai Rundu Pharmaceutical Co., Ltd., valid till 10-04-2024 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Rosuvastatin Calcium:** Firm has submitted copy of commercial invoice number WIS200291 dated December, mentioning 50Kg quantity of Rosuvastatin Calcium attested by Assistant Director, I & E, DRAP Karachi dated 23-12-2020. ADC signed Form 5 & Invoice are available while Form 3 & Form 7 are also available. **Valsartan:** Firm has submitted copy of commercial invoice No. RD-2020041301-1 dated 16-04-2020 mentioning 650Kg quantity of Valsartan with Batch No. 67820030607, Mfg. date March, 2020 & retest date of February, 2023 attested by Assistant Director I & E, DRAP Karachi dated 27-04-2020. *The utilization is restricted for sampling and for submission & endorsement of certificate of analysis for NDMA & EDMA impurities.* ADC signed Form 5 & Invoice are available while Form 3 & Form 7 are also available.

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section No.	Observation	Response by the firm
1.	3.2.S.4.1	• Justification for specification for water determination shall be submitted as the Finished Product manufacturer has provided NMT 6% while drug substance manufacturer has NMT 3.5%. • Assay limit of valsartan is 98% in USP while FPP has mentioned 98.5%. justify.	Firm has submitted that they have followed USP specification for the testing of Rosuvastatin calcium & in USP monograph limit of water content is NMT 6% while drug substance manufacturer has 3.5-4.5% which is in-house. Assay limit of valsartan in USP is 98-102% and we have followed for the same & submitted accordingly.
2.	3.2.S.4.2	Analytical procedures for the drug substance rosuvastatin calcium used by the drug substance manufacturer shall be submitted.	Submitted.
3.	3.2.S.4.4	Certificate of analysis for NDMA and EDMA impurities in the drug substance i.e. valsartan after clearance from DRAP shall be submitted as the utilization was restricted for sampling and for submission & endorsement of certificate of analysis for NDMA & EDMA impurities.	Firm has submitted the same commercial invoice submitted above with following remarks of the Assistant Director, DRAP, Karachi; "COA regarding impurities was checked and utilization allowed." They further referred to a decision of Registration Board in its 312th meeting, wherein in point "a" it is decided by the Board that; *a. The manufacturers of Valsartan API which have valid certificate of suitability as per EDQM or any other Reference Regulatory Authorities (RRAs), as adopted by the Registration Board, are exempted from NDMA/NDEA testing on every consignment.* *b. Import of Valsartan API by DML holders from manufacturers not covered in point a shall be subject to testing as per decision of 291st meeting of Registration Board.* *However, neither any certificates for NDMA and EDMA impurities in the drug*

			substance is provided by the firm nor any valid certificate of suitability as per EDQM or any other Reference Regulatory Authorities (RRAs), as adopted by the Registration Board.
4.	3.2.P.2.2	Justification for not performing CDP & PE against the Reference Regulatory Authority country product.	Firm has stated that Pharmaceutical equivalence and CDP studies against the reference product of "Valarox Tablets" in three dissolution medium has been submitted with a acceptance level of F2 results. Although the product is available in Germany with the brand name of Rosuvastatin/valsartan HCS film coated tablets which is sufficient reference for RRA country. Furthermore, based on reference regulatory authorities by the DRAP in 275th DRB meeting, in which it has clearly mentioned that at least three EU countries product should be available as reference for consideration of registration board of the product. Reference products are also available more than three EU countries which are as follows: • Bulgaria & Latvia with the brand name of Valarox. Slovenia & Hungry with the brand name of Ravalsyo.
5.	3.2.P.5.2	Provide scientific rationale for selection of dissolution parameters including type of apparatus, rpm, dissolution medium, sampling time and the analytical method.	The scientific rational for selection of dissolution medium and type of apparatus carried out, based on FPP of Valsartan Tablets in the USP monograph, however, rpm and sample elapsed time set the parameters grounded on practical observation and In-House analytical method was developed, Dissolution method validation is being submitted as per ICH guidelines.
6.	3.2.P.3.3	• Manufacturing process has mentioned bilayer tablets however, label claim has not mentioned. Justification shall be submitted. • Evidence of availability of bilayer tablet machine shall be submitted.	Firm has submitted that they have followed same manufacturing procedure as similar as reference product. It is bilayer tablet & finally covered with film coating. Supportive/ Orientation document is attached for your ready reference where it is evidently mentioned film coated tablets, Hence, we are claiming film coated tablets. Firm has submitted that they are manufacturing the "**Cresar-AM**" bi-layer tablets on commercial scale and marketed accordingly since long time.

			They further submitted routine GMP inspection report of October, 2018 wherein it is mentioned in the report that the firm has recently purchased Rotary tablet press Machine ZP-31 (for double layer tablet manufacturing).
7.	3.2.P.2.2	• The chromatograms provided for dissolution studies have run time of 6 minutes and column temperature is mentioned 40ºC. The method validated for assay has a run time of 65 minutes and column temperature is less than 40ºC. It appears as if the HPLC method used in dissolution is not validated. • Justify/provide validation studies for HPLC method used in dissolution for the applied formulation.	Firm has submitted that the assay of SIM method and Dissolution method are developed separately having different chromatographic conditions, hence, both chromatographic conditions are seeming to be different. They further submitted dissolution method validation report which was not submitted in the initial submission.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

430.	Name, address of Applicant / Marketing Authorization Holder	M/s Tabros Pharma (Pvt.) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Tabros Pharma (Pvt.) Ltd., L-20/B, Sector-22, F.B. Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11097 dated 07-05-2022.
	Details of fee submitted	PKR 75,000/- dated 23-04-2022.
	The proposed proprietary name / brand name	RAST-VT TABLET 20mg/160mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Rosuvastatin Calcium equivalent to Rosuvastatin ……. 20mg Valsartan ……... 160mg
	Pharmaceutical form of applied drug	Light yellow color, oblong, biconvex film coated tablets.

	Pharmacotherapeutic Group of (API)	Lipid modifying agents in combination with other drugs (C10BX)
	Reference to Finished product specifications	Tabros Specifications.
	Proposed Pack size	2×14's
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	Rosuvastatin/Valsartan HCS, Marketing Authorization Holder HCS bvba, Germany, (10 mg/80 mg, 20 mg/80 mg, 10 mg/160 mg, 20mg/160 mg) Germany Approved. Belgium approved.
	For generic drugs (me-too status)	N/A.
	GMP status of the Finished product manufacturer	GMP certificate issued based upon inspection conducted on 28-02-2020
	Evidence of section approval.	Tablet section vide letter No. F.2-5/87-Lic. (Vol-III) 30-06-2020.
	Name and address of API manufacturer.	Rosuvastatin Calcium: Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. The firm has submitted copy of GMP certificate No. DE-BE-01-GMP-2019-0042 for M/s Ruyuan HEC Pharm Co. Ltd., wherein the competent authority of Germany has confirmed that the knowledge gained during the inspection of the above said manufacturer, the latest of which was conducted on 29-11-2019, it is considered that it complies with the Good Manufacturing Practice requirements referred to in "the principles of GMP for active substances referred to in" Article 47 of Directive 2001/83/EC. The certificate is valid till 29th 11, 2022. Valsartan: Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China. Copy of GMP certificate No. GD20190988 dated 11-04-2019 in the name of M/s Zhuhai Rundu Pharmaceutical Co., Ltd., valid till 10-04-2024 is submitted.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per template provided in 293rd meeting of Registration Board.
	Module III (Drug Substance)	Firm has submitted detailed drug substance data for rosuvastatin calcium related to general information, nomenclature, structure, general properties, solubility, physical description, manufacturer, Characterization, impurities, Specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Firm has also submitted detailed drug substance data for Valsartan related to general information, nomenclature, structure, general properties, solubility,

		physical description, manufacturer, Characterization, impurities, Specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies (Drug Substance)	**Rosuvastatin Calcium;** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (RSV-201803001, RSV-201803002 & RSV-201803003). **Valsartan;** Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (64614080101, 64614080102 & 64614080103)
	Module-III (Drug Product):	Firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, control of critical steps and intermediate, process validation protocols , control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the VALAROX 20/160mg, batch No. NJ58338 Tablet manufactured by KRKA. d.d., Novomesto, Bulgaria by performing quality tests including Identification, water content, Assay, Dissolution, Disintegration. CDP has been performed against the same brand that is VALAROX 20/160mg Tablet manufactured by KRKA. d.d., Novomesto, in Acid media (0.1N HCl), acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The F2 values are found satisfactory.
	Analytical method validation /verification of product	Method validation studies for finished product have submitted including following parameters: Linearity & range, Accuracy, Precision, Specificity, Detection limit, Quantitation limit, Robustness, Stability indicating, Solution stability, Analytical method validation for drug substance performed by drug product manufacturer also submitted including following parameters: Linearity & Range, Accuracy, Precision & Specificity.
STABILITY STUDY DATA		
Manufacturer of API		**Rosuvastatin Calcium:** Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. **Valsartan:** Zhuhai Rundu Pharmaceutical Co., Ltd.,

	No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China.		
API Lot No.	Valsartan: 67820030607 Rosuvastatin Calcium: RSV-(RD)202010604(WI)		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×14's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	TR001-1/RVT	TR002-1/RVT	TR003-1/RVT
Batch Size	1500 Tablets	1500 Tablets	1500 Tablets
Manufacturing Date	09.2021	09-2021	09-2021
Date of Initiation	22.11.2021	22.11.2021	22.11.2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred last onsite panel inspection for instant dosage form conducted during last two years BAXIB (Apixaban) 2.5mg & 5mg Tablets on 5th January, 2021 by following panel: 1. Prof. Dr. Rafeeq Alam Khan, Dean, Faculty of Pharmacy, Zia Uddin University, Karachi. (Member Registration Board). 2. Dr. Saif-ur-Rehman Khattak, Director / FGA, CDL, DRAP, Karachi. • The HPLC software is 21 CFR complaint. • Audit trials on the testing reports of Baxib tablets were available.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Rosuvastatin Calcium:** Ruyuan HEC Pharm Co., Ltd., Xiaba Development Zone, Ruyuan County, Shaoguan City, Guangdong Province, P.R. China. The firm has submitted copy of GMP certificate No. DE-BE-01-GMP-2019-0042 for M/s Ruyuan HEC Pharm Co. Ltd., wherein the competent authority of Germany has confirmed that the knowledge gained during the inspection of the above said manufacturer, the latest of which was conducted on 29-11-2019, it is considered that it complies with the Good Manufacturing Practice requirements referred to in "the principles of GMP for active substances referred to in" Article 47 of Directive 2001/83/EC. The certificate is valid till 29th 11, 2022. **Valsartan:** Zhuhai Rundu Pharmaceutical Co., Ltd., No. 6, North Airport Road, Sanzao Town, Jinwan District, Zhuhai City, Guangdong Province, 519041 P.R. China. Copy of GMP certificate No. GD20190988 dated 11-04-2019 in the name of M/s Zhuhai Rundu

		Pharmaceutical Co., Ltd., valid till 10-04-2024 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Rosuvastatin Calcium:** Firm has submitted copy of commercial invoice number WIS200291 dated December, mentioning 50Kg quantity of Rosuvastatin Calcium attested by Assistant Director, I & E, DRAP Karachi dated 23-12-2020. ADC signed Form 5 & Invoice are available while Form 3 & Form 7 are also available. **Valsartan:** Firm has submitted copy of commercial invoice No. RD-2020041301-1 dated 16-04-2020 mentioning 650Kg quantity of Valsartan with Batch No. 67820030607, Mfg. date March, 2020 & retest date of February, 2023 attested by Assistant Director I & E, DRAP Karachi dated 27-04-2020. *The utilization is restricted for sampling and for submission & endorsement of certificate of analysis for NDMA & EDMA impurities.* ADC signed Form 5 & Invoice are available while Form 3 & Form 7 are also available.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section No.	Observation	Response by the firm
1.	3.2.S.4.1	• Justification for specification for water determination shall be submitted as the Finished Product manufacturer has provided NMT 6% while drug substance manufacturer has NMT 3.5%. • Assay limit of valsartan is 98% in USP while FPP has mentioned 98.5%. justify.	Firm has submitted that they have followed USP specification for the testing of Rosuvastatin calcium & in USP monograph limit of water content is NMT 6% while drug substance manufacturer has 3.5-4.5% which is in-house. Assay limit of valsartan in USP is 98-102% and we have followed for the same & submitted accordingly.
2.	3.2.S.4.2	Analytical procedures for the drug substance rosuvastatin calcium used by the drug substance manufacturer shall be submitted.	Submitted.

3.	3.2.S.4.4	Certificate of analysis for NDMA and EDMA impurities in the drug substance i.e. valsartan after clearance from DRAP shall be submitted as the utilization was restricted for sampling and for submission & endorsement of certificate of analysis for NDMA & EDMA impurities.	Firm has submitted the same commercial invoice submitted above with following remarks of the Assistant Director, DRAP, Karachi; "COA regarding impurities was checked and utilization allowed." They further referred to a decision of Registration Board in its 312th meeting, wherein in point "a" it is decided by the Board that; *a. The manufacturers of Valsartan API which have valid certificate of suitability as per EDQM or any other Reference Regulatory Authorities (RRAs), as adopted by the Registration Board, are exempted from NDMA/NDEA testing on every consignment.* *b. Import of Valsartan API by DML holders from manufacturers not covered in point a shall be subject to testing as per decision of 291st meeting of Registration Board.* *However, neither any certificates for NDMA and EDMA impurities in the drug substance is provided by the firm nor any valid certificate of suitability as per EDQM or any other Reference Regulatory Authorities (RRAs), as adopted by the Registration Board.*
4.	3.2.P.2.2	Justification for not performing CDP & PE against the Reference Regulatory Authority country product.	Firm has stated that Pharmaceutical equivalence and CDP studies against the reference product of "Valarox Tablets" in three dissolution medium has been submitted with a acceptance level of F2 results. Although the product is available in Germany with the brand name of Rosuvastatin/valsartan HCS film coated tablets which is sufficient reference for RRA country. Furthermore, based on reference regulatory authorities by the DRAP in 275th DRB meeting, in which it has clearly mentioned that at least three EU countries product should be available as reference for consideration of registration board of the product. Reference products are also available more than three EU countries which are as follows: • Bulgaria & Latvia with the brand name of Valarox. Slovenia & Hungry with the brand name of Ravalsyo.
5.	3.2.P.5.2	Provide scientific rationale for selection of dissolution parameters	The scientific rational for selection of dissolution medium and type of apparatus

		including type of apparatus, rpm, dissolution medium, sampling time and the analytical method.	carried out, based on FPP of Valsartan Tablets in the USP monograph, however, rpm and sample elapsed time set the parameters grounded on practical observation and In-House analytical method was developed, Dissolution method validation is being submitted as per ICH guidelines.
6.	3.2.P.3.3	• Manufacturing process has mentioned bilayer tablets however, label claim has not mentioned. Justification shall be submitted. • Evidence of availability of bilayer tablet machine shall be submitted.	Firm has submitted that they have followed same manufacturing procedure as similar as reference product. It is bilayer tablet & finally covered with film coating. Supportive/ Orientation document is attached for your ready reference where it is evidently mentioned film coated tablets, Hence, we are claiming film coated tablets. Firm has submitted that they are manufacturing the "**Cresar-AM**" bi-layer tablets on commercial scale and marketed accordingly since long time. They further submitted routine GMP inspection report of October, 2018 wherein it is mentioned in the report that the firm has recently purchased Rotary tablet press Machine ZP-31 (for double layer tablet manufacturing).
7.	3.2.P.2.2	• The chromatograms provided for dissolution studies have run time of 6 minutes and column temperature is mentioned 40ºC. The method validated for assay has a run time of 65 minutes and column temperature is less than 40ºC. It appears as if the HPLC method used in dissolution is not validated. Justify/provide validation studies for HPLC method used in dissolution for the applied formulation.	Firm has submitted that the assay of SIM method and Dissolution method are developed separately having different chromatographic conditions, hence, both chromatographic conditions are seeming to be different. They further submitted dissolution method validation report which was not submitted in the initial submission.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the *pharmaceutical* i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year.

In compliance to the aforementioned decision of the Authority, Assistant Director (PR-I/EFD) vide letter No. F.1-6/2019-PR-I (EFD) dated 06th October, 2022 has informed that **M/s Atco Laboratories Ltd, Karachi** has achieved the benchmark of more than **100,000 USD (542,854.81 USD)** during the fiscal Year 2019-2020 and submitted their applications for priority consideration/ evaluation.
Following products are presented before the Board in light of the decision of the 133rd meeting of DRAP Authority held on 13th April 2022 for consideration.

431.	Name, address of Applicant / Marketing Authorization Holder	M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi.
	Name, address of Manufacturing site.	M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi.
	Status of the applicant	☒ Manufacturer. ☐ Importer. ☐ Is involved in none of the above (contract giver).
	Status of application	☐ New Drug Product (NDP). ☒ Generic Drug Product (GDP).
	Intended use of pharmaceutical product	☐ Domestic sale. ☐ Export sale. ☒ Domestic and Export sales.
	Dy. No. and date of submission	Dy. No 3726 dated 09-02-2022.
	Details of fee submitted	Rs.30,000/- dated 21-12-2021.
	The proposed proprietary name / brand name	Lenalidomide 5mg Capsule.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Lenalidomide ……..…5mg
	Pharmaceutical form of applied drug	Oral Capsule.
	Pharmacotherapeutic Group of (API)	L04 Immunosuppressant's.
	Reference to Finished product specifications	Innovator's specifications.
	Proposed Pack size	7's, 10's, 14's, 20's, 21's, 28's, 30's, 60's, & 100's.
	Proposed unit price	As per policy.
	The status in reference regulatory authorities	Revlimid 5mg Capsules USFDA approved.
	For generic drugs (me-too status)	Not submitted.
	GMP status of the Finished product manufacturer	Not submitted.
	Evidence of section approval.	Capsule general section approved vide letter No. F. No.F.2-5/85-Lic (Vol-VI) dated 23-01-2019.
	Name and address of API manufacturer.	M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template.
	Module III (Drug Substance)	Firm has submitted detail of the drug substance regarding nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures

		and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of both drug substances.
	Stability studies (Drug substance.)	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 12 months Batches: (ELNB210401, ELNB210501 & ELNB210701) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (LNB-161002, LNB-161003 & LNB-161004)
	Module-III (Drug Product):	The firm has submitted detail of the drug product including its composition, formulation development, pharmaceutical equivalence, comparative dissolution profile, manufacturer, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Not submitted.
	Analytical method validation/verification of product	Method Validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China.		
API Lot No.	ZSELNB210201.		
Description of Pack (Container closure system)	7's Capsule in Alu-Alu blisters, packed in a printed carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	AP166C	AP167C	AP168C
Batch Size	6000 capsules	6000 capsules	6000 capsules
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	10-06-2021	10-06-2021	10-06-2021
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product "Rofl 500mcg Tablets" which was conducted on 10-10-2017, and was presented in 277th meeting of Registration Board (27 - 29 December, 2017). Following observations were reported in the report: ✓ The HPLC software is 21CFR Compliant. ✓ Audit trail reports on the testing were verifiable. Firm has adequate monitoring and controls for stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued in the name of M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China issued by Jiangsu Changzhou Drug Administration. The certificate remains valid till 27-08-2022. Firm has also submitted copy of license for drug production No. Su20160138 for M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China valid till 24-09-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of form 6 No. 1088 dated 01/04/2021 issued in the name M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi mentioning 0.965kg quantity of Lenalidomide attested by Assistant Director, DRAP, Karachi. Firm has also submitted copy of commercial invoice No. CYI20457 dated 11-03-2021 mentioning 0.965kg quantity of Lenalidomide, Batch No. ZSELNB210201 attested by Assistant Director, DRAP, Karachi dated 01/04/2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Section	Observation	Reply by the firm
1.	1.3.4	• Valid copy of DML of the applicant shall be submitted as the provide one is w.e.f. 11-04-2016.	Firm has replied that they submitted application for renewal of Drug Manufacturing License before the expiry of license i.e., on 17th March, 2021. Therefore, as per the conditions of Rule 6 of Drugs Licensing, Registering and Advertising Rules, 1976 our DML is still valid.

		• Latest GMP certificate/last inspection report conducted within last three years of the finished product manufacturer shall be submitted.	Copy of GMP certificate No. 160/2020-DRAP (K) dated 24-12-2020 on the basis of inspection conducted on 06-11-2020 is submitted by the firm
2.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer issued by concerned/relevant regulatory authority shall be submitted.	Firm has submitted a document with heading of "written confirmation for active substances exported to EU" issued by Jiangsu Drug Administration wherein the issuing authority confirms that the manufacturing plant complies with the requirements of Chinese Good Manufacturing Practices (GMP of EU, WHO/ICT Q7) and this written confirmation remains valid till 23-08-2024. Copy of GMP certificate (No.JS20180928) of Changzhou Pharmaceutical Factory issued by China Food and Drug Administration. The certificate is valid till 12-11-2023. The certificate is also verified online from NMPA database.
3.	1.5.8	Evidence of approval of applied formulation already approved by DRAP with brand name, Registration number and manufacturer name shall be submitted.	Firm has submitted differential fee of 45000/- vide slip No. 7965161967 dated 17-10-2022.
4.	3.2.S.4.3	Validation studies of the drug substance performed by the drug product manufacturer shall be submitted.	Firm has submitted method verification studies for the drug substance including Specificity, Accuracy, Precision and Range.
5.	3.2.S.7.3	Complete real time stability studies for the drug substance shall be submitted.	Real time stability data of three batches i.e. ELNB210401, ELNB210501 & ELNB210701 only for 12 months is provided. While the accelerated stability data of three batches i.e. ELNB210401, ELNB210501 & ELNB210701 for 06 months is provided. ***Real time Stability study data is only for one year.***
6.	3.2.P.2.2	• Composition of finished product has mentioned 147mg of Lenalidomide per capsule. Justification shall be submitted.	Firm has submitted that in Module 3, section 3.2.P.2.2, in submitted product development document, page number 16 clearly indicates the quantity of API in finished product as 5mg but, on page number 10 we have mentioned the quantities of excipients only in which 147mg quantity is mentioned against

		• Comparison of the developed formulation and the innovator / reference / comparator product including the results of all the quality tests shall be submitted and discussed (Pharmaceutical Equivalence studies. • The results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 shall be submitted and discussed (Comparative dissolution profile.)	Lactose Anhydrous to be used in the manufacturing of Lenalidomide capsule 5mg. ***However, the said page has mentioned Lenalidomide 147mg.*** Firm has submitted that they have already submitted *Pharmaceutical Equivalence through Comparative Dissolution Profile* for our product Lenalidomide Capsule 5mg in which drug release is greater than 85% within 15minutes and no need to calculate f_2 factor as the Innovator product for Lenalidomide Capsule 5mg is not available locally or internationally. Further, Pharmaceutical Equivalence and Comparative Dissolution Profile against innovator product for Lenalidomide Capsule 10mg and Lenalidomide Capsule 25mg have also been submitted which indicates the equivalency of Lenalidomide Capsule 5mg as the formulation of Lenalidomide Capsule 5mg is based on dose proportion with other strengths of Lenalidomide Capsule. Pharmaceutical Equivalence report for Lenalidomide Capsule 5mg containing our product results is being submitted for your ready reference. *Firm has neither submitted any Pharmaceutical equivalence and Comparative dissolution studies against the innovator/comparator/reference product.* *They just provided release studies of the applied formulation in different medias.*
7.	3.2.P.5.2	Sample preparation method in the dissolution studies shall be submitted.	Submitted.
8.	3.2.P.8	• Stability condition for real time stability studies of the drug product are 30˚C ± 2˚C / 75% ± 5%RH instead of 30˚C ± 2˚C / 65% ± 5%RH. Justification shall be submitted.	Firm has submitted that they conduct stability studies on more worst condition than those data is also acceptable for comparatively relaxed condition. As per policy we conduct the stability studies for real time as per Zone IV(b) requirement which is more stringent and acceptable for DRAP requirement for Zone IV(a) as well as for those regulatory authorities where requirement is IV(b).

Decision: Deferred for the following;

- **Pharmaceutical Equivalence studies of the developed formulation and the innovator / reference / comparator product including the results of all the quality tests shall be submitted.**

• **The results of comparative dissolution profile conducted in three BCS media across the physiological pH range along with calculation of similarity factor f2 against the innovator product shall be submitted.**		
432.	Name, address of Applicant / Marketing Authorization Holder	M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi.
	Name, address of Manufacturing site.	M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi.
	Status of the applicant	☒ Manufacturer. ☐ Importer. ☐ Is involved in none of the above (contract giver).
	Status of application	☐ New Drug Product (NDP). ☒ Generic Drug Product (GDP).
	Intended use of pharmaceutical product	☒ Domestic sale. ☐ Export sale. ☐Domestic and Export sales.
	Dy. No. and date of submission	Dy. No 1741 dated 18-01-2022
	Details of fee submitted	Rs.30,000/- dated 21-12-2021
	The proposed proprietary name / brand name	Lenalidomide 10mg Capsule.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Lenalidomide ……..…10mg
	Pharmaceutical form of applied drug	Oral Capsule.
	Pharmacotherapeutic Group of (API)	L04 Immunosuppressant's.
	Reference to Finished product specifications	Innovator's specifications.
	Proposed Pack size	7's, 10's, 14's, 20's, 21's, 28's, 30's, 60's, & 100's.
	Proposed unit price	As per policy.
	The status in reference regulatory authorities	Revlimid 10mg Capsules USFDA approved.
	For generic drugs (me-too status)	Lenalidomide 10mg Capsule, Lab diagnostic system, Reg. No. 110507.
	GMP status of the Finished product manufacturer	Not submitted.
	Evidence of section approval.	Capsule general section approved vide letter No. F. No.F.2-5/85-Lic (Vol-VI) dated 23-01-2019.
	Name and address of API manufacturer.	M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template.
	Module III (Drug Substance)	Firm has submitted detail of the drug substance regarding nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure

		system and stability studies of both drug substances.
	Stability studies (Drug substance.)	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 12 months Batches: (ELNB210401, ELNB210501 & ELNB210701) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (LNB-161002, LNB-161003 & LNB-161004)
	Module-III (Drug Product):	The firm has submitted detail of the drug product including its composition, formulation development, pharmaceutical equivalence, comparative dissolution profile, manufacturer, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the reference product Lenalidomide 10mg capsules batch number 2730017 manufactured by Beacon Pharmaceuticals Limited by performing quality tests (Identification, Description, Disintegration time, Dissolution & Assay). CDP has been performed against the Linamide 10mg capsules batch number 2730017 Mfg. date 01-2021, Exp. Date 12-2022 in in three different mediums i.e. pH 1.2 in 0.1 N HCl, pH 4.5 Acetate buffer & pH 6.8 Phosphate buffer. In all the three mediums, both the reference product and test product have shown more than 85% release in 15 minutes, therefore, F2 is not calculated.
	Analytical method validation/verification of product	Method Validation studies have submitted including specificity, linearity, range, accuracy, precision, robustness.

STABILITY STUDY DATA

Manufacturer of API	M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China.		
API Lot No.	ZSELNB210201.		
Description of Pack (Container closure system)	7's Capsule in Alu-Alu blisters, packed in a printed carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	AP155C	AP156C	AP157C
Batch Size	3000 capsules	3000 capsules	3000 capsules

Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	20-06-2021	20-06-2021	20-06-2021
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product "Rofl 500mcg Tablets" which was conducted on 10-10-2017, and was presented in 277th meeting of Registration Board (27 - 29 December, 2017). Following observations were reported in the report: ✓ The HPLC software is 21CFR Compliant. ✓ Audit trail reports on the testing were verifiable. ✓ Firm has adequate monitoring and controls for stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued in the name of M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China issued by Jiangsu Changzhou Drug Administration. The certificate remains valid till 27-08-2022. Firm has also submitted copy of license for drug production No. Su20160138 for M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China valid till 24-09-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of form 6 No. 1088 dated 01/04/2021 issued in the name M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi mentioning 0.965kg quantity of Lenalidomide attested by Assistant Director, DRAP, Karachi. Firm has also submitted copy of commercial invoice No. CYI20457 dated 11-03-2021 mentioning 0.965kg quantity of Lenalidomide, Batch No. ZSELNB210201 attested by Assistant Director, DRAP, Karachi dated 01/04/2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Section	Observation	Reply by the firm
1.	1.3.4	• Valid copy of DML of the applicant shall be submitted as the provide one is w.e.f. 11-04-2016. • Latest GMP certificate/last inspection report conducted within last three years of the finished product manufacturer shall be submitted.	Firm has replied that they submitted application for renewal of Drug Manufacturing License before the expiry of license i.e., on 17th March, 2021. Therefore, as per the conditions of Rule 6 of Drugs Licensing, Registering and Advertising Rules, 1976 our DML is still valid. Copy of GMP certificate No. 160/2020-DRAP (K) dated 24-12-2020 on the basis of inspection conducted on 06-11-2020 is submitted by the firm
2.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer issued by concerned/relevant regulatory authority shall be submitted.	Firm has submitted a document with heading of "written confirmation for active substances exported to EU" issued by Jiangsu Drug Administration wherein the issuing authority confirms that the manufacturing plant complies with the requirements of Chinese Good Manufacturing Practices (GMP of EU, WHO/ICT Q7) and this written confirmation remains valid till 23-08-2024. Copy of GMP certificate (No.JS20180928) of Changzhou Pharmaceutical Factory issued by China Food and Drug Administration. The certificate is valid till 12-11-2023. The certificate is also verified online from NMPA China database.
3.	3.2.S.4.3	Validation studies of the drug substance performed by the drug product manufacturer shall be submitted.	Firm has submitted method verification studies for the drug substance including Specificity, Accuracy, Precision and Range.
4.	3.2.S.7.3	Complete real time stability studies for the drug substance shall be submitted.	Real time stability data of three batches i.e. ELNB210401, ELNB210501 & ELNB210701 only for 12 months is provided. While the accelerated stability data of three batches i.e. ELNB210401, ELNB210501 & ELNB210701 for 06 months is provided. ***Real time Stability study data is only for one year.***
5.	3.2.P.2.2	In both Pharmaceutical Equivalence and Comparative Dissolution Profile two different brand names are mentioned while formulation development has mentioned product of Celgene pharma. In some places Beacon	Firm has submitted that in product development data we have mentioned details of brand leader as reference product which is REVLIMID CAPSULE manufactured by Celgene Corporation Summit, NJ 07901, but, due to unavailability of this reference product in Pakistan, we have performed

		pharma products are mentioned. Clarification shall be submitted.	pharmaceutical equivalence and Comparative Dissolution Profile studies against locally available brand i.e., Linamide Capsule manufactured by Beacon Pharmaceuticals Limited Bangladesh. This is in accordance with the decision of Drug Registration Board taken in its 307th meeting.
6.	3.2.P.2.2.1	Justification shall be submitted regarding the selection of only two time points and paddle speed of 75 rpm in comparative dissolution studies. Reference product has used 50rpm and sampling time of 10, 15, 20, 30 & 45.	As per WHO, Annex 6, Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, 10.1.2 Determination of dissolution characteristics of multisource products in consideration of a bio waiver based on the Biopharmaceutics Classification System, for very rapid release product use paddle apparatus at 75 rpm therefore subjected speed conducted for CDP. Also Minutes of 293rd Meeting of Registration Board (6 – 8th January, 2020), USFDA Guidance for Industry Dissolution Testing of Immediate Release Solid Oral Dosage Forms was followed for guidance which states "with the paddle method, it is 50-75 rpm (Shah et al., 1992)." (Section 3.2.P.2.2.1). While reference product manufacturer used 50 rpm for finish product dissolution testing and we also performed the same for submitted initial & stability studies. Further regarding the selection of only two time points, same above references are adopted as the test product releases above 85% in 10 minutes then only further one-time point included in report and dissolution release achieved 85% for both of test and reference products within 15 minutes due to this no need to calculate f_2 factor therefore 3rd time point is not the part of test report. Reference of above guidelines attached in the section of (3.2.P.2.2.1).
7.	3.2.P.5.2	Sample preparation method in the dissolution studies shall be submitted.	Submitted.
8.	3.2.P.8	• Date of manufacturing of all the three trial batches 04-2021 while the analysis date is 20-06-2021. Justification for this delay shall be submitted.	Firm has submitted that as per their policy, they allocate the manufacturing date by date of dispensing of raw material and for this product the date of dispensing/manufacturing is 28/04/2021. You may realize that this is oral solid dosage form which requires more process time as compare to other dosage forms.

		• Stability condition for real time stability studies of the drug product are 30°C ± 2°C / 75% ± 5%RH instead of 30°C ± 2°C / 65% ± 5%RH. Justification shall be submitted.	Mostly an oral solid dosage form batch requires Twenty (20) days to one (1) month to complete the manufacturing process then QC testing and then subjected the finish form for stability studies so, in normal course of action forty-five (45) to sixty (60) days is required to put the batches in stability chamber since dispensing of the material (28/04/2021). Firm has submitted that they conduct stability studies on more worst condition than those data is also acceptable for comparatively relaxed condition. As per policy we conduct the stability studies for real time as per Zone IV(b) requirement which is more stringent and acceptable for DRAP requirement for Zone IV(a) as well as for those regulatory authorities where requirement is IV(b).
9.			Firm has also submitted differential fee of 45000/- vide slip No. 4580801013 dated 17-10-2022.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

433.	Name, address of Applicant / Marketing Authorization Holder	M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi.
	Name, address of Manufacturing site.	M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi.
	Status of the applicant	☒ Manufacturer. ☐ Importer. ☐ Is involved in none of the above (contract giver).
	Status of application	☐ New Drug Product (NDP). ☒ Generic Drug Product (GDP).
	Intended use of pharmaceutical product	☒ Domestic sale. ☐ Export sale. ☐Domestic and Export sales.
	Dy. No. and date of submission	Dy. No 1742 dated 19-01-2022
	Details of fee submitted	Rs.30,000/- dated 21-12-2021
	The proposed proprietary name / brand name	Lenalidomide 25mg Capsule.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Lenalidomide ……..…25mg
	Pharmaceutical form of applied drug	Oral Capsule.
	Pharmacotherapeutic Group of (API)	L04 Immunosuppressant's.
	Reference to Finished product specifications	Innovator's specifications.

	Proposed Pack size	7's, 10's, 14's, 20's, 21's, 28's, 30's, 60's, & 100's.
	Proposed unit price	As per policy.
	The status in reference regulatory authorities	Revlimid 25mg Capsules USFDA approved.
	For generic drugs (me-too status)	Firm has submitted copy of minutes of minutes of 283rd meeting of Registration Board wherein the product of M/s Helix Pharma, Relidomide 25mg imported from India, is approved by the Board as per policy of inspections of manufacturer abroad. Lenoma 25mg Capsule, Gene Tech laboratories, Reg. No. 110502.
	GMP status of the Finished product manufacturer	Not submitted.
	Evidence of section approval.	Capsule general section approved vide letter No. F. No.F.2-5/85-Lic (Vol-VI) dated 23-01-2019.
	Name and address of API manufacturer.	M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS details as per WHO QOS PD template.
	Module III (Drug Substance)	Firm has submitted detail of the drug substance regarding nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of both drug substances.
	Stability studies (Drug substance.)	Stability study conditions: Real time: 30°C ± 2°C / 75% ± 5%RH for 12 months Batches: (ELNB210401, ELNB210501 & ELNB210701) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (LNB-161002, LNB-161003 & LNB-161004)
	Module-III (Drug Product):	The firm has submitted detail of the drug product including its composition, formulation development, pharmaceutical equivalence, comparative dissolution profile, manufacturer, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the reference product Lenalidomide 25mg capsules batch number 2740007 manufactured by Beacon Pharmaceuticals Limited by performing quality tests (Identification, Description, Disintegration

		time, Dissolution & Assay). CDP has been performed against the Linamide 25mg capsules batch number 2730017 Mfg. date 12-2020, Exp. Date 11-2022 in in three different mediums i.e. pH 1.2 in 0.1 N HCl, pH 4.5 Acetate buffer & pH 6.8 Phosphate buffer. In all the three mediums, both the reference product and test product have shown more than 85% release in 15 minutes, therefore, F2 is not calculated.
	Analytical method validation/verification of product	Method Validation studies have submitted including specificity, linearity, range, accuracy, precision, robustness.

STABILITY STUDY DATA

Manufacturer of API	Nantong Chanyoo Pharmatech Co. Ltd., No. 2 Tonghai Si Road, Rudong Coastal Economic Development Zone, Nantong, Jiangsu Province China.		
API Lot No.	RD-TG-201907211.		
Description of Pack (Container closure system)	7's Capsule in Alu-Alu blisters, packed in a printed carton.		
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	MY171C	MY172C	MY173C
Batch Size	3000 capsules.	3000 capsules.	3000 capsules.
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	01-07-2021	01-07-2021	01-07-2021
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has referred to onsite inspection report of their product "Rofl 500mcg Tablets" which was conducted on 10-10-2017, and was presented in 277th meeting of Registration Board (27 - 29 December, 2017). Following observations were reported in the report: ✓ The HPLC software is 21CFR Compliant. ✓ Audit trail reports on the testing were verifiable. ✓ Firm has adequate monitoring and controls for stability chambers.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate issued in the name of M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou,

		Jiangsu 213018, China issued by Jiangsu Changzhou Drug Administration. The certificate remains valid till 27-08-2022. Firm has also submitted copy of license for drug production No. Su20160138 for M/s Changhzhou Pharmaceutical Factory, No. 518, Laodong East Road, Changhzhou, Jiangsu 213018, China valid till 24-09-2025.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of form 6 No. 1088 dated 01/04/2021 issued in the name M/s Atco Laboratories Limited., B-18, S.I.T.E. Karachi mentioning 0.965kg quantity of Lenalidomide attested by Assistant Director, DRAP, Karachi. Firm has also submitted copy of commercial invoice No. CYI20457 dated 11-03-2021 mentioning 0.965kg quantity of Lenalidomide, Batch No. ZSELNB210201 attested by Assistant Director, DRAP, Karachi dated 01/04/2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section	Observation	Reply by the firm
1.	1.3.4	• Valid copy of DML of the applicant shall be submitted as the provide one is w.e.f. 11-04-2016. • Latest GMP certificate/last inspection report conducted within last three years of the finished product manufacturer shall be submitted.	Firm has replied that they submitted application for renewal of Drug Manufacturing License before the expiry of license i.e., on 17th March, 2021. Therefore, as per the conditions of Rule 6 of Drugs Licensing, Registering and Advertising Rules, 1976 our DML is still valid. Copy of GMP certificate No. 160/2020-DRAP (K) dated 24-12-2020 on the basis of inspection conducted on 06-11-2020 is submitted by the firm
2.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer issued by concerned/relevant regulatory authority shall be submitted.	Firm has submitted a document with heading of "written confirmation for active substances exported to EU" issued by Jiangsu Drug Administration wherein the issuing authority confirms that the manufacturing plant complies with the requirements of Chinese Good Manufacturing Practices (GMP of EU,

			WHO/ICT Q7) and this written confirmation remains valid till 23-08-2024. Copy of GMP certificate (No.JS20180928) of Changzhou Pharmaceutical Factory issued by China Food and Drug Administration. The certificate is valid till 12-11-2023. The certificate is also verified online from NMPA database.
3.	1.5.8	Evidence of approval of applied formulation already approved by DRAP with brand name, Registration number and manufacturer name shall be submitted.	Firm has also submitted differential fee of 45000/- vide slip No. 4265665526 dated 17-10-2022.
4.	3.2.S.4.3	Validation studies of the drug substance performed by the drug product manufacturer shall be submitted.	Firm has submitted method verification studies for the drug substance including Specificity, Accuracy, Precision and Range.
5.	3.2.S.7.3	Complete real time stability studies for the drug substance shall be submitted.	Real time stability data of three batches i.e. ELNB210401, ELNB210501 & ELNB210701 only for 12 months is provided. While the accelerated stability data of three batches i.e. ELNB210401, ELNB210501 & ELNB210701 for 06 months is provided. *Real time Stability study data is only for one year*.
6.	3.2.P.2.2	In both Pharmaceutical Equivalence and Comparative Dissolution Profile two different brand names are mentioned while formulation development has mentioned product of Celgene pharma. In some places Beacon pharma products are mentioned. Clarification shall be submitted.	Firm has submitted that in product development data we have mentioned details of brand leader as reference product which is REVLIMID CAPSULE manufactured by Celgene Corporation Summit, NJ 07901, but, due to unavailability of this reference product in Pakistan, we have performed pharmaceutical equivalence and Comparative Dissolution Profile studies against locally available brand i.e., Linamide Capsule manufactured by Beacon Pharmaceuticals Limited Bangladesh. This is in accordance with the decision of Drug Registration Board taken in its 307th meeting.
7.	3.2.P.2.2.1	Justification shall be submitted regarding the selection of only two time points and paddle speed of 75 rpm in comparative dissolution studies. Reference product has used 50rpm and sampling time of 10, 15, 20, 30 & 45.	As per WHO, Annex 6, Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability, 10.1.2 Determination of dissolution characteristics of multisource products in consideration of a bio waiver based on the Biopharmaceutics Classification System,

			for very rapid release product use paddle apparatus at 75 rpm therefore subjected speed conducted for CDP. Also Minutes of 293rd Meeting of Registration Board (6 – 8th January, 2020), USFDA Guidance for Industry Dissolution Testing of Immediate Release Solid Oral Dosage Forms was followed for guidance which states "with the paddle method, it is 50-75 rpm (Shah et al., 1992)." (Section 3.2.P.2.2.1). While reference product manufacturer used 50 rpm for finish product dissolution testing and we also performed the same for submitted initial & stability studies. Further regarding the selection of only two time points, same above references are adopted as the test product releases above 85% in 10 minutes then only further one-time point included in report and dissolution release achieved 85% for both of test and reference products within 15 minutes due to this no need to calculate f_2 factor therefore 3rd time point is not the part of test report. Reference of above guidelines attached in the section of (3.2.P.2.2.1).
8.	3.2.P.5.2	Sample preparation method in the dissolution studies shall be submitted.	Submitted.
9.	3.2.P.8	• Stability condition for real time stability studies of the drug product are 30°C ± 2°C / 75% ± 5%RH instead of 30°C ± 2°C / 65% ± 5%RH. Justification shall be submitted.	Firm has submitted that they conduct stability studies on more worst condition than those data is also acceptable for comparatively relaxed condition. As per policy we conduct the stability studies for real time as per Zone IV(b) requirement which is more stringent and acceptable for DRAP requirement for Zone IV(a) as well as for those regulatory authorities where requirement is IV(b).

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the *pharmaceutical* i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year.

In compliance to the aforementioned decision of the Authority, Assistant Director (PR-I/EFD) vide letter No. F.1-6/2019-PR-I (EFD) dated 06th October, 2022 has informed that **M/s Pharmedic Laboratories (Pvt.) Ltd, Lahore** has achieved the benchmark of more than **100,000 USD (1576776.335 USD)** during the fiscal Year 2019-2020 and submitted their applications for priority consideration/ evaluation.

Following products are presented before the Board in light of the decision of the 133rd meeting of DRAP

Authority held on 13th April 2022 for consideration.		
434.	Name, address of Applicant / Marketing Authorization Holder	Pharmedic Laboratories (Pvt.) Ltd., 16Km Multan Road, Lahore.
	Name, address of Manufacturing site.	Pharmedic Laboratories (Pvt.) Ltd., 16Km Multan Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13722: dated 07-06-2022.
	Details of fee submitted	PKR 30,000/- vide slip No. 4235445044 dated 11-05-2022.
	The proposed proprietary name / brand name	Rovastin 5mg Tablet.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains; Rosuvastatin as Calcium ……..5mg
	Pharmaceutical form of applied drug	Light yellow color, round, biconvex film coated tablets.
	Pharmacotherapeutic Group of (API)	HMG CoA reductase inhibitors.
	Reference to Finished product specifications	USP specifications.
	Proposed Pack size	10’s.
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	CRESTOR (rosuvastatin as calcium) 5mg, 10mg, 20 mg & 40 mg coated tablets, USFDA approved.
	For generic drugs (me-too status)	Rovista tablet 5mg, Getz Pharma, Reg. No. 044043.
	GMP status of the Finished product manufacturer	GMP certificate No. 93/2020-DRAP (AD-2003099-790) dated 09-06-2020 issued on the basis of inspection conducted on 04-02-2020 is submitted.
	Evidence of section approval.	Tablet Non antibiotic, Antibiotic, Psychotropic, Cephalosporin & Anit-Cancer are mentioned in the above submitted GMP certificate.
	Name and address of API manufacturer.	Holder; M/s Changzhou Pharmaceutical Factory, No. 518 East Laodong Road, Jiangsu Province China. GMP certificate No. JS20180848 issued by the Jiangsu Food and Drug Administration valid till 09-07-2023 is provided.

		Manufacturer; M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road,v Yangkou chemical industrial Park, Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China. Copy of License for drug production in the name of Nantong Chanyoo Pharmatech., Co., Ltd., with license No. Su20160512 issued by Jiangsu Food and Drug Administration dated 03-12-2020 is submitted.
	Module-II (Quality Overall Summary)	Firm has nor submitted QOS as per WHO QOS-PD template.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubility, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies (Drug substance.)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 24 months. Batches:(RS-190308, RS-190309 & RS-109311).
	Module-III (Drug Product):	Firm has submitted detail of drug product including its description, composition, pharmaceutical development, manufacturer, manufacturing process and process control, process validation protocols, control of drug product, specifications, analytical procedures, analytical method verification studies, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the competitor product i.e. Rovista 5mg tablets manufactured by M/s Getz Pharma having batch No. 293F17, Exp. Date 10-2023 by performing quality tests (Disintegration, Dissolution, and Assay). CDP has been performed against the same brand Rovista 5mg tablets manufactured by M/s Getz Pharma having batch No. 293F17, Exp. Date 10-2023 in three different mediums. F2 values for all the three mediums are in acceptable range.

	Analytical method validation/verification of product.	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Holder;** M/s Changzhou Pharmaceutical Factory, No. 518 East Laodong Road, Jiangsu Province China. GMP certificate No. JS20180848 issued by the Jiangsu Food and Drug Administration valid till 09-07-2023 is provided. **Manufacturer;** M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road,v Yangkou chemical industrial Park, Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China. Copy of License for drug production in the name of Nantong Chanyoo Pharmatech., Co., Ltd., with license No. Su20160512 issued by Jiangsu Food and Drug Administration dated 03-12-2020 is submitted.		
API Lot No.	RS-701-200603.		
Description of Pack (Container closure system)	Alu-Alu blister sealed with Aluminum foil of 1×10's.		
Stability Storage Condition	Long term: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Long term: 6 months Accelerated: 12 months		
Frequency	Accelerated: 0, 3, 6 (Months) Long term: 0, 3, 6, 9, 12 (Months)		
Batch No.	ROS5-TR005	ROS5-TR006	ROS5-TR007
Batch Size	1000 Tablets.	1000 Tablets.	1000 Tablets.
Manufacturing Date	02-2021.	02-2021.	02-2021.
Date of Initiation	10-03-2021.	15-12-2021.	15-12-2021.
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION		
The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.		
Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted.
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Holder;** M/s Changzhou Pharmaceutical Factory, No. 518 East Laodong Road, Jiangsu Province China. GMP certificate No. JS20180848 issued by the Jiangsu Food and Drug Administration valid till 09-07-2023 is provided. **Manufacturer;** M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road,v Yangkou chemical industrial Park, Coastal Economic Development

		Zone, Nantong, Jiangsu Province 226407, China. Copy of License for drug production in the name of Nantong Chanyoo Pharmatech., Co., Ltd., with license No. Su20160512 issued by Jiangsu Food and Drug Administration dated 03-12-2020 is submitted.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice No. CY120236 dated 10-06-2020 mentioning Rosuvastatin calcium with quantity of 625gm, Batch No. RS-701-200603 attested by Assistant Director I&E DRAP, Lahore.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted.
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section	Observations	Reply by the firm
1.	1.3.4	Valid copy of DML of the finished product manufacturer shall be submitted. As submitted one is w.e.f. 07-04-2010.	
2.	1.6.5	Valid copy of GMP certificate for the drug substance manufacturer issued by the concerned/relevant regulatory authority shall be submitted.	
3.	2.3	Table of literature references has not mention BP for drug substance. Table of literature references has also shown JP for the finished product. Clarification shall be submitted.	
4.	3.2.S.4.1	Drug substance manufacturer has used Ph. Eur. specification for the drug substance while drug product manufacturer has used USP specifications. Justification shall be submitted.	
5.	3.2.S.4.2	Analytical procedures provided by the drug substance manufacturer are different from that of the drug product manufacturer. Justification shall be submitted.	
6.	3.2.S.4.3	Verification studies of the drug substance performed by the drug	

		product manufacturer shall be submitted.	
7.	3.2.S.4.4	• Clear and readable copies of COAs for the drug substance from drug substance manufacturer shall be submitted. • Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacturer shall also be submitted	
8.	3.2.S.5	Clear and readable copies of COAs for the reference/working standard shall be submitted.	
9.	3.2.P.2	Qualitative composition of the applied formulation is different from the innovator product. Justification shall be submitted.	
10.	3.2.P.2.2	Justification shall be submitted for not performing CDP and Pharmaceutical equivalence against the innovator product.	
11.	3.2.P.5.1	• Specifications has mentioned dissolution specification of NLT 75% Q while CDP has mentioned NLT 80% Q. Justification shall be submitted. • Value for weight variation in the specifications and stability data sheets are different from each other. Justify.	
12.	3.2.P.8.3	• 06th month time point accelerated stability study and real time stability study for Batch No. ROS5-006 and ROS5-007 shall be submitted. • Date of manufacture on BMR and stability data sheets are not similar. • Reference of previous approval of applications with stability study data of the firm (if any) shall be submitted.	
13.		Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	

Decision: Deferred for submission of above cited observations within six months.

435.	Name, address of Applicant / Marketing Authorization Holder	Pharmedic Laboratories (Pvt.) Ltd., 16Km Multan Road, Lahore.
	Name, address of Manufacturing site.	Pharmedic Laboratories (Pvt.) Ltd., 16Km Multan Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract

		giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13723: dated 07-06-2022.
	Details of fee submitted	PKR 30,000/- vide slip No. 639696389234 dated 11-05-2022.
	The proposed proprietary name / brand name	Rovastin 10mg Tablet.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains; Rosuvastatin as Calcium ……..10mg
	Pharmaceutical form of applied drug	Pink color, round shaped biconvex film coated tablets.
	Pharmacotherapeutic Group of (API)	HMG CoA reductase inhibitors.
	Reference to Finished product specifications	USP specifications.
	Proposed Pack size	10's.
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	CRESTOR (rosuvastatin as calcium) 5mg, 10mg, 20 mg & 40 mg coated tablets, USFDA approved.
	For generic drugs (me-too status)	Rovista tablet 10mg, Getz Pharma, Reg. No. 044044.
	GMP status of the Finished product manufacturer	GMP certificate No. 93/2020-DRAP (AD-2003099-790) dated 09-06-2020 issued on the basis of inspection conducted on 04-02-2020 is submitted.
	Evidence of section approval.	Tablet Non antibiotic, Antibiotic, Psychotropic, Cephalosporin & Anit-Cancer are mentioned in the above submitted GMP certificate.
	Name and address of API manufacturer.	**Holder;** M/s Changzhou Pharmaceutical Factory, No. 518 East Laodong Road, Jiangsu Province China. GMP certificate No. JS20180848 issued by the Jiangsu Food and Drug Administration valid till 09-07-2023 is provided. **Manufacturer;** M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road,v Yangkou chemical industrial Park, Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China. Copy of License for drug production in the name of Nantong Chanyoo Pharmatech., Co., Ltd., with license No. Su20160512 issued by Jiangsu

		Food and Drug Administration dated 03-12-2020 is submitted.
	Module-II (Quality Overall Summary)	Firm has nor submitted QOS as per WHO QOS-PD template.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubility, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies (Drug substance.)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 24 months. Batches:(RS-190308, RS-190309 & RS-109311).
	Module-III (Drug Product):	Firm has submitted detail of drug product including its description, composition, pharmaceutical development, manufacturer, manufacturing process and process control, process validation protocols, control of drug product, specifications, analytical procedures, analytical method verification studies, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the competitor product i.e. Rovista 10mg tablets manufactured by M/s Getz Pharma having batch No. 359F18, Exp. Date 01-2023 by performing quality tests (Disintegration, Dissolution, and Assay). CDP has been performed against the same brand Rovista 10mg tablets manufactured by M/s Getz Pharma having batch No. 359F18, Exp. Date 01-2023 in three different mediums. F2 calculations for Acetate buffer and phosphate buffer are not performed. The values for f2 in 1.2 pH is in the acceptable range.
	Analytical method validation/verification of product.	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	**Holder;**	

	M/s Changzhou Pharmaceutical Factory, No. 518 East Laodong Road, Jiangsu Province China. GMP certificate No. JS20180848 issued by the Jiangsu Food and Drug Administration valid till 09-07-2023 is provided. **Manufacturer;** M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road,v Yangkou chemical industrial Park, Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China.		
API Lot No.	RS-701-200603.		
Description of Pack (Container closure system)	Alu-Alu blister sealed with Aluminum foil of 1×10's.		
Stability Storage Condition	Long term: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Long term: 6 months Accelerated: 12 months		
Frequency	Accelerated: 0, 3, 6 (Months) Long term: 0, 3, 6, 9, 12 (Months)		
Batch No.	ROS10-TR005	ROS10-TR006	ROS10-TR007
Batch Size	1000 Tablets.	1000 Tablets.	1000 Tablets.
Manufacturing Date	02-2021.	02-2021.	02-2021.
Date of Initiation	10-03-2021.	15-12-2021.	15-12-2021.
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of the Holder is submitted while GMP certificate of the manufacturer is not submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice No. CY120236 dated 10-06-2020 mentioning Rosuvastatin calcium with quantity of 625gm, Batch No. RS-701-200603 attested by Assistant Director I&E DRAP, Lahore.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section	Observations	Reply by the firm
1.	1.3.4	Valid copy of DML of the finished product manufacturer shall be submitted. As submitted one is w.e.f. 07-04-2010.	
2.	1.6.5	Valid copy of GMP certificate for the drug substance manufacturer issued by the concerned/relevant regulatory authority shall be submitted.	
3.	2.3	Table of literature references has not mention BP for drug substance. Table of literature references has also shown JP for the finished product. Clarification shall be submitted.	
4.	3.2.S.4.1	Drug substance manufacturer has used Ph. Eur. specification for the drug substance while drug product manufacturer has used USP specifications. Justification shall be submitted.	
5.	3.2.S.4.2	Analytical procedures provided by the drug substance manufacturer are different from that of the drug product manufacturer. Justification shall be submitted.	
6.	3.2.S.4.3	Verification studies of the drug substance performed by the drug product manufacturer shall be submitted.	
7.	3.2.S.4.4	• Clear and readable copies of COAs for the drug substance from drug substance manufacturer shall be submitted. • Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacturer shall also be submitted	
8.	3.2.S.5	Clear and readable copies of COAs for the reference/working standard shall be submitted.	
9.	3.2.P.2	Qualitative composition of the applied formulation is different from the innovator product. Justification shall be submitted.	
10.	3.2.P.2.2	• Justification shall be submitted for not performing CDP and Pharmaceutical equivalence against the innovator product. • F2 calculations for acetate buffer and phosphate buffer shall be submitted.	
11.	3.2.P.5.1	• Specifications has mentioned dissolution specification of NLT	

		75% Q while CDP has mentioned NLT 80% Q. Justification shall be submitted. • Value for weight variation in the specifications and stability data sheets are different from each other. Justify.	
12.	3.2.P.8.3	• Weight variation test in the stability data is out of specification. Clarification shall be submitted. • Manufacturing date of batch No. ROS10-006 is December, 2021 and 06th month time point accelerated stability study and real time stability study shall be submitted. • 06th month time point accelerated stability study and real time stability study for Batch No. ROS10-007 shall be submitted. • Date of manufacture on BMR and stability data sheets are not similar. • Reference of previous approval of applications with stability study data of the firm (if any) shall be submitted.	
13.		Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	

Decision: Deferred for submission of above cited observations within six months.

436.	Name, address of Applicant / Marketing Authorization Holder	Pharmedic Laboratories (Pvt.) Ltd., 16Km Multan Road, Lahore.
	Name, address of Manufacturing site.	Pharmedic Laboratories (Pvt.) Ltd., 16Km Multan Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13724: dated 07-06-2022.
	Details of fee submitted	PKR 30,000/- vide slip No. 41094042890 dated 11-05-2022.
	The proposed proprietary name / brand name	Rovastin 20mg Tablet.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains; Rosuvastatin as Calcium ……..20mg
	Pharmaceutical form of applied drug	White color, round shaped, biconvex core

		tablets.
	Pharmacotherapeutic Group of (API)	HMG CoA reductase inhibitors.
	Reference to Finished product specifications	USP specifications.
	Proposed Pack size	10's.
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	CRESTOR (rosuvastatin as calcium) 5mg, 10mg, 20 mg & 40 mg coated tablets, USFDA approved.
	For generic drugs (me-too status)	Rovista tablet 20mg, Getz Pharma, Reg. No. 044045.
	GMP status of the Finished product manufacturer	GMP certificate No. 93/2020-DRAP (AD-2003099-790) dated 09-06-2020 issued on the basis of inspection conducted on 04-02-2020 is submitted.
	Evidence of section approval.	Tablet Non antibiotic, Antibiotic, Psychotropic, Cephalosporin & Anit-Cancer are mentioned in the above submitted GMP certificate.
	Name and address of API manufacturer.	Holder; M/s Changzhou Pharmaceutical Factory, No. 518 East Laodong Road, Jiangsu Province China. GMP certificate No. JS20180848 issued by the Jiangsu Food and Drug Administration valid till 09-07-2023 is provided. Manufacturer; M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road,v Yangkou chemical industrial Park, Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China. Copy of License for drug production in the name of Nantong Chanyoo Pharmatech., Co., Ltd., with license No. Su20160512 issued by Jiangsu Food and Drug Administration dated 03-12-2020 is submitted.
	Module-II (Quality Overall Summary)	Firm has nor submitted QOS as per WHO QOS-PD template.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubility, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies (Drug substance.)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions.

		The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 24 months. Batches:(RS-190308, RS-190309 & RS-109311).
	Module-III (Drug Product):	Firm has submitted detail of drug product including its description, composition, pharmaceutical development, manufacturer, manufacturing process and process control, process validation protocols, control of drug product, specifications, analytical procedures, analytical method verification studies, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the competitor product i.e. Rovista 20mg tablets manufactured by M/s Getz Pharma having batch No. 215F19, Exp. Date 01-2023 by performing quality tests (Disintegration, Dissolution, and Assay). CDP has been performed against the same brand Rovista 5mg tablets manufactured by M/s Getz Pharma having batch No. 215F19, Exp. Date 01-2023 in three different mediums. In all the three mediums more than 85% release is observer in 15minut time point and hence F2 values are not calculated.
	Analytical method validation/verification of product.	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	**Holder;** M/s Changzhou Pharmaceutical Factory, No. 518 East Laodong Road, Jiangsu Province China. GMP certificate No. JS20180848 issued by the Jiangsu Food and Drug Administration valid till 09-07-2023 is provided. **Manufacturer;** M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road,v Yangkou chemical industrial Park, Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China.
API Lot No.	RS-701-200603.
Description of Pack (Container closure system)	Alu-Alu blister sealed with Aluminum foil of 1×10's.
Stability Storage Condition	Long term: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Long term: 03 months Accelerated: 03 months
Frequency	Accelerated: 0, 3 (Months)

	Long term: 0, 3 (Months)		
Batch No.	ROS20-TR002	ROS20-TR003	ROS20-TR004
Batch Size	1000 Tablets.	1000 Tablets.	1000 Tablets.
Manufacturing Date	02-2021.	02-2021.	02-2021.
Date of Initiation	15-12-2021.	15-12-2021.	15-12-2021.
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not submitted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Holder;** M/s Changzhou Pharmaceutical Factory, No. 518 East Laodong Road, Jiangsu Province China. GMP certificate No. JS20180848 issued by the Jiangsu Food and Drug Administration valid till 09-07-2023 is provided. **Manufacturer;** M/s Nantong Chanyoo Pharmatech Co., Ltd., No. 2 Tonghai Si Road,v Yangkou chemical industrial Park, Coastal Economic Development Zone, Nantong, Jiangsu Province 226407, China. Copy of License for drug production in the name of Nantong Chanyoo Pharmatech., Co., Ltd., with license No. Su20160512 issued by Jiangsu Food and Drug Administration dated 03-12-2020 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of commercial invoice No. CY120236 dated 10-06-2020 mentioning Rosuvastatin calcium with quantity of 625gm, Batch No. RS-701-200603 attested by Assistant Director I&E DRAP, Lahore.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section	Observations	Reply by the firm

1.	1.3.4	Valid copy of DML of the finished product manufacturer shall be submitted. As submitted one is w.e.f. 07-04-2010.	
2.	1.6.5	Valid copy of GMP certificate for the drug substance manufacturer issued by the concerned/relevant regulatory authority shall be submitted.	
3.	2.3	Table of literature references has not mention BP for drug substance. Table of literature references has also shown JP for the finished product. Clarification shall be submitted.	
4.	3.2.S.4.1	Drug substance manufacturer has used Ph. Eur. specification for the drug substance while drug product manufacturer has used USP specifications. Justification shall be submitted.	
5.	3.2.S.4.2	Analytical procedures provided by the drug substance manufacturer are different from that of the drug product manufacturer. Justification shall be submitted.	
6.	3.2.S.4.3	Verification studies of the drug substance performed by the drug product manufacturer shall be submitted.	
7.	3.2.S.4.4	• Clear and readable copies of COAs for the drug substance from drug substance manufacturer shall be submitted. • Certificate of Analysis (COA) of the same batch from Drug Substance / API manufacturer shall also be submitted	
8.	3.2.S.5	Clear and readable copies of COAs for the reference/working standard shall be submitted.	
9.	3.2.P.2	Qualitative composition of the applied formulation is different from the innovator product. Justification shall be submitted.	
10.	3.2.P.2.2	• Justification shall be submitted for not performing CDP and Pharmaceutical equivalence against the innovator product. • F2 calculations for acetate buffer and phosphate buffer shall be submitted.	
11.	3.2.P.5.1	• Specifications has mentioned dissolution specification of NLT 75% Q while CDP has mentioned	

		NLT 80% Q. Justification shall be submitted. • Value for weight variation in the specifications and stability data sheets are different from each other. Justify.	
12.	3.2.P.8.3	• 06th month time point accelerated stability study and real time stability study for all the batches shall be submitted. • Date of manufacture on BMR and stability data sheets are not similar. • Reference of previous approval of applications with stability study data of the firm (if any) shall be submitted.	
13.		Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	

Decision: Deferred for submission of above cited observations within six months.

b. Registration applications of locally manufactured Human Drugs of Export Facilitation on form 5D.

In pursuance of decision of 133rd meeting of DRAP Authority held on 13th April 2022, wherein it was decided to grant registration on priority basis to the *pharmaceutical* i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year.
In compliance to the aforementioned decision of the Board, Assistant Director (PR-I/EFD) vide letter No. F.1-6/2019-PR-I (EFD) dated 06th October, 2022 has informed that **M/s Surge Laboratories (Pvt.) Ltd, Sheikhupura** has achieved the benchmark of more than **100,000 USD (790529.78 USD)** during the fiscal Year 2019-2020 and submitted their applications for priority consideration/ evaluation.
Following products are presented before the Board in light of the decision of the 133rd meeting of DRAP Authority held on 13th April 2022 for consideration.

437.	Name and address of manufacturer / Applicant	M/s Surge Laboratories (Pvt.) Ltd, 10-Km, Faisalabad Road, Sheikhupura.
	Brand Name +Dosage Form + Strength	Neofen Injection 200mg/2ml.
	Diary No. Date of R& I & fee	Form-5D, 17-06-2010, diary #_____ **Photocopy**& 15-08-2013 diary No.____ **Photocopy** Rs.35000 Only Photocopies are attached.
	Composition	Each 2ml contains: - Ibuprofen……..…….200mg
	Pharmacological Group	Analgesic.
	Type of Form	Form 5.
	Finished Product Specification	Manufacturers specification
	Pack size & Demanded Price	Rs.435 per ampoule
	Approval status of product in Reference Regulatory Authorities.	The product is not confirmed in this volume in FDA, require to be submitted.
	Me-too status	N/A
	GMP status	

	Previous remarks of the Evaluator.	The local and international availability of the applied formulation could not be confirmed.
	Decision of 254th meeting of Registration Board.	International availability in same strength and dosage form is not confirmed. As per the decision of RB in its 251st meeting following is required: - • Certificate of Analysis of API. • Approval of API by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin. • Manufacturer will follow Drug Specification Rules, 1986. • Protocols followed for conduction of stability study and details of tests. • Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc. • Documents confirming import of API etc. • All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents. • Shelf life of two years shall be granted based upon the results 06 month accelerated and real time stability study data. • Commitment to continue real time stability study till assigned shelf life of the product.

STABILITY STUDY DATA			
Drug	Neofen Injection (Ibuprofen 200mg/2ml).		
Name of Manufacturer	M/s Surge Laboratories (Pvt.) Ltd, 10-Km, Faisalabad Road, Sheikhupura.		
Manufacturer of API	M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State Of America.		
API Lot No.	Initially not submitted. (C100-1607094M)		
Description of Pack (Container closure system)	Initially not submitted. (2ml clear glass ampoule USP type I)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6 (months)		
Batch No.	IBI-2-004	IBI-2-005	IBI-2-006
Batch Size	238 ampoules	238 ampoules	238 ampoules
Manufacturing Date	12-2019	12-2019	12-2019
Date of Initiation	16-12-2019	16-12-2019	28-12-2019
No. of Batches	03		
Date of Submission	20-04-2021 (Dy. No. 11773)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION		
DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
S. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Not submitted.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA from SI group with Lot No. 4050-3070 for Ibuprofen. However, COA from the finished product manufacturer is not provided.
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Not submitted.
4.	Stability study data of API from API manufacturer	Not submitted.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. MI-2015-CE-03496-1 dated 31-03-2020 issued to M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America by TGA Australia. The certificate is valid till 16-04-2022.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has provided copy of commercial invoice No. 434651 dated 29-03-2017 without any attestation from the DRAP. Furthermore, the invoice has only mentioned 0.5kg quantity of Ibuprofen while there is no lot number on the invoice.
7.	Protocols followed for conduction of stability study	Submitted.
8.	Method used for analysis of FPP	Not Submitted.
9.	Drug-excipients compatibility studies (where applicable)	Not submitted.
10.	Complete batch manufacturing record of three stability batches.	Not submitted.
11.	Record of comparative dissolution data (where applicable)	N/A
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

Remarks of the Evaluator:

Sr. No.	Observations	Submission by the firm.
1.	Valid copy of the DML and latest GMP certificate/inspection report conducted within last three years of the finished product manufacturer shall be submitted.	**M/s Surge Laboratories;** Copy of DML No. 000484 w.e.f. 19-12-2020 is submitted. Copy of GMP certificate No. 41/202-DRAP(Ad-9978029213) dated 05-04-2022 issued on the basis of inspection conducted on 05-10-2021 is submitted.
2.	Evidence of approval of applied formulation in Reference Regulatory Authorities as defined by the Registration Board in its 275th meeting shall be submitted.	Not Submitted.
3.	Valid copy of GMP certificate of the drug substance manufacturer issued by concerned/relevant regulatory authority shall be submitted.	Firm has submitted a document with heading of "written confirmation for active substances exported to EU" issued by Hubei Medical Products Administration wherein the issuing authority confirms that the manufacturing plant i.e. Hubei Biocause Heilen Pharmaceutical Co. Ltd., complies with the requirements of Chinese Good Manufacturing Practices (GMP of EU, WHO/ICT Q7) and this written confirmation remains valid till 27-08-2023. ***However, initially submitted dossier has mentioned M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America as drug substance manufacturer. While in reply they have changed it to Hubei Biocause Heilen Pharmaceutical Co. Ltd., China.***
4.	COA of the drug substance by the finished product manufacturer shall be submitted.	Firm has submitted copy of COA from M/s Surge Laboratories having name of supplier as Hubei Granules-Biocause Heilen Pharmaceutical Co. Ltd., Batch No. C100-1607094M. ***However, COA submitted in the initial dossier was from SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America with Lot No. 4050-3070 for Ibuprofen.*** ***Furthermore, COA from the drug substance manufacturer of China is also not provided.***
5.	Stability study data of the drug substance for both accelerated and real time from drug substance manufacturer shall be submitted.	Firm has submitted stability study data of 03 batches for the drug substance from M/s Hubei Granules-Biocause Heilen Pharmaceutical Co. Ltd., China. Real time: 30°C ± 2°C / 75% ± 5%RH for 72 months. Batches; (C100-1305307M, C100-1305308M & C100-1305309M) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06

		months. Batches; (C100-1812264M, C100-1812265M & C100-1812266M). ***Both real time and accelerated stability studies of the drug substance are for different batches.***
6.	Specifications of drug substance from both drug substance manufacturer and Finished Product manufacturer shall be submitted.	Submitted. ***Specifications from Hubei Biocause Heilen Pharmaceutical Co. Ltd., China is submitted instead of SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America***
7.	Analytical method used for analysis of drug substance from both drug substance manufacturer and Finished Product manufacturer shall be submitted.	Submitted. ***Analytical procedures from Hubei Biocause Heilen Pharmaceutical Co. Ltd., China is submitted instead of SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America***
8.	Analytical method along with specifications used for analysis of Finished Product shall be submitted.	Submitted.
9.	Specifications has mentioned pH from 7.3 to 8.3 while COA has pH specifications from 7.3 to 7.8. clarification shall be submitted.	Firm has submitted that pH limit of this product is from 7.3 to 7.8 while the pH mentioned on the stability data sheets was 7.3 to 8.3 by typographic mistake which has been corrected and revised stability sheets have also been submitted by the firm.
10.	Complete formulation including the inactive used in the applied formulation shall be submitted.	Submitted.
11.	Complete batch manufacturing record of three stability batches shall be submitted.	Submitted.
12.	Stability data sheets shall be as per decision of 293rd meeting of Registration Board with inclusion of API lot number, batch size etc.	Firm has submitted stability data summary sheets as per decision of 293rd meeting of Registration Board with inclusion of API lot number (C100-1607094M) and total batch size (238 ampoules). They have also included bacterial endotoxins and sterility test in the revised stability data sheets.
13.	Justification shall be submitted for not performing the sterility testing in the stability data for the applied formulation.	Firm has submitted that in routine they use to conduct the sterility testing of injectable products at each time point during stability, the reports were kept at microbiology section, and unfortunately we do not use to make them part of the final stability reports, since major focus were on potency degradation. They further submitted that they now collected the said reports from microbiology and make them part of the revised stability summary data sheets.
14.	Documents for the procurement of API with approval from DRAP with mentioning batch number of the drug substance shall be submitted.	Firm has submitted copy document having invoice No. W170217-035 dated 22-02-2017 mentioning 2kg of Ibuprofen, batch No. C100-1607094M attested by ADC, DRAP, Lahore

		dated 24-03-2017. ***In the initially submitted dossier copy of commercial invoice No. 434651 dated 29-03-2017 without any attestation from the DRAP.***
15.	Reference of previous approval of applications with stability study data of the firm shall be submitted.	Firm has submitted reference of their product Nervlok-Heavy Injection, approved in 313th meeting of the Registration Board. The applied product was on form 5F.
16.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	Only compliance certificate is submitted however no audit trial is submitted.
17.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) shall be submitted.	Hand written digital logger is submitted.

Decision: Deferred for following;

- **Valid copy of GMP certificate/DML of the drug substance manufacturer issued by concerned/relevant regulatory authority.**
- **COA of the drug substance from drug substance manufacturer with lot number used in the development of the product shall be submitted.**
- **Justification for change of source of drug substance as initially drug substance Source was from USA while afterward it was changed to China.**
- **Justification shall be submitted for the batch size as only 238 ampoules were manufactured in each trial batch while sterility is also claimed in the submitted data.**
- **Evidence of approval of applied formulation in Reference Regulatory Authorities as defined by the Registration Board in its 275th meeting shall be submitted.**
- **Confirmation of submission of Form 5 application from R&I record.**

438.	Name and address of manufacturer / Applicant	M/s Surge Laboratories (Pvt.) Ltd, 10-Km, Faisalabad Road, Sheikhupura.
	Brand Name +Dosage Form + Strength	Neofen Injection 400mg/4ml.
	Diary No. Date of R& I & fee	Form-5D, 17-06-2010, diary #_____ **Photocopy**& 15-08-2013 diary No.____ **Photocopy** Rs.35000 Only Photocopies are attached.
	Composition	Each 4ml contains: - Ibuprofen…….……400mg
	Pharmacological Group	Analgesic.
	Type of Form	Form 5D.
	Finished Product Specification	Manufacturers specification
	Pack size & Demanded Price	Rs.435 per ampoule
	Approval status of product in Reference Regulatory Authorities.	Caldolor 400mg/4ml, USFDA approved.
	Me-too status	N/A
	GMP status	
	Decision of 254th meeting of Registration Board.	As per the decision of RB in its 251st meeting following is required: - • Certificate of Analysis of API. • Approval of API by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin.

		• Manufacturer will follow Drug Specification Rules, 1986. • Protocols followed for conduction of stability study and details of tests. • Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc. • Documents confirming import of API etc. • All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents. • Shelf life of two years shall be granted based upon the results 06 month accelerated and real time stability study data. • Commitment to continue real time stability study till assigned shelf life of the product.

STABILITY STUDY DATA			
Drug	Neofen Injection (Ibuprofen 400mg/4ml).		
Name of Manufacturer	M/s Surge Laboratories (Pvt.) Ltd, 10-Km, Faisalabad Road, Sheikhupura.		
Manufacturer of API	M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State Of America.		
API Lot No.	Initially not submitted. (C100-1607094M)		
Description of Pack (Container closure system)	Initially not submitted. (5ml clear glass ampoule USP type I)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6 (months)		
Batch No.	IBI-4-004	IBI-4-005	IBI-4-006
Batch Size	121 ampoules	121 ampoules	121 ampoules
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	14-01-2020	25-01-2020	25-01-2020
No. of Batches	03		
Date of Submission	20-04-2021 (Dy. No. 11774)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

S. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Not submitted.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA from SI group with Lot No. 4050-3070 for Ibuprofen.

		However, COA from the finished product manufacturer is not provided.
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Not submitted.
4.	Stability study data of API from API manufacturer	Not submitted.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. MI-2015-CE-03496-1 dated 31-03-2020 issued to M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America by TGA Australia. The certificate is valid till 16-04-2022.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided.
7.	Protocols followed for conduction of stability study	Submitted.
8.	Method used for analysis of FPP	Not Submitted.
9.	Drug-excipients compatibility studies (where applicable)	Not submitted.
10.	Complete batch manufacturing record of three stability batches.	Not submitted.
11.	Record of comparative dissolution data (where applicable)	N/A
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

Remarks of the Evaluator:

Sr. No.	Observations	Submission by the firm.
1.	Valid copy of the DML and latest GMP certificate/inspection report conducted within last three years of the finished product manufacturer shall be submitted.	**M/s Surge Laboratories;** Copy of DML No. 000484 w.e.f. 19-12-2020 is submitted. Copy of GMP certificate No. 41/202-DRAP(Ad-9978029213) dated 05-04-2022 issued on the basis of inspection conducted on 05-10-2021 is submitted.
2.	Valid copy of GMP certificate of the drug substance manufacturer issued by concerned/relevant regulatory authority shall be submitted.	Firm has submitted a document with heading of "written confirmation for active substances exported to EU" issued by Hubei Medical Products Administration wherein the issuing authority confirms that the manufacturing plant i.e. Hubei Biocause Heilen Pharmaceutical Co. Ltd., complies with the

		requirements of Chinese Good Manufacturing Practices (GMP of EU, WHO/ICT Q7) and this written confirmation remains valid till 27-08-2023. ***However, initially submitted dossier has mentioned M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America as drug substance manufacturer. While in reply they have changed it to Hubei Biocause Heilen Pharmaceutical Co. Ltd., China.***
3.	COA of the drug substance by the finished product manufacturer shall be submitted.	Firm has submitted copy of COA from M/s Surge Laboratories having name of supplier as Hubei Granules-Biocause Heilen Pharmaceutical Co. Ltd., Batch No. C100-1607094M. ***However, COA submitted in the initial dossier was from SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America with Lot No. 4050-3070 for Ibuprofen.*** ***Furthermore, COA from the drug substance manufacturer of China is also not provided.***
4.	Stability study data of the drug substance for both accelerated and real time from drug substance manufacturer shall be submitted.	Firm has submitted stability study data of 03 batches for the drug substance from M/s Hubei Granules-Biocause Heilen Pharmaceutical Co. Ltd., China. Real time: 30°C ± 2°C / 75% ± 5%RH for 72 months. Batches; (C100-1305307M, C100-1305308M & C100-1305309M) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months. Batches; (C100-1812264M, C100-1812265M & C100-1812266M). ***Both real time and accelerated stability studies of the drug substance are for different batches.***
5.	Specifications of drug substance from both drug substance manufacturer and Finished Product manufacturer shall be submitted.	Submitted. ***Specifications from Hubei Biocause Heilen Pharmaceutical Co. Ltd., China is submitted instead of SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America***
6.	Analytical method used for analysis of drug substance from both drug substance manufacturer and Finished Product manufacturer shall be submitted.	Submitted. ***Analytical procedures from Hubei Biocause Heilen Pharmaceutical Co. Ltd., China is submitted instead of SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America***
7.	Analytical method along with specifications used for analysis of Finished Product shall be submitted.	Submitted.

8.	Specifications has mentioned pH from 7.3 to 8.3 while COA has pH specifications from 7.3 to 7.8. clarification shall be submitted.	Firm has submitted that pH limit of this product is from 7.3 to 7.8 while the pH mentioned on the stability data sheets was 7.3 to 8.3 by typographic mistake which has been corrected and revised stability sheets have also been submitted by the firm.
9.	Complete formulation including the inactive used in the applied formulation shall be submitted.	Submitted.
10.	Complete batch manufacturing record of three stability batches shall be submitted.	Submitted.
11.	Stability data sheets shall be as per decision of 293rd meeting of Registration Board with inclusion of API lot number, batch size etc.	Firm has submitted stability data summary sheets as per decision of 293rd meeting of Registration Board with inclusion of API lot number (C100-1607094M) and total batch size (121 ampoules). They have also included bacterial endotoxins and sterility test in the revised stability data sheets.
12.	Justification shall be submitted for not performing the sterility testing in the stability data for the applied formulation.	Firm has submitted that in routine they use to conduct the sterility testing of injectable products at each time point during stability, the reports were kept at microbiology section, and unfortunately we do not use to make them part of the final stability reports, since major focus were on potency degradation. They further submitted that they now collected the said reports from microbiology and make them part of the revised stability summary data sheets.
13.	Documents for the procurement of API with approval from DRAP with mentioning batch number of the drug substance shall be submitted.	Firm has submitted copy document having invoice No. W170217-035 dated 22-02-2017 mentioning 2kg of Ibuprofen, batch No. C100-1607094M attested by ADC, DRAP, Lahore dated 24-03-2017. ***In the initially submitted dossier copy of commercial invoice No. 434651 dated 29-03-2017 without any attestation from the DRAP.***
14.	Reference of previous approval of applications with stability study data of the firm shall be submitted.	Firm has submitted reference of their product Nervlok-Heavy Injection, approved in 313th meeting of the Registration Board. The applied product was on form 5F.
15.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	Only compliance certificate is submitted however no audit trial is submitted.
16.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) shall be submitted.	Hand written digital logger is submitted.

Decision: Deferred for following;

- **Valid copy of GMP certificate/DML of the drug substance manufacturer issued by concerned/relevant regulatory authority.**
- **COA of the drug substance from drug substance manufacturer with lot number used in the development of the product shall be submitted.**

- **Justification for change of source of drug substance as initially drug substance source was from USA while afterward it was changed to China.**
- **Justification shall be submitted for the batch size as only 121 ampoules were manufactured in each trial batch while sterility is also claimed in the submitted data.**
- **Confirmation of submission of Form 5 application from R&I record.**

439.	Name and address of manufacturer / Applicant	M/s Surge Laboratories (Pvt.) Ltd, 10-Km, Faisalabad Road, Sheikhupura.
	Brand Name +Dosage Form + Strength	Neofen Injection 800mg/8ml.
	Diary No. Date of R& I & fee	Form-5D, 17-06-2010, diary #_____ **Photocopy**& 15-08-2013 diary No.____ **Photocopy** Rs.35000 Only Photocopies are attached.
	Composition	Each 8ml contains: - Ibuprofen…….…….800mg
	Pharmacological Group	Analgesic.
	Type of Form	Form 5D.
	Finished Product Specification	Manufacturers specification
	Pack size & Demanded Price	Rs.540 per ampoule
	Approval status of product in Reference Regulatory Authorities.	Caldolor 800mg/8ml, USFDA approved.
	Me-too status	N/A
	GMP status	
	Decision of 254th meeting of Registration Board.	Deferred for completion of application as under:- As per the decision of RB in its 251st meeting following is required: - • Certificate of Analysis of API. • Approval of API by regulatory authority of country of origin or GMP certificate of API manufacturer issued by regulatory authority of country of origin. • Manufacturer will follow Drug Specification Rules, 1986. • Protocols followed for conduction of stability study and details of tests. • Data of 03 batches will be supported by attested respective documents like chromatograms, laboratory reports, data sheets etc. • Documents confirming import of API etc. • All provided documents will be attested (name, sign and stamp) for ensuring authenticity of data / documents. • Shelf life of two years shall be granted based upon the results 06 month accelerated and real time stability study data. • Commitment to continue real time stability study till assigned shelf life of the product.

STABILITY STUDY DATA	
Drug	Neofen Injection (Ibuprofen 800mg/8ml).
Name of Manufacturer	M/s Surge Laboratories (Pvt.) Ltd, 10-Km, Faisalabad Road, Sheikhupura.

Manufacturer of API	M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State Of America.		
API Lot No.	Initially not submitted. (C100-1607094M)		
Description of Pack (Container closure system)	Initially not submitted. (10ml clear glass ampoule USP type I)		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Real time: 0,3,6 (months) Accelerated: 0,3,6 (months)		
Batch No.	IBI-8-004	IBI-8-005	IBI-8-006
Batch Size	60 ampoules.	60 ampoules.	60 ampoules.
Manufacturing Date	01-2020	01-2020	01-2020
Date of Initiation	08-01-2020	14-01-2020	14-01-2020
No. of Batches	03		
Date of Submission	20-04-2021 (Dy. No. 11775)		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT FOR EXEMPTION

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

S. No.	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm	Not submitted.
2.	Certificate of Analysis of API from both API Manufacturer and Finished Product manufacturer.	Firm has submitted copy of COA from SI group with Lot No. 4050-3070 for Ibuprofen. However, COA from the finished product manufacturer is not provided.
3.	Method used for analysis of API from both API Manufacturer and Finished Product manufacturer	Not submitted.
4.	Stability study data of API from API manufacturer	Not submitted.
5.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted copy of GMP certificate No. MI-2015-CE-03496-1 dated 31-03-2020 issued to M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America by TGA Australia. The certificate is valid till 16-04-2022.
6.	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided.
7.	Protocols followed for conduction of stability study	Submitted.
8.	Method used for analysis of FPP	Not Submitted.
9.	Drug-excipients compatibility studies (where applicable)	Not submitted.
10.	Complete batch manufacturing record of three stability batches.	Not submitted.

11.	Record of comparative dissolution data (where applicable)	N/A
12.	Data of 03 batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
13.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not Submitted
14.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Not Submitted

Remarks of the Evaluator:

Sr. No.	Observations	Submission by the firm.
1.	Valid copy of the DML and latest GMP certificate/inspection report conducted within last three years of the finished product manufacturer shall be submitted.	**M/s Surge Laboratories;** Copy of DML No. 000484 w.e.f. 19-12-2020 is submitted. Copy of GMP certificate No. 41/202-DRAP(Ad-9978029213) dated 05-04-2022 issued on the basis of inspection conducted on 05-10-2021 is submitted.
2.	Valid copy of GMP certificate of the drug substance manufacturer issued by concerned/relevant regulatory authority shall be submitted.	Firm has submitted a document with heading of "written confirmation for active substances exported to EU" issued by Hubei Medical Products Administration wherein the issuing authority confirms that the manufacturing plant i.e. Hubei Biocause Heilen Pharmaceutical Co. Ltd., complies with the requirements of Chinese Good Manufacturing Practices (GMP of EU, WHO/ICT Q7) and this written confirmation remains valid till 27-08-2023. ***However, initially submitted dossier has mentioned M/s SI Group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America as drug substance manufacturer. While in reply they have changed it to Hubei Biocause Heilen Pharmaceutical Co. Ltd., China.***
3.	COA of the drug substance by the finished product manufacturer shall be submitted.	Firm has submitted copy of COA from M/s Surge Laboratories having name of supplier as Hubei Granules-Biocause Heilen Pharmaceutical Co. Ltd., Batch No. C100-1607094M. ***However, COA submitted in the initial dossier was from SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America with Lot No. 4050-3070 for Ibuprofen.*** ***Furthermore, COA from the drug substance manufacturer of China is also not provided.***
4.	Stability study data of the drug substance	Firm has submitted stability study data of 03

	for both accelerated and real time from drug substance manufacturer shall be submitted.	batches for the drug substance from M/s Hubei Granules-Biocause Heilen Pharmaceutical Co. Ltd., China. Real time: 30°C ± 2°C / 75% ± 5%RH for 72 months. Batches; (C100-1305307M, C100-1305308M & C100-1305309M) Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months. Batches; (C100-1812264M, C100-1812265M & C100-1812266M). ***Both real time and accelerated stability studies of the drug substance are for different batches.***
5.	Specifications of drug substance from both drug substance manufacturer and Finished Product manufacturer shall be submitted.	Submitted. ***Specifications from Hubei Biocause Heilen Pharmaceutical Co. Ltd., China is submitted instead of SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America***
6.	Analytical method used for analysis of drug substance from both drug substance manufacturer and Finished Product manufacturer shall be submitted.	Submitted. ***Analytical procedures from Hubei Biocause Heilen Pharmaceutical Co. Ltd., China is submitted instead of SI group Inc. 725 Cannon Bridge Road Orangeburg SC United State of America***
7.	Analytical method along with specifications used for analysis of Finished Product shall be submitted.	Submitted.
8.	Specifications has mentioned pH from 7.3 to 8.3 while COA has pH specifications from 7.3 to 7.8. clarification shall be submitted.	Firm has submitted that pH limit of this product is from 7.3 to 7.8 while the pH mentioned on the stability data sheets was 7.3 to 8.3 by typographic mistake which has been corrected and revised stability sheets have also been submitted by the firm.
9.	Complete formulation including the inactive used in the applied formulation shall be submitted.	Submitted.
10.	Complete batch manufacturing record of three stability batches shall be submitted.	Submitted.
11.	Stability data sheets shall be as per decision of 293rd meeting of Registration Board with inclusion of API lot number, batch size etc.	Firm has submitted stability data summary sheets as per decision of 293rd meeting of Registration Board with inclusion of API lot number (C100-1607094M) and total batch size (121 ampoules). They have also included bacterial endotoxins and sterility test in the revised stability data sheets.
12.	Justification shall be submitted for not performing the sterility testing in the stability data for the applied formulation.	Firm has submitted that in routine they use to conduct the sterility testing of injectable products at each time point during stability, the reports were kept at microbiology section, and unfortunately we do not use to make them part of the final stability reports, since major focus

		were on potency degradation. They further submitted that they now collected the said reports from microbiology and make them part of the revised stability summary data sheets.
13.	Documents for the procurement of API with approval from DRAP with mentioning batch number of the drug substance shall be submitted.	Firm has submitted copy document having invoice No. W170217-035 dated 22-02-2017 mentioning 2kg of Ibuprofen, batch No. C100-1607094M attested by ADC, DRAP, Lahore dated 24-03-2017. ***In the initially submitted dossier copy of commercial invoice No. 434651 dated 29-03-2017 without any attestation from the DRAP.***
14.	Reference of previous approval of applications with stability study data of the firm shall be submitted.	Firm has submitted reference of their product Nervlok-Heavy Injection, approved in 313th meeting of the Registration Board. The applied product was on form 5F.
15.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	Only compliance certificate is submitted however no audit trial is submitted.
16.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) shall be submitted.	Hand written digital logger is submitted.

Decision: Deferred for following;

- **Valid copy of GMP certificate/DML of the drug substance manufacturer issued by concerned/relevant regulatory authority.**
- **COA of the drug substance from drug substance manufacturer with lot number used in the development of the product shall be submitted.**
- **Justification for change of source of drug substance as initially drug substance Source was from USA while afterward it was changed to China.**
- **Justification shall be submitted for the batch size as only 60 ampoules were manufactured in each trial batch while sterility is also claimed in the submitted data.**
- **Confirmation of submission of Form 5 application from R&I record.**

Case No. 02 Registration applications of newly granted DML or New section (Human) drugs on Form 5F.

CLB in its 282nd meeting held on 31st August 2021 has considered and approved the grant of Drug Manufacturing License by way of formulation with following six (06) sections to M/s Swera Pharmaceuticals.

1	Tablet (General)	4	Cream / Gel (general)
2	Capsule (General)	5	Lotion section (General)
3	Sachet (General)	6	Dry powder injection (General)

440.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals Islamabad.
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals, Plot No. 27, Street S-4, Industrial Area, Rawat.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28941 dated 12/10/2022.
	Details of fee submitted	PKR 30,000/-: vide slip No. 41557437353 dated 06/09/2022.
	The proposed proprietary name / brand name	Cipday 250mg Tablets.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet contains: Ciprofloxacin as hydrochloride ……..250mg
	Pharmaceutical form of applied drug	White to off white film coated tablets packed in Alu-Alu blister.
	Pharmacotherapeutic Group of (API)	Fluoroquinolones (J01MA)
	Reference to Finished product specifications	USP specs
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	Ciprofloxacin 250 mg, film coated tablets, MHRA approved.
	For generic drugs (me-too status)	Invoflox 250mg Tablet, Innvotek Pharmaceuticals, Reg. No. 096628.
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021.
	Evidence of section approval	Tablet (General) section approved vide letter No. F. 1-42/2011-Lic. Dated 16-09-2021.
	Name and address of API manufacturer.	Pharmagen Limited, Kot Nabi, Buksh Wala, 34-km Ferozepur Road, Lahore. Copy of GMP certificate No. 06/2019 DRAP (AD/607409-530) issued on the basis of inspection conducted on 09-01-2019 by DRAP valid till 08/01/2022 is submitted .
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official Monograph of Ciprofloxacin HCl is present in USP. The firm as submitted detail of

		nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis (00510011/244/2021) and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (RD-T001, RD-T002, RD-T003)
	Module-III (Drug Product):	The firm has submitted detail of the drug product including its description, composition, formulation development, manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the Innovator that is Ciproxin 250mg Tablets, Batch No. BAA954, Mfg. date 01-2022 manufactured by Bayer Pakistan by performing quality tests (Identification, weight variation, Disintegration, Dissolution & Assay). CDP has been performed against the same innovator that is Ciproxin 250mg Tablets, Batch No. BAA954, Mfg. date 01-2022 manufactured by Bayer Pakistan in pH 1.2, 4.5 and 6.8 media in pH 1.2, 4.5 more than 85% of the release is observed within 15minutes hence, F2 is not calculated. While in pH 6.8 release was lower than 85% in 15 minute and F2 is calculated for this medium and is in acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	Pharmagen Limited, Kot Nabi, Buksh Wala, 34-km Ferozepur Road, Lahore.
API Lot No.	00510011/244/2021.
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Batch No.	RD-T001	RD-T002	RD-T003
Batch Size	900 tablets	900 tablets	900 tablets
Manufacturing Date	03-2022	03-2022	03-2022
Date of Initiation	01-04-2022	01-04-2022	02-04-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 06/2019 DRAP (AD/607409-530) issued on the basis of inspection conducted on 09-01-2019 by DRAP valid till 08/01/2022 is submitted .
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice No. 2208 dated 12-03-2022 wherein they have purchased 25kg of Ciprofloxacin hydrochloride with batch No. of 00510011/244/2021 from M/s Pharmagen Limited.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section	Observation	Reply by the firm
1.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer shall be submitted.	Firm has submitted copy of GMP certificate No. 129/2020-DRAP (AD/1998630-53-) dated 02-09-2020 in the name of M/s Pharmagen Ltd., issued on the basis of inspection conducted on 22-06-2020.
2.	3.2.S.7.3	Complete real time and accelerated stability data sheets for the drug substance shall be submitted.	Firm has submitted both real time and accelerated stability study data for the drug substance. Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months

			Batches:(00510011/001/2014, 00510011/002/2014 & 00510011/003/2014)
3.	3.2.P.2.2	Qualitative composition is different from innovator product. Clarification shall be submitted.	Firm has submitted that the product is stable during the entire time for stability study. Moreover, the same excipients have been used in development of drug product as innovator product. They also provided leaflet of Ciproxin film coated tablet manufactured by Novartis pharma for Bayer Pakistan (Pvt.) Ltd., having the same excipients as that of the applied formulation.
4.	3.2.P.2.2	Justification shall be submitted for using 75 RPM in dissolution.	Firm has submitted that the 75 RPM is typographical mistake. Actual value is 50RPM.
5.	3.2.P.5.2	Injection volume in the assay method is 10µL in USP while firm has claimed 20 µL.	Firm has submitted that due to availability of 20µL injector we have used 20µL injection volume.
6.		Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	The firm submitted that they have new DML. They will make assure the compliance of 21CFR HPLC in nearby future.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

441.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals Islamabad.
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals, Plot No. 27, Street S-4, Industrial Area, Rawat.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28942 dated 12/10/2022.
	Details of fee submitted	PKR 30,000/-: vide slip No. 7137429249 dated 06/09/2022.
	The proposed proprietary name / brand name	Cipday 500mg Tablets.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Film Coated Tablet contains: Ciprofloxacin as hydrochloride ……..500mg

	Pharmaceutical form of applied drug	White to off white film coated tablets packed in Alu-Alu blister.
	Pharmacotherapeutic Group of (API)	Fluoroquinolones (J01MA)
	Reference to Finished product specifications	USP specs
	Proposed Pack size	1×10's
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	Ciprofloxacin 500 mg, film coated tablets, MHRA approved.
	For generic drugs (me-too status)	Invoflox 500mg Tablet, Innvotek Pharmaceuticals, Reg. No. 096629.
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021.
	Evidence of section approval	Tablet (General) section approved vide letter No. F. 1-42/2011-Lic. Dated 16-09-2021.
	Name and address of API manufacturer.	Pharmagen Limited, Kot Nabi, Buksh Wala, 34-km Ferozepur Road, Lahore. Copy of GMP certificate No. 06/2019 DRAP (AD/607409-530) issued on the basis of inspection conducted on 09-01-2019 by DRAP valid till 08/01/2022 is submitted .
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official Monograph of Ciprofloxacin HCl is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis (00510011/244/2021) and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(00510011/001/2014, 00510011/002/2014 & 00510011/003/2014)
	Module-III (Drug Product):	The firm has submitted detail of the drug product

		including its description, composition, formulation development, manufacturers, description of manufacturing process and controls, specifications, analytical procedure (including dissolution testing) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the Innovator that is Ciproxin 500mg Tablets, Batch No. BAA846, Mfg. date 11-2021 manufactured by Bayer Pakistan by performing quality tests (Identification, weight variation, Disintegration, Dissolution & Assay). CDP has been performed against the same innovator that is Ciproxin 500mg Tablets, Batch No. BAA846, Mfg. date 11-2021 manufactured by Bayer Pakistan in pH 1.2, 4.5 and 6.8 media in pH 1.2, 4.5 more than 85% of the release is observed within 15minutes hence, F2 is not calculated. While in pH 6.8 release was lower than 85% in 15 minute and F2 is calculated for this medium and is in acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Pharmagen Limited, Kot Nabi, Buksh Wala, 34-km Ferozepur Road, Lahore.		
API Lot No.	00510011/244/2021.		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	RD-T004	RD-T005	RD-T006
Batch Size	900 tab	900 tab	900 tab
Manufacturing Date	04-2022	04-2022	04-2022
Date of Initiation	07-04-2022	07-04-2022	07-04-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 06/2019 DRAP (AD/607409-530) issued on the basis of inspection conducted on 09-01-2019 by DRAP valid till 08/01/2022 is submitted .
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted copy of invoice No. 2208 dated 12-03-2022 wherein they have purchased 25kg of Ciprofloxacin hydrochloride with batch No. of 00510011/244/2021 from M/s Pharmagen Limited.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Section	Observation	Reply by the firm
1.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer shall be submitted.	Firm has submitted copy of GMP certificate No. 129/2020-DRAP (AD/1998630-53-) dated 02-09-2020 in the name of M/s Pharmagen Ltd., issued on the basis of inspection conducted on 22-06-2020.
2.	3.2.S.7.3	Complete real time and accelerated stability data sheets for the drug substance shall be submitted.	Firm has submitted boh real time and accelerated stability study data for the drug substance. Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(00510011/001/2014, 00510011/002/2014 & 00510011/003/2014)
3.	3.2.P.2.2	Qualitative composition is different from innovator product. Clarification shall be submitted.	Firm has submitted that the product is stable during the entire time for stability study. Moreover, the same excipients have been used in development of drug product as innovator product. They also provided leaflet of Ciproxin film coated tablet manufactured by Novartis pharma for Bayer Pakistan (Pvt.) Ltd., having the same excipients as that of the applied formulation.

4.	3.2.P.2.2	Justification shall be submitted for using 75 RPM in dissolution.	Firm has submitted that the 75 RPM is typographical mistake. Actual value is 50RPM.
5.	3.2.P.5.2	Injection volume in the assay method is 10µL in USP while firm has claimed 20 µL.	Firm has submitted that due to availability of 20µL injector we have used 20µL injection volume.
6.		Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	The firm submitted that they have new DML. They will make assure the compliance of 21CFR HPLC in nearby future.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

442.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals Islamabad.
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals, Plot No. 27, Street S-4, Industrial Area, Rawat.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales.
	Dy. No. and date of submission	Dy. No. 27131 dated 26/09/2022.
	Details of fee submitted	PKR 30,000/-: vide slip No. 8510651844 dated 13/09/2022.
	The proposed proprietary name / brand name	Emozol 40mg Injection.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Esomeprazole sodium eq. to Esomeprazole……. 40mg
	Pharmaceutical form of applied drug	White to off white color powder filled in transparent glass vial.
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor.
	Reference to Finished product specifications	Manufacturer's Specs.
	Proposed Pack size	1's.
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	NEXIUM® I.V. (esomeprazole sodium) for injection, for intravenous use Manufactured by: AstraZeneca Pharmaceuticals LP, USFDA approved.

	For generic drugs (me-too status)	Koncept 40mg Injection, M/s McOlson Research Laboratories, Reg. No. 060700.
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021.
	Evidence of section approval	Dry powder injection (General) section approved vide letter No. F. 1-42/2011-Lic. Dated 16-09-2021.
	Name and address of API manufacturer.	Vision Pharmaceuticals, Plot # 22-23, Industrial Triangle, Kahutta Road, Islamabad. Copy of GMP certificate No. F.3-26/2019-Addl. Dir. (QA & LT-I) dated 31-07-2019 issued on the basis of inspection conducted on 11-02-2019 valid till 10/02/2022 is submitted.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Firm has submitted detail of drug substance regarding to its nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis (2112901) and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (1703901, 1805901, 1708902)
	Module-III (Drug Product):	The firm has submitted detail of description and composition of the drug product, formulation development, manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the brand leader that is Nexum 40mg Injection, batch No. 152P07, Mfg. date 12-2021 manufactured by Getz Pharma by performing quality tests (Identification, Clarity of solution, particulate matter, pH & Assay).

	Analytical method validation/verification of product	Method validation studies have submitted including specificity, accuracy, precision, Linearity, range and Robustness.

STABILITY STUDY DATA			
Manufacturer of API	Vision Pharmaceuticals, Plot # 22-23, Industrial Triangle, Kahutta Road, Islamabad.		
API Lot No.	2112901		
Description of Pack (Container closure system)	glass vial packed in unit carton (1's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 3 months Accelerated: 3 months		
Frequency	Accelerated: 0, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.	RD-I001	RD-I002	
Batch Size	2133 Injection.	2132 Injection	
Manufacturing Date	01-2022	01-2022	
Date of Initiation	19-01-2022	19-01-2022	
No. of Batches	02		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. F.3-26/2019-Addl. Dir. (QA & LT-I) dated 31-07-2019 issued on the basis of inspection conducted on 11-02-2019 valid till 10/02/2022 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section	Observation	Reply by the firm.

1.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer shall be submitted.	Copy of GMP certificate No.F.3-26/2019-Addl. Dir. (QA&LT-I)-56 dated 22-08-2022 in the name of M/s Vision Pharmaceuticals (Pvt.) Ltd., issued on the basis of inspection conducted on 14-06-2022 is submitted.
2.	2.3.R	Copies of executed BMRs along with blank production document shall be submitted.	Submitted.
3.	3.2.S.4.1	Submit the composition of the drug substance since the submitted specifications declare the assay limit of 34% – 38% for Esomeprazole.	Firm has submitted that the drug substance contains 34-38% of Omeprazole while the remaining 62-66% is mannitol as mentioned in the Certificate of analysis of drug substance manufacturer. They also provided Certificate of analysis of drug substance from the manufacturer.
4.	3.2.S.7.3	Clear and readable copies of the stability data sheets of the drug substance shall be submitted.	Firm has submitted clear and readable copies of the stability data sheets of the drug substance.
5.	3.2.P.2.2	Justifications for developing only two trial batches in the formulation development and stability studies.	Firm has submitted that in selection of trial batches, they have followed "Guidance document for submission of application on form 5-F (CTD) (Edition 1)" which clearly indicates that: At least 2 batches having the following minimum batch size considering the scientific reliability • OSDs: 5000 Units • Oral Liquid/Suspension: 2000 • Injectable: 2000 As our batch size is greater than 2000 units, so we have proceeded for two trial batches.
6.	3.2.P.8.3	06th month time point stability data for both accelerated and real time of all the trial batches shall be submitted.	Firm has initially submitted 03 months stability data and now they provided 06 months stability data both real time and accelerated for the applied formulation.
7.	3.2.P.8.3	Raw data sheets and chromatograms for assay studies of both the batches for initial, 3rd and six month time point shall be submitted.	Submitted.
8.	3.2.P.8.3	Documents for the procurement of API shall be submitted.	Firm has submitted copy of invoice No. 801597 dated 29-12-2021 mentioning 0.45 kg of Omeprazole sodium lyophilized powder with batch No. 2112901 from M/s Vision pharma.
9.	3.2.P.8.3	Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	The firm submitted that they have new DML. They will make assure the compliance of 21CFR HPLC in nearby future.

Decision: Approved with innovator's specifications.

• **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**		
443.	Name, address of Applicant / Marketing Authorization Holder	M/s Swera Pharmaceuticals Islamabad.
	Name, address of Manufacturing site.	M/s Swera Pharmaceuticals, Plot No. 27, Street S-4, Industrial Area, Rawat.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐Domestic sale ☐ Export sale ☒ Domestic and Export sales.
	Dy. No. and date of submission	Dy. No. 27130 dated 26/09/2022.
	Details of fee submitted	PKR 30,000/-: vide slip No. 802460765103 dated 13/09/2022.
	The proposed proprietary name / brand name	Mepra 40mg Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole ……40mg.
	Pharmaceutical form of applied drug	White to off white color powder filled in transparent glass vial
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor.
	Reference to Finished product specifications	Sawera's Specs.
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole 40mg powder for solution for infusion, MHRA approved.
	For generic drugs (me-too status)	Somezol Injection, Bosch Pharma, Reg. No. 045386.
	GMP status of the Finished product manufacturer	New license granted on 13/09/2021.
	Evidence of section approval	Dry powder injection (General) section approved vide letter No. F. 1-42/2011-Lic. Dated 16-09-2021.
	Name and address of API manufacturer.	Vision Pharmaceuticals, Plot # 22-23, Industrial Triangle, Kahutta Road, Islamabad.

		Copy of GMP certificate No. F.3-26/2019-Addl. Dir. (QA & LT-I) dated 31-07-2019 issued on the basis of inspection conducted on 11-02-2019 valid till 10/02/2022 is submitted.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted detail of the drug substance regarding its nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its validation, batch analysis (2112902) and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months. Batches: (1709901, 1607901, 1704901)
	Module-III (Drug Product):	The firm has submitted detail of description and composition of the drug product, formulation development, manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the brand leader that is Rizek 40mg Injection, batch No. 954P06, Mfg. date 01-2022 manufactured by Getz Pharma by performing quality tests (Identification, Clarity of the solution, Particulate matters, pH & Assay).
	Analytical method validation/verification of product	Method validation studies have submitted including specificity, accuracy, precision, Linearity, range and Robustness.

STABILITY STUDY DATA

Manufacturer of API	Vision Pharmaceuticals (Pvt.) Ltd. Plot # 22-23, Industrial Triangle, Kahutta Road, Islamabad-Pakistan.
API Lot No.	2112902
Description of Pack	glass vial packed in unit carton (1's)

(Container closure system)			
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 03 months Accelerated: 03 months		
Frequency	Accelerated: 0, 3 (Months) Real Time: 0, 3 (Months)		
Batch No.	RD-I003	RD-I004	
Batch Size	2006 Injections	2005 Injections	
Manufacturing Date	01-2022	01-2022	
Date of Initiation	19-01-2022	19-01-2022	
No. of Batches	02		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. F.3-26/2019-Addl. Dir. (QA & LT-I) dated 31-07-2019 issued on the basis of inspection conducted on 11-02-2019 valid till 10/02/2022 is submitted.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Not Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr. No.	Section	Observation	Reply by the firm.
1.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer shall be submitted.	Copy of GMP certificate No.F.3-26/2019-Addl. Dir. (QA&LT-I)-56 dated 22-08-2022 in the name of M/s Vision Pharmaceuticals (Pvt.) Ltd., issued on the basis of inspection conducted on 14-06-2022 is submitted.
2.	2.3.R	Copies of executed BMRs along with blank production document shall be submitted.	Submitted.

3.	3.2.S.4.1	Submit the composition of the drug substance since the submitted specifications declare the assay limit of 34% – 38% for omeprazole.	Firm has submitted that the drug substance contains 36-40% of Omeprazole while the remaining 60-64% is mannitol as mentioned in the Certificate of analysis of drug substance manufacturer. They also provided Certificate of analysis of drug substance from the manufacturer.
4.	3.2.S.7.3	Clear and readable copies of the stability data sheets of the drug substance shall be submitted.	Submitted. Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months. Batches: (1702901, 1704901, 1709901)
5.	3.2.P.2.2	Justifications for developing only two trial batches in the formulation development and stability studies.	Firm has submitted that in selection of trial batches, they have followed "Guidance document for submission of application on form 5-F (CTD) (Edition 1)" which clearly indicates that: At least 2 batches having the following minimum batch size considering the scientific reliability • OSDs: 5000 Units • Oral Liquid/Suspension: 2000 • Injectable: 2000 As our batch size is greater than 2000 units, so we have proceeded for two trial batches.
6.	3.2.P.8.3	06th month time point stability data for both accelerated and real time of all the trial batches shall be submitted.	Firm has initially submitted 03 months stability data and now they provided 06 months stability data both real time and accelerated for the applied formulation.
7.	3.2.P.8.3	Raw data sheets and chromatograms for assay studies of both the batches for initial, 3rd and 06th month time point shall be submitted.	Submitted.
8.	3.2.P.8.3	Documents for the procurement of API shall be submitted.	Firm has submitted copy of invoice No. 801682 dated 05-01-2022 mentioning 0.43 kg of Omeprazole sodium lyophilized powder with batch No. 2112902 from M/s Vision pharma.
9.	3.2.P.8.3	Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	The firm submitted that they have new DML. They will make assure the compliance of 21CFR HPLC in nearby future.

Decision: Approved with innovator's specifications.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

- **Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

CLB in its 282nd meeting held on 31st August 2021 has considered and approved the grant of Drug Manufacturing License by way of formulation with following one (01) sections to M/s World Biz Pharmaceutical Company Plot No. 340, Multan Industrial Estate, Multan.

- Oral liquid syrup section (General).

Accordingly following two products of the firm are placed before the Board for consideration.

444.	Name, address of Applicant / Marketing Authorization Holder	World Biz Pharmaceutical Company Plot No. 340, Multan Industrial Estate, Multan.
	Name, address of Manufacturing site.	World Biz Pharmaceutical Company Plot No. 340, Multan Industrial Estate, Multan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22535: dated 10-08-2022.
	Details of fee submitted	PKR 30,000/- vide slip No. 39078566893 dated 09-06-2022.
	The proposed proprietary name / brand name	Ibubiz 100mg/5ml suspension.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains; Ibuprofen ……. ….. 100mg.
	Pharmaceutical form of applied drug	Oral suspension.
	Pharmacotherapeutic Group of (API)	M01A Anti-inflammatory And Anti-rheumatic Products, Non-Steroids.
	Reference to Finished product specifications	USP specifications.
	Proposed Pack size	As per DPC.
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	Tesco Health Ibuprofen 100 mg/5ml Oral Suspension, MHRA Approved.
	For generic drugs (me-too status)	Brufen Suspension, Abbot laboratories, Reg. No. 004595.
	GMP status of the Finished product manufacturer	New license issued dated 14-09-2021 w.e.f. 13-09-2021.
	Evidence of section approval.	Oral liquid syrup section (general) is approved vide letter No. F. 1-25/2008-Lic dated 17-09-2021.

	Name and address of API manufacturer.	Zenith Chemical Industries (Pvt.) Limited, 16 Km off Ferozpur-Road, Behind Wapda Grid Station, 1 Km of Chandrai Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has nor submitted QOS as per WHO QOS-PD template.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubility, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies (Drug substance.)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 36 months. Batches:(ZIBU11-001, ZIBU11-002, & ZIBU11-003).
	Module-III (Drug Product):	Firm has submitted detail of drug product including its description, composition, pharmaceutical development, manufacturer, manufacturing process and process control, process validation protocols, control of drug product, specifications, analytical procedures, analytical method verification studies, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the brand Ibuprofen manufactured by Abbott Laboratories by performing quality tests (Identification, pH and Assay). Results of both the products are similar.
	Analytical method validation/verification of product.	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Zenith Chemical Industries (Pvt.) Limited, 16 Km off Ferozpur-Road, Behind Wapda Grid Station, 1 Km of Chandrai Road, Lahore.
API Lot No.	
Description of Pack (Container closure system)	Orange colour viscous liquid suspension filled in amber colour bottle.
Stability Storage Condition	Long term: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Long term: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Long term: 0, 3, 6 (Months)		
Batch No.	RD-IS-001	RD-IS-002	RD-IS-003
Batch Size	2000 bottles.	2000 bottles.	2000 bottles.
Manufacturing Date	11-2021	11-2021	11-2021
Date of Initiation	11-11-2021.	11-11-2021.	11-11-2021.
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. 75/2021-DRAP (AD-2027105-531) dated 24-09-2021 issued on the basis of inspection conducted on 14-07-2021 is submitted by the firm.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section	Observation	Response by the firm
1.	1.1	Fee slip is for syrup Ibubiz while applied formulation is Ibubiz suspension. Clarification shall be submitted.	Firm has submitted that applied formulation is Ibubiz suspension. Due to typographic error, word syrup was written.
2.	1.5.2	Section 1.5.2 has mentioned BP specifications while 1.5.6 has mentioned USP specifications. Clarification shall be submitted	Firm has submitted that we applied BP specifications so we mentioned on BP monograph. As per CTD requirements, the table is revised and document is attached.

		regarding the specifications of the finished product.	***However, no revised document is attached. Same document is again submitted wherein USP specification are still written.***
3.	2.3	Table for literature references has mentioned only BP pharmacopoeia for both the drug substance and drug product. However, official monograph is available in other pharmacopoeias also. Clarification shall be submitted.	Firm has submitted that we applied BP specifications so we mentioned on BP monograph. As per CTD requirements, the table is revised and document is attached. Revised document is attached.
4.	3.2.S.4.3	Verification studies of drug substance performed by the drug product manufacturer shall be submitted.	Firm has submitted verification studies for the drug substance including Linearity, Precision, Accuracy, Range, Specificity etc.
5.	3.2.P.5.1	• This section has mentioned USP specification while the limits for test are of BP. Clarification shall be submitted regarding specifications of the drug product. • Dissolution test is not mentioned in the specification. However, both the USP and BP monograph has mentioned dissolution test. Clarification shall be submitted.	Firm has revised their specifications to BP. Firm has submitted that they applied BP specifications and dissolution test parameter was not available in BP 2020 monograph.
6.	3.2.P.5.2	• Analytical procedure has mentioned dissolution for the drug product while specification has no dissolution. • Assay test in the analytical procedure has no formula for calculation of the content.	Firm has submitted that as the analysis of stability samples was performed as per BP monograph so the procedure is revised and attached. Formula for calculation of the content is added in the revised analytical procedures.
7.	3.2.P.5.8	• Stability data sheets shall be as per decision of 293rd meeting of Registration Board with inclusion of API lot number. • Official monograph of the applied formulation has dissolution test while the drug product manufacturer has not performed any dissolution. Justification shall be submitted. • Justification shall be submitted regarding the retention time of	Revised stability data sheets as per decision of 293rd meeting of RB are provided. API lot No. ZIBU21-029 is used in stability data and COA of the same has already been submitted. Firm has submitted that applied product was developed as per BP 2020 specifications and BP 2020 was not having dissolution test. Stability studies for the applied formulation were started in November, 2021 while monograph of BP 2022 was available after January, 2022. They further submitted that after registration of their product, they will perform stability of first three commercial batches as per new monograph and will perform dissolution studies. Firm has submitted that we are new DML, so due to limited resources and column unavailability, we used Column of 15cm x 4.6mm and 5µm, C18 that's why peak

		Ibuprofen in the submitted chromatograms as the monograph has mentioned that under the prescribed condition the retention time of ibuprofen is about 21 minutes.	obtained earlier than prescribed retention time. ***Chromatograms submitted by the firm are revealing all the conditions mentioned in the pharmacopoeia, while the retention time in the chromatograms is 2.1 to 2.2 minutes while BP monograph has mentioned that under the prescribed condition the retention time of ibuprofen is about 21 minutes.***
8.		• Documents for the procurement of API used in the development of trial batches shall be submitted. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	Firm has submitted Sales tax invoice No. 00014/1021 dated 29-10-2021 mentioning 12 kg quantity of Ibuprofen. ***No batch number and manufacturing date is mentioned.*** ***Not submitted.***

Decision: Deferred for justification regarding the retention time of Ibuprofen in the submitted chromatograms as the monograph has mentioned that under the prescribed condition the retention time of ibuprofen is about 21 minutes whereas submitted chromatograms reflect retention time of about 2 minutes.

- **Firm will also submit revised 1.5.2 section and fee of Rs. 7,500/- for correction/pre-approval change in the table for literature references, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**

445.	Name, address of Applicant / Marketing Authorization Holder	World Biz Pharmaceutical Company Plot No. 340, Multan Industrial Estate, Multan.
	Name, address of Manufacturing site.	World Biz Pharmaceutical Company Plot No. 340, Multan Industrial Estate, Multan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 22534: dated 10-08-2022.
	Details of fee submitted	PKR 30,000/- vide slip No. 3138737615 dated 09-06-2022.
	The proposed proprietary name / brand name	Poly Biz 50mg/5ml syrup.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains; Iron-III hydroxide polymaltose complex eq. to elemental iron …… 50mg.
	Pharmaceutical form of applied drug	Oral liqid.
	Pharmacotherapeutic Group of (API)	B03AB05 Iron Preparations.

	Reference to Finished product specifications	Innovator's specifications.
	Proposed Pack size	As per PRC.
	Proposed unit price	As per PRC.
	The status in reference regulatory authorities	Maltofer Syrup (iron polymaltose 37 mg/mL Equivalent: iron 10mg/ml), Vifor Pharma Pty Ltd, TGA Approved.
	For generic drugs (me-too status)	Bisleri Syrup, Sami Pharma, Reg. No. 033003.
	GMP status of the Finished product manufacturer	New license issued dated 14-09-2021 w.e.f. 13-09-2021.
	Evidence of section approval.	Oral liquid syrup section (general) is approved vide letter No. F. 1-25/2008-Lic dated 17-09-2021.
	Name and address of API manufacturer.	M/s Chemiworld (Pvt.) Ltd., Plot No. 97-J, Industrial Estate, Hayatabad, Peshawar.
	Module-II (Quality Overall Summary)	Firm has nor submitted QOS as per WHO QOS-PD template.
	Module III (Drug Substance)	Firm has submitted detail of nomenclature, structure, general properties, solubility, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies (Drug substance.)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 60 months. Batches:(F15-IPC-270, F15-IPC-271 & F15-IPC-272).
	Module-III (Drug Product):	Firm has submitted detail of drug product including its description, composition, pharmaceutical development, manufacturer, manufacturing process and process control, process validation protocols, control of drug product, specifications, analytical procedures, analytical method verification studies, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the Bisleri syrup manufactured by Sami pharmaceuticals by performing quality tests (Identification, filled volume, leakage teat, pH

		and Assay). Results of both the products are similar.
	Analytical method validation/verification of product.	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Chemiworld (Pvt.) Ltd., Plot No. 97-J, Industrial Estate, Hayatabad, Peshawar.		
API Lot No.	G20-IPC-351._		
Description of Pack (Container closure system)	Amber glass bottle of 60ml containing a dark brown colour liquid syrup with characteristic pleasant flavour sealed with pp-aluminum cap and packed in a specific unit carton.		
Stability Storage Condition	Long term: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Long term: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 1, 3, 6 (Months) Long term: 0, 3, 6 (Months)		
Batch No.	RD-IPS-001	RD-IPS-002	RD-IPS-003
Batch Size	2000 bottles.	2000 bottles.	2000 bottles.
Manufacturing Date	11-2021	11-2021	11-2021
Date of Initiation	05-11-2021.	05-11-2021.	05-11-2021.
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION		
The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.		
Administrative Portion		
13.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A.
14.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	
15.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted.
16.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	N/A
17.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted.

18.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks by the Evaluator:

Sr. No.	Section	Observation	Reply by the firm
1.	1.6.5	GMP certificate of the drug substance manufacturer shall be submitted.	Firm has submitted copy of GMP certificate No. F.3-20/2017-DRAP-90 dated 15-02-2017 issued on the basis of inspection conducted on 29-11-2016. **Not Valid.**
2.	2.3.R	Justify the dispensed quantity of the drug substance in the executed BMR's with respect to the COA of the drug substance used in the developmental studies.	Firm has submitted that it was a calculation error in the quantity of drug substance that is corrected.
3.	3.2.S.4.1	Specification of the drug substance by the drug product manufacturer shall be submitted.	Specifications from both the drug substance manufacturer and drug product manufacturer for the drug substance is submitted.
4.	3.2.S.4.3	Verification studies of drug substance performed by the drug product manufacturer shall be submitted.	Validation studies of the drug substance by the finished product manufacturer is submitted including Linearity, Precision, Accuracy, Range, Specificity, LOD & LOQ etc.
5.	3.2.S.4.4	Submitted COA of the drug substance manufacturer has Iron assay limit of NLT 30% while COA of the drug product manufacturer has NLT 25%. Justification shall be submitted.	Firm has submitted that it was typographic mistake and also provided revised COA for the drug substance having has Iron assay limit of NLT 30% without submission of any fee for revision.
6.	3.2.S.7	• Limits of iron & polymaltose content in the submitted COA by the drug substance manufacturer are different in the stability data sheets of the drug substance. Justification shall be submitted. • Two different drug substance source are present in the dossier i.e. Chemiworld and Biocon. Justification shall be submitted.	Firm has submitted new stability data sheets for both real time and accelerated stability data from API manufacturer for 60 months and 6 months respectively with batch No. F15-IPC-270, F15-IPC-271 & F15-IPC-272. In these new data sheets Limits of iron & polymaltose content are as per specifications. Firm has clarified that Chemiworld is the drug substance source while the working standard provided from the drug substance manufacturer was from Biocon source.
7.	3.2.P.2.2	• Qualitative composition of the applied formulation is different from the reference product. Clarification shall be submitted. •	Firm has submitted that Qualitative composition of the applied formulation is same as of the reference product. ***However, reference product has different excipients from the applied formulation.***

		• Formulation development has mentioned some infusion product. Clarification shall be submitted.	Firm has submitted that it was a typographic mistake and submitted revised document.
8.	3.2.P.8.3	• Documents for the procurement of API used in the development of trial batches shall be submitted. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing shall be submitted.	Firm has submitted invoice No. 3053 dated 27-10-2021 mentioning 15kg of Iron poly maltose complex with batch No. G20-IPC-351. Firm has submitted that as the product contains elemental Iron so the testing was performed through titration method.

Decision: Approved. Registration letter will be issued after submission of compatibility studies of the drug product with excipients as Qualitative composition of the applied formulation is different from the reference product.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

Case no. 03 Registration applications of locally manufactured Human Drugs (Routine) drugs on Form 5F.

446.	Name, address of Applicant / Marketing Authorization Holder	Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Name, address of Manufacturing site.	Jaskan Pharmaceuticals (Pvt.) Ltd., 50-Sundar Industrial Estate, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 31871: dated 19-11-2021.
	Details of fee submitted	PKR 30,000/-: dated 08/10/2021.
	The proposed proprietary name / brand name	Clua 75mg Tablet.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains; Clopidogrel bisulphate equivalent to Clopidogrel ……... 75mg
	Pharmaceutical form of applied drug	Film coated Tablet.
	Pharmacotherapeutic Group of (API)	B01AC Platelet aggregation inhibitors excl. heparin.

	Reference to Finished product specifications	USP specifications
	Proposed Pack size	As per SRO
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Plavix 75 mg (Clopidogrel bisulphate) film coated tablets, USFDA approved.
	For generic drugs (me-too status)	Lowplate 75mg Tablet, PharmEvo (Pvt.) Ltd, Reg. No. 029174.
	GMP status of the Finished product manufacturer	GMP certificate No. 10/2021-DRAP (FID-797667-1346) dated 18-02-2021 issued on the basis of inspection conducted on 26-10-2020 is submitted.
	Evidence of section approval.	Tablet general section is approved vide letter No. F. 1-16/2006-Lic (Vol-I) dated 02-04-2021.
	Name and address of API manufacturer.	Aarti Drugs Limited, Plot No. G-60, MIDC, Tarapur, Tal. – Palghar, Dist. Thane – 401 506, Maharashtra, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related compounds, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. Firm has also summarized drug product information including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related compounds, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Stability studies (Drug substance.)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. Batches:(CLOPI/509041, CLOPI/510042 & CLOPI/511043). The real time stability data is conducted at 30°C ± 2°C / 65 ± 5% RH for 48 months. Batches:(CLOPI/509041, CLOPI/510042 & CLOPI/511043).
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence is established against the Lowolat tablets manufactured by PharmEvo Pharma Batch No. 06192 by performing quality tests (description, identification, Disintegration, Assay, Dissolution). Both the products have shown similar results. CDP has been performed against the same brand that is Lowolat tablets manufactured by PharmEvo Pharma in Acid media (pH 1.2), Acetate buffer (pH 4.5) & Phosphate Buffer (pH 6.8). However, F2 factor is only calculated for acidic media and limit is in acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	Aarti Drugs Limited, Plot No. G-60, MIDC, Tarapur, Tal. – Palghar, Dist. Thane – 401 506, Maharashtra, India.
API Lot No.	2006-5091FP013.
Description of Pack (Container closure system)	Alu Alu blister pack of 1 x 10's.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5% RH Accelerated: 40°C ± 2°C / 75% ± 5% RH
Time Period	Real time: 03 months Accelerated: 03 months
Frequency	Accelerated: 0, 1, 2, 3, 6 (Months)

	Real Time: 0, 3, 6 (Months)		
Batch No.	KO-01	KO-02	KO-03
Batch Size	1000 Tablets.	1000 Tablets.	1000 Tablets.
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	20-03-2021	20-03-2021	20-03-2021
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

7.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Not submitted.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section	Observation	Response by the firm
1.	1.4.2	This section has contradictory information. Table of content has mentioned only domestic sale while annexure has mentioned Domestic and Export sales. Clarification shall be submitted.	Firm has submitted that it is for domestic sale only and also provided corrected annexure.
2.	1.6.5	Valid copy of GMP certificate of the drug substance manufacturer shall be submitted.	Firm has submitted copy of GMP certificate No. 20031933 issued in the name of Aarti Drugs Limited (Unit-II), Plot No. 211 & 213, Road-2, GIDC at & Post; Sarigam, Dist. Valsad Gujrat State, India. *However, information submitted in 1.6.5 has mentioned Aarti Drugs*

			Limited, Plot No. G-60, MIDC, Tarapur, Tal. – Palghar, Dist. Thane – 401 506, Maharashtra, India.
3.	3.2.S.4.1	Drug substance manufacturer has total impurities limit of 1.5% while the official monograph has mentioned NMT 0.5%. COA provided by the drug substance manufacturer has 0.93% of total impurities which is out of specifications of USP Clarification shall be submitted.	Firm has submitted that impurities mentioned by the drug substance manufacturer is NMT 1.5% whereas USP monograph for Clopidogrel bisulphate shows as NMT 1.0% i.e. (Impurities A+B= 0.5% + C= 0.5% total 1%). However, COA of the API shows impurities A+B+C = 0.93% within limits of USP monograph. You may kindly overlook the variation from USP of mentioning NMT 1.5% and accept the COA figure of 0.93% as within the USP limits.
4.	3.2.S.4.1	Specifications of the drug substance by the finished product manufacturer shall be submitted.	Submitted.
5.	3.2.S.4.2	Analytical procedures for the dug substance by the finished product manufacturer shall be submitted.	Submitted. *However, composition of the mobile phase provided by the FPP is acetonitrile and buffer in the ratio of 70:30 while USP has mentioned Acetonitrile and Buffer (25:75).*
6.	3.2.S.4.3	Analytical Method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Submitted.
7.	3.2.S.4.4	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture.	Firm has submitted copy of COA from M/s Aarti Drugs Limited with Batch No. CLOPI/19030076 with manufacturing date of March 2019. Drug product manufacturer has also submitted their COA with same batch number as that of the drug substance manufacturer.
8.	3.2.S.7.3	Real time stability data at 09-month time point for batch No. CLOPI/509041 is out of specification for the assay test. Clarify.	Firm has submitted that we contacted principal manufacturer through our vendor regarding out of specification assay (94.24%) at 09-month time point for batch No. CLOPI/509041 and they informed that it was a typographic mistake and actual figure was 99.24%. this fact is substantiated from the observation "No significant change" recorded in the remarks column relating to this data. They have requested us to

			correct the typographic mistake as the data relates to 17 years old batch. Applicant has also provided hand written corrected page of the stability data.
9.	3.2.P.2	Justification shall be submitted regarding the quantity of Clopidogrel bisulphate used per tablet.	No justification submitted.
10.	3.2.P.2.2.1	• Justification of selection of time points for CDP shall be submitted. • Similarity factor F2 calculation for pH 4.5 & pH 6.8 shall be submitted. • Raw data sheets for dissolution test shall be submitted.	*No justification submitted. Firm has used 30, 45 & 60-minute time points.* Firm has new CDP results for the applied formulation having 30, 45 & 60-minute time points against Lowpat 75mg tablets, batch No. 06192 manufactured by PharmEvo in three medium of pH **2.0**, 4.5 & 6.8. Firm has also submitted F2 values for all the three mediums. *Firm has used pH 2.0 in their medium instead of pH 1.2. Furthermore, the calculated values for pH 4.5 & 6.8 are less than 3.* *The firm also concluded that dissolution similarity factor F2 between the two product is more than the limit in acidic medium pH 2.0 at 30 minutes, hence the product dissolution medium is set in acidic media at 30 minutes.*
11.	3.2.P.5.2	• Standard preparation and sample preparation in analytical procedures for assay test are completely different from official monograph. Justification shall be submitted. • Standard preparation, sample preparation, dissolution medium, wavelength and calculation formula in analytical procedures for dissolution test are completely different from the official monograph. • Justification shall be submitted for the analytical procedure as it is for clarithromycin instead of Clopidogrel.	Firm has submitted revised document of the analytical procedure. *In the initially submitted data, Standard preparation was having final concentration of 0.1mg/ml Clopidogrel as bisulphate RS while the USP has mentioned final concentration of about 0.1 mg of Clopidogrel bisulfate per mL.* *In the revised document, the final concentration of the sample solution for assay test is still again different from that of the USP.* Firm has also revised the document for dissolution test. *In the initial submitted data wavelength of 210nm was mentioned while USP has 240nm. Dissolution medium of pH 6.5 buffer was mentioned while USP has pH 2.0 hydrochloric acid buffer.*

			No justification submitted.
12.	3.2.P.5.4	Complete batch analysis for all the three trial batches (COA) shall be submitted.	Submitted.
13.	3.2.P.8.3	• Complete six-month stability data shall be submitted. • Submit stability data sheets as per approved format by the Registration Board with inclusion of API lot number.	Submitted. Submitted. API lot No. CLOPI/19030076 is mentioned in the new stability summary data sheets.
14.		Documents for the procurement of API used in the development of trial batches with approval from DRAP shall be submitted.	Firm has submitted copy of Invoice No. ADL/INV/15/29-21 dated 29-01-2021 mentioning Clopidogrel bisulphate USP, batch No. CLOPI/101120328, Mfg. date of December, 2020 having quantity of 300gm. ***However, the Summary data sheets have mentioned API lot No. CLOPI/19030076 and COA of the same is also submitted.***
15.		Reference of previous approval of applications with stability study data of the firm shall be submitted.	**Not submitted.**
16.		Compliance Record of HPLC software 21CFR & audit trail reports on product testing	**Not submitted.**

Decision: Deferred for following;

- **Justification regarding the GMP certificate of the drug substance manufcaturer as information submitted in section 1.6.5 has mentioned Aarti Drugs Limited, Plot No. G-60, MIDC, Tarapur, Tal. – Palghar, Dist. Thane – 401 506, Maharashtra, India while GMP certificate provided is for Aarti Drugs Limited (Unit-II), Plot No. 211 & 213, Road-2, GIDC at & Post; Sarigam, Dist. Valsad Gujrat State, India.**
- **Justification for variation in mobile phase composition for the assay test of drug substance from that recommended by USP monograph.**
- **Justification of selection of time points, dissolution medium of pH 2.0 and results of similarity factor (f_2) reported below 3.0 for CDP studies shall be submitted.**
- **Justification regarding variation in the final concentration of the sample solution for assay test in the revised analytical procedures from that recommended by USP monograph.**
- **Documents for the procurement of API used in the development of trial batches with approval from DRAP shall be submitted**

Case no. 04; Registration applications Deferred Human drugs on Form 5F.

a. Locally Manufactured Deferred products.

447.	Name, address of Applicant / Marketing Authorization Holder	Wilson's Pharmaceuticals, Plot No. 387-388, Sector I-9, Industrial Area, Islamabad.
	Name, address of Manufacturing site.	Wilson's Pharmaceuticals, Plot No. 387-388, Sector I-9, Industrial Area, Islamabad.
	Status of the applicant	☒ Manufacturer

		☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales.
	Dy. No. and date of submission	Form-5F Dy. No. 26709 dated 27-09-2021.
	Details of fee submitted	PKR 75,000/-: dated 20-09-2021.
	The proposed proprietary name / brand name	Coldenol Sinus Severe Caplets (day).
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated Caplet contains; Paracetamol …… 325mg Phenylephrine HCl …… 5mg Guaifenesin …… 200mg
	Pharmaceutical form of applied drug	Oral tablet.
	Pharmacotherapeutic Group of (API)	Paracetamol, combinations excl. Psycholeptics. (N02BE51)
	Reference to Finished product specifications	Manufacturer specifications.
	Proposed Pack size	10's, 20's & 30's.
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	Tylenol Sinus Severe (day), USFDA is provided by the firm. However, the same could not be found in USFDA data. Daily med has the same product as OTC product with the following disclaimer: *Most OTC drugs are not reviewed and approved by FDA, however they may be marketed if they comply with applicable regulations and policies. FDA has not evaluated whether this product complies.*
	For generic drugs (me-too status)	Could not be confirmed.
	GMP status of the Finished product manufacturer	Inspection report of 24-01-2018. Not valid.
	Evidence of section approval.	Tablet (general) section approved vide No. F. 1-19/92-Lic (P1) dated 27-07-2015.
	Name and address of API manufacturer.	Paracetamol: Saakh Pharma (Pvt.) Ltd., C-7/1, North Western Industrial Zone. Port Qasim, Karachi. Guaifenesin: Zhejiang Haizhou Pharmaceutical Co., Ltd., linhai Industrial Zone, Linhai Zhejiang China. Phenylephrine Hydrochloride. M/s Shenzhen Oriental Pharmaceutical Co., Ltd., No. 43, Dakeng Road, Tongle village, Longgang District, Shenzhen China.

	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its validation, batch analyses and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Paracetamol (USP/BP), Guaifenesin (USP) and Phenylephrine HCl (USP/BP) is present respectively. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests impurities B,C,D, Individual Impurity I & any unspecified for Paracetamol, Impurities A,B,C and D for Guaifenesin and Impurities A,C,D,E and unspecified impurity for Phenylephrine HCl, specifications, analytical procedures and its validation, batch analyses and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies (Drug substance.)	Firm has submitted stability study data of 3 batches of the following drug substances as per Zone IV-a for both accelerated as well as real time conditions: Paracetamol: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months. (Batch No. 18GN60001, 18GN60002, and 18GN60003) Guaifenesin: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months. (Batch No. 08GF04156, 08GF04157, and 08GF04158) Phenylephrine hydrochloride. Real time: 30°C ± 2°C / 65% ± 5%RH for 48 months. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months. (Batch No. PEH-160404, PEH-160405, and PEH-160406)
	Module-III (Drug Product):	The firm has submitted detail of description, composition, pharmaceutical development, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference

		standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against Tylenol Sinus Severe Caplets DAY by performing quality tests (Assay, Dissolution, Disintegration Time test). CDP has been performed against the same product that is Tylenol Sinus Severe Caplets DAY, Lot No. 485556 made in Italy, distributed by M/s Johnson & Johnson Consumer Inc., Mc Neil Consumer Healthcare Division USA in 0.1 N HCl, Acetate buffer pH 4.5 & Phosphate Buffer pH 6.8. The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have been submitted including: system suitability, accuracy, and precision.

STABILITY STUDY DATA			
Manufacturer of API	Paracetamol: Saakh Pharma (Pvt.) Ltd., C-7/1, North Western Industrial Zone. Port Qasim, Karachi. Guaifenesin: Zhejiang Haizhou Pharmaceutical Co., Ltd., Linhai Industrial Zone, Linhai Zhejiang China. Phenylephrine Hydrochloride. M/s Shenzhen Oriental Pharmaceutical Co., Ltd., No. 43, Dakeng Road, Tongle village, Longgang District, Shenzhen China.		
API Lot No.	Paracetamol (Batch No.19GN60209, Batch No.19GN60213) Guaifenesin (Batch No.18GF03204) Phenylephrine HCl (Batch No.PEH-180101Y1)		
Description of Pack (Container closure system)	Alu-Alu blister packed in card box unit carton of 10's, 20's & 30's.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 01	Trial 02	Trial 03
Batch Size	1500 caplets	1500 caplets	1500 caplets
Manufacturing Date	17-12-2019	23-12-2019	23-12-2019
Date of Initiation	01-01-2020	01-01-2020	01-01-2020
No. of Batches	03		
REQUEST OF EXEMPTION FROM ON SITE INSPECTION			

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.		
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Firm has submitted Reference of previous approval of applications with stability study data.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted GMP certificates of: Paracetamol: Copy of GMP certificate No. 83/2020-DRAP(K) of M/s Saakh Pharma (Pvt.) Ltd., C-7/1, North Western Industrial Zone. Port Qasim, Karachi issued by DRAP Karachi valid till 18/06/2022. Guaifenesin: Copy of GMP certificate No. ZJ20180122 of Zhejiang Haizhou Pharmaceutical Co., Ltd., Linhai Industrial Zone, Linhai city Zhejiang China issued by China food & Drug Administration valid until 09-25-2023. Phenylephrine Hydrochloride. Not provided.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Paracetamol Copy of commercial invoice No. PRT/2019/0191 dated 18/03/2019 is submitted. Copy of commercial invoice No. PRT/2019/0197 dated 25/03/2019 is submitted. • Guaifenesin Copy of clearance certificate attested by AD (I&E) DRAP, Islamabad dated 16/07/2018 along with commercial invoice No.130128 dated 22/06/2018 with quantity of 0.75Kg is submitted. • Phenylephrine HCl Copy of clearance certificate attested by AD (I&E) DRAP, Islamabad dated 10/05/2018 along with commercial invoice No. SZ-1803039 dated 12/04/2018 with quantity of 308.25 Gram is submitted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted
Remarks of Evaluator:		

Sr. No.	Section No.	Observation	Response by the firm
1.	1.3	Valid copy of DML and latest GMP certificate/inspection report conducted within last three years of the finished product manufacturer shall be provided.	Firm has not provided any renewal of DML. Firm has submitted GMP inspection report dated 24-01-2018. *Provided GMP inspection report is not within last three years.*
2.	1.5.9	Evidence of approval of applied formulation in reference regulatory authorities as decided by the registration board shall be submitted as the provided reference could not be confirmed.	Tylenol Sinus Severe (day), USFDA is provided by the firm. However, the same could not be found in USFDA data. Daily med has the same product as OTC product with the following disclaimer: *Most OTC drugs are not reviewed and approved by FDA, however they may be marketed if they comply with applicable regulations and policies. FDA has not evaluated whether this product complies.*
3.	1.6.5	• Address of the API manufacturer for guaifenesin provided in section 1.6.5 is different from that of mentioned in GMP certificate. Clarification is required. • Valid GMP certificate of the drug substance manufacturer (phenylephrine HCL) issued by the concerned / relevant regulatory authority shall be submitted.	• Firm has submitted that due to typographical error, the address of the drug substance manufacturer mentioned in section 1.6.5 was written wrong. *Firm has submitted a document "Announcement of the state drug administration on matters concerning the implementation of the Drug Administration Law of the People's Republic of China" wherein under the heading of drug GMP & GSP management requirements following is stated.* *'starting from December 1, 2019 the pharmaceutical GMP and GSP certifications will be cancelled, GMP and GSP certificates will no longer be accepted and pharmaceutical GMP and GSP certificates will no longer be issued. Where current regulation require on site inspection, on-site inspection shall be continued after December 1, 2019 and the company shall be notified of the on-site inspection results. '*
4.	3.2.S.4.2	Guaifenesin: • Analytical method used for drug substance (guaifenesin) by the drug substance manufacturer shall be submitted.	Submitted.

		• Analytical method provided by the drug product manufacturer for drug substance (guaifenesin) has mentioned 40g/ml while the pharmacopoeia has mentioned 40mcg/ml in Identification test. Clarification is required. Phenylephrine HCL: • Analytical method used for drug substance (phenylephrine HCL) by drug substance manufacturer shall be submitted.	Firm has submitted that due typographic error 40g/ml was written instead of 40mcg/ml. However, finished product manufacturer has followed USP method for drug substance. Submitted.
5.	3.2.S.4.3	Verification studies of all the three drug substances performed by the drug product manufacturer shall be submitted.	Submitted.
6.	3.2.S.4.4	Batch analysis of paracetamol from Wilson pharma has not mentioned whether USP specifications or BP. Clarification is required.	Firm has submitted COA's wherein it is mentioned that the samples complies with both USP and BP.
7.	3.2.S.7.3	Both real time and accelerated stability study data for phenylephrine HCl from drug substance manufacturer shall be submitted.	Firm has submitted real time and accelerated stability study data for Phenylephrine HCl.
8.	3.2.P.2.	Qualitative composition of the applied formulation is different from reference product. Clarification is required.	• Firm has submitted that they used PVP K30 instead of HPC as binder in their formulation as both the materials are safely used in pharmaceutical industry for granulation purpose can be used interchangeably because of their excellent binding profiles, as mentioned in the hand book of pharmaceutical excipients. • Triacetin is used as plasticizer in the formulation and is used in the film coating to add plasticity to the film. Our film coating yields excellent film without use of plasticizer, so we didn't add triacetin in the formulation. • Carnauba wax is used to polish the caplet which is not necessarily required in our formulation. • Sucralose is not added in the formulation as it is used as sweetener and our formulation is neither chewable nor dispersible.
9.	3.2.P.2.2.1	Average weight of 10 tablets in pharmaceutical equivalence is 776.7gm. clarification is required.	Firm submitted that due to typographic error average weight of 10 tablets was mentioned 776.7 gm rather than 7.767gm.

10.	3.2.P.3.2	Batch formula has mentioned innovator's specification for paracetamol. clarification is required.	Firm has submitted new batch formula wherein USP specification is mentioned against paracetamol.
11.		Clearance certificate for Guaifenesin provided by the firm has mentioned 750Gm (0.75 Kg) quantity. While the firm has manufactured three trial batches of 1500 tablets each. With this respect only 900gm is required for the manufacturing of the said three trial batches. Clarification is required.	Firm has submitted that drug substance B. No. 18GF03204, quantity 750Gm was used in the manufacturing of trial 01, 02 trial batches. While B. No. 18GF03204 750gm & B. No. 18GF09667, 03 Kg respectively were used in the manufacturing of trial 03. We had submitted the clearance certificate of one batch 18GF03204 at the time of registration application submission, whereas the clearance certificate of the second batch was unintentionally overlooked. They also submitted the clearance certificate of the second batch. *However, there is no record of the second batch in the submitted application nor any verification studies of the said batch.*
12.	2.3.R	Dispensing of active materials without potency adjustment for Guaifenesin and Phenylephrine HCl. Justification is required.	Firm has submitted that potency was not adjusted for trial manufacturing batches (pilot scale) due to small batch size (1500 caplets) the adjustment amount was very low and does not affect the quality, efficacy and safety of the drug product. It is pertinent to mention here, that the finished drug product release limit is 90% - 110%. They also undertake that they will adjust the potency of drug substance at commercial batch for said drug product.

Decision of 321st meeting of Registration Board:
Deferred for further deliberation regarding regulatory status of applied formulation in reference regulatory authorities adopted by Registration Board in its 275th meeting.
Reply by the firm;
Firm has stated that that, they have applied for drug registration of our product namely Conofen 10/200mg tablet having composition (Phenylephrine HCl…..10mg, Ibuprofen…..200mg) on Form 5F (CTD) and submitted the dailymed reference i.e. Advil Congestion Relief Tablet 200mg/10mg https://dailymed.nlm.nih.gov/ dailymed/ drugInfo.cfm?setid=b1e29c19-fe03-4d2b-9660adf4eb4b4cf which was considered and no objection raised by Drug Registration Board in its 313th meeting of held on 16th -18th Nov, 2021 regarding dailymed reference.
They also submitted copy of that decision. Wherein the product is deferred for following submissions:

- *Pharmaceutical equivalence data of the applied product along with innovator / reference or comparator product.*
- *Comparative Dissolution Profile (CDP) data of the applied product along with innovator / reference or comparator product.*

Moreover, the firm M/s Vision Pharmaceuticals, Islamabad had applied for drug registration of their product namely, Mensodol Tablet 500/25mg with composition: Paracetamol 500mg and Pamabrom

25mg and provided "Proof of International availability of same formulation with same strength in RRA": https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=fb9a5647-b7c9-4820-b148-91060e34cb83 which was approved in 296th meeting of Drug registration Board held on 8-10th September, 2020. The product is approved. In the light of above, it is requested to kindly registration of our aforementioned applied drug product Colynol Multi Symptom Severe Cold sachet may please be granted in the upcoming meeting of Drug Registration Board.		
Decision: Deferred for deliberation regaring approval of applied formulation by reference regulatory authorities.		
448.	Name, address of Applicant / Marketing Authorization Holder	Wilson's Pharmaceuticals, Plot No. 387-388, Sector I-9, Industrial Area, Islamabad.
	Name, address of Manufacturing site.	Wilson's Pharmaceuticals, Plot No. 387-388, Sector I-9, Industrial Area, Islamabad.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales.
	Dy. No. and date of submission	Form-5F Dy. No. 3336 dated 03-02-2022.
	Details of fee submitted	PKR 75,000/-: dated 07-01-2022.
	The proposed proprietary name / brand name	Colynol Multi Symptom Severe Cold Sachet.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Sachet contains; Paracetamol ……... 500mg Phenylephrine HCl …… 10mg Dextromethorphan HBr ……. 20mg
	Pharmaceutical form of applied drug	Sachet.
	Pharmacotherapeutic Group of (API)	Cough Suppressants and expectorants. (R05FB02)
	Reference to Finished product specifications	Manufacturer specifications.
	Proposed Pack size	10's.
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	Theraflu Multi Symptom Severe Cold Sachet. However, the same could not be found in USFDA data. Daily med has the same product as OTC product with the following disclaimer: *Most OTC drugs are not reviewed and approved by FDA, however they may be marketed if they comply with applicable regulations and policies. FDA has not evaluated whether this product complies.*

	For generic drugs (me-too status)	Could not be confirmed.
	GMP status of the Finished product manufacturer	Inspection report of 24-01-2018. Not valid.
	Evidence of section approval.	Tablet (general) section approved vide No. F. 1-19/92-Lic (P1) dated 27-07-2015.
	Name and address of API manufacturer.	**Paracetamol:** Saakh Pharma (Pvt.) Ltd., C-7/1, North Western Industrial Zone. Port Qasim, Karachi. Copy of GMP certificate No. 83/2020-DRAP(K) of M/s Saakh Pharma (Pvt.) Ltd., C-7/1, North Western Industrial Zone. Port Qasim, Karachi issued by DRAP Karachi valid till 18/06/2022. **Dextromethorphan hydro bromide:** Onerio Chemicals (Pvt.) Limited, S. No. 475/P, At & Po Ekalbara – 391 440, Ta. Padra, Distt. Vadodara, Gujrat, India. Firm has submitted license to manufacture for sale of drugs in the name of M/s Onerio Chemicals (Pvt.) Limited, issued by the Food & Drug Administration Gujrat State India valid till 13-07-2022. **Phenylephrine Hydrochloride.** M/s Shenzhen Oriental Pharmaceutical Co., Ltd., No. 43, Dakeng Road, Tongle village, Longgang District, Shenzhen China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its validation, batch analyses and justification of specification, reference standard, container closure system and stability studies of all the three drug substances and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Paracetamol (USP/BP/EP), Dextromethorphan HBr (USP/BP/EP) and Phenylephrine HCl (USP/BP/EP) is present respectively. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests impurities, specifications, analytical procedures and its validation, batch analyses and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies (Drug substance.)	Firm has submitted stability study data of 3 batches of the following drug substances as per Zone IV-a for both accelerated as well as real time conditions:

		Paracetamol: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 12 months. (Batch No. 18GN60001, 18GN60002, and 18GN60003) **Dextromethorphan hydro bromide:** Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months. Accelerated: 40°C ± 2°C / 75% ± 5%RH for 06 months. (Batch No. DX/B/054/12, DX/B/055/12 and DX/B/056/12) **Phenylephrine hydrochloride.** Not provided.
	Module-III (Drug Product):	The firm has submitted detail of description, composition, pharmaceutical development, manufacturers, description of manufacturing process and controls, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence has been established against the innovator product that is Theraflu Multi symptom Severe Cold Sachet by performing quality tests (Assay). Assay of both the products are in acceptable range. CDP has not been performed because our applied dosage form is powder (sachet).
	Analytical method validation/verification of product	Method validation studies have been submitted including: system suitability, accuracy, and precision.

STABILITY STUDY DATA	
Manufacturer of API	**Paracetamol:** Copy of GMP certificate No. 83/2020-DRAP(K) of M/s Saakh Pharma (Pvt.) Ltd., C-7/1, North Western Industrial Zone. Port Qasim, Karachi issued by DRAP Karachi valid till 18/06/2022. **Dextromethorphan hydro bromide:** Firm has submitted copy of license to manufacture for sale of drugs in the name of M/s Onerio Chemicals (Pvt.) Limited, issued by the Food & Drug Administration Gujrat State India valid till 13-07-2022. **Phenylephrine Hydrochloride.** Not provided.
API Lot No.	**Paracetamol** (Batch No.19GN60228, Batch No. 19GN60222) **Dextromethorphan HBr** (Batch No. DX/L/017/18) **Phenylephrine HCl** (Batch No.PEH-180101Y1)
Description of Pack (Container closure system)	Peach colored flavored powder packed in aluminum foil.
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH

Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	Trial 01	Trial 02	Trial 03
Batch Size	1200 sachet	1200 sachet	1200 sachet
Manufacturing Date	04-2020	05-2020	05-2020
Date of Initiation	22-05-2020	22-05-2020	22-05-2020
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Firm has submitted GMP certificates of: Paracetamol: Copy of GMP certificate No. 83/2020-DRAP(K) of M/s Saakh Pharma (Pvt.) Ltd., C-7/1, North Western Industrial Zone. Port Qasim, Karachi issued by DRAP Karachi valid till 18/06/2022. Guaifenesin: Copy of GMP certificate No. ZJ20180122 of Zhejiang Haizhou Pharmaceutical Co., Ltd., Linhai Industrial Zone, Linhai city Zhejiang China issued by China food & Drug Administration valid until 09-25-2023. Phenylephrine Hydrochloride. Not provided.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• **Paracetamol;** Copy of commercial invoice No. PRT/2019/0208 dated 30/03/2019 is submitted. Copy of commercial invoice No. PRT/2019/0197 dated 25/03/2019 is submitted. • **Dextromethorphan HBr;** Clearance certificate No. 794 dated 14-03-2019 mentioning 300 gm quantity of Dextromethorphan HBr EP, batch No. DX/L/017/18 attested by Assistant Director I&E is submitted by the firm. • **Phenylephrine HCl** Copy of clearance certificate attested by AD (I&E) DRAP, Islamabad dated 10/05/2018 along with commercial invoice No. SZ-1803039 dated 12/04/2018 with quantity of 308.25 Gram is submitted.

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr. No.	Section No.	Observation	Response by the firm
1.	1.3	Valid copy of DML and latest GMP certificate/inspection report conducted within last three years of the finished product manufacturer shall be provided.	
2.	1.6.5	• Valid copy of GMP certificate for drug substance manufacturer (Paracetamol) shall be submitted. • Valid copy of GMP certificate drug substance manufacturer (Phenylephrine Hydrochloride) shall be submitted. • Valid copy of manufacturing license or GMP certificate for the drug substance manufacturer (Dextromethorphan HBr) issued by concerned regulatory authority shall be submitted.	
3.	2.3.R.1	• Provide blank master production document/batch manufacturing record to be used during the commercial manufacturing of the applied product. • Provide copy of Batch manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3.	
4.	3.2.S.4.2	• Analytical method used for drug substance (Paracetamol) used by the drug Product manufacturer shall be submitted. • Analytical method used for drug substance (Dextromethorphan	

		HBr) used by the drug Product manufacturer shall be submitted. • Analytical method used for drug substance (Phenylephrine hydrochloride) used by both the drug substance manufacturer and drug Product manufacturer shall be submitted.	
5.	3.2.S.4.3	• Verification studies of the drug substance (Paracetamol) performed by the drug product manufacturer shall be submitted. • Verification studies of the drug substance (Dextromethorphan HBr) performed by the drug product manufacturer shall be submitted. • Verification studies of the drug substance (Phenylephrine hydrochloride) performed by the drug product manufacturer shall be submitted.	
6.	3.2.S.4.4	Provide results of analysis of relevant batch(es) of all the three Drug Substances (Paracetamol, Dextromethorphan HBr & Phenylephrine hydrochloride) performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance / /Active Pharmaceutical Ingredient manufacture.	
7.	3.2.S.8.3	Stability study data for the drug substance (Phenylephrine hydrochloride) from concerned manufacturer shall be submitted.	
8.	3.2.P.8.	Reference of previous approval of applications with stability study data of the firm shall be submitted.	

Decision of 321st meeting of Registration Board;

The Board deferred the case for the following:

- Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.
- Submission of valid copy of DML and latest GMP certificate/inspection report conducted within last three years of the finished product manufacturer shall be provided.
- Submission of valid copy of GMP certificate for drug substance manufacturer (Paracetamol) shall be submitted.
- Submission of valid copy of GMP certificate drug substance manufacturer (Phenylephrine Hydrochloride) shall be submitted.

- Submission of valid copy of manufacturing license or GMP certificate for the drug substance manufacturer (Dextromethorphan HBr) issued by concerned regulatory authority shall be submitted.
- Submission of blank master production document/batch manufacturing record to be used during the commercial manufacturing of the applied product.
- Submission of copy of Batch manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3.
- Submission of analytical method used for drug substance (Paracetamol) used by the drug Product manufacturer shall be submitted.
- Submission of analytical method used for drug substance (Dextromethorphan HBr) used by the drug Product manufacturer shall be submitted.
- Submission of analytical method used for drug substance (Phenylephrine hydrochloride) used by both the drug substance manufacturer and drug Product manufacturer shall be submitted.
- Verification studies of the drug substance (Paracetamol) performed by the drug product manufacturer shall be submitted.
- Verification studies of the drug substance (Dextromethorphan HBr) performed by the drug product manufacturer shall be submitted.
- Verification studies of the drug substance (Phenylephrine hydrochloride) performed by the drug product manufacturer shall be submitted.
- Submission of results of analysis of relevant batch(es) of all the three Drug Substances (Paracetamol, Dextromethorphan HBr & Phenylephrine hydrochloride) performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance /Active Pharmaceutical Ingredient manufacture.
- Submission of stability study data for the drug substance (Phenylephrine hydrochloride) from concerned manufacturer shall be submitted.
- Reference of previous approval of applications with stability study data of the firm shall be submitted.

Reply submitted by the firm;

Sr. No.	Observation	Reply by the firm
1.	Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.	Firm has stated that that, they have applied for drug registration of our product namely Conofen 10/200mg tablet having composition (Phenylephrine HCl…..10mg, Ibuprofen…..200mg) on Form 5F (CTD) and submitted the dailymed reference i.e. Advil Congestion Relief Tablet 200mg/10mg https://dailymed.nlm.nih.gov/ dailymed/ drugInfo.cfm?setid=b1e29c19-fe03-4d2b-9660adf4eb4b4cf which was considered and no objection raised by Drug Registration Board in its 313th meeting of held on 16th -18th Nov, 2021 regarding dailymed reference. ***They also submitted copy of that decision. Wherein the product is deferred for following submissions:*** • ***Pharmaceutical equivalence data of the applied product along with innovator / reference or comparator product.*** • ***Comparative Dissolution Profile (CDP) data of the applied product along with innovator / reference or comparator product.*** Moreover, the firm M/s Vision Pharmaceuticals, Islamabad had applied for drug registration of their product namely, Mensodol Tablet 500/25mg with composition: Paracetamol 500mg and Pamabrom 25mg and provided "Proof of International availability of same formulation with same strength in RRA":

		https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=fb9a5647-b7c9-4820-b148-91060e34cb83 which was approved in 296th meeting of Drug registration Board held on 8-10th September, 2020. The product is approved. In the light of above, it is requested to kindly registration of our aforementioned applied drug product Colynol Multi Symptom Severe Cold sachet may please be granted in the upcoming meeting of Drug Registration Board.
2.	Submission of valid copy of DML and latest GMP certificate/inspection report conducted within last three years of the finished product manufacturer shall be provided.	GMP certificate No.F.3-96/2022-Addl.Dir. (QA&LT-I) dated August, 2022 on the basis of inspection conducted on 28-07-2022 is submitted by the applicant.
3.	Submission of valid copy of GMP certificate for drug substance manufacturer (Paracetamol) shall be submitted.	Copy of GMP certificate No.83/2020-DRAP (K) dated 23-06-2020 issued on the basis of inspection conducted on 18-06-2020 in the name of M/s Saakh pharma is submitted.
4.	Submission of valid copy of GMP certificate drug substance manufacturer (Phenylephrine Hydrochloride) shall be submitted.	Firm has submitted copy of License No. Y.20160118 issued in the name of M/s Shenzhen Oriental Pharmaceutical Co., Ltd., No. 43, Dakeng Road, Tongle village, Longgang District, Shenzhen China by Guangdong Food & Drug Administration valid till December, 2025.
5.	Submission of valid copy of manufacturing license or GMP certificate for the drug substance manufacturer (Dextromethorphan HBr) issued by concerned regulatory authority shall be submitted.	Firm has submitted copy of GMP certificate No. S-GMP/22023157 issued in the name of M/s Onerio Chemicals (Pvt.) Ltd., valid till 22-02-2024.
6.	Submission of blank master production document/batch manufacturing record to be used during the commercial manufacturing of the applied product.	Submitted.

7.	Submission of copy of Batch manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3.	Submitted.
8.	Submission of analytical method used for drug substance (Paracetamol) used by the drug Product manufacturer shall be submitted.	Submitted.
9.	Submission of analytical method used for drug substance (Dextromethorphan HBr) used by the drug Product manufacturer shall be submitted.	Submitted.
10.	Submission of analytical method used for drug substance (Phenylephrine hydrochloride) used by both the drug substance manufacturer and drug Product manufacturer shall be submitted.	Submitted.
11.	Verification studies of the drug substance (Paracetamol) performed by the drug product manufacturer shall be submitted.	Firm has submitted verification studies for the drug substance including Accuracy, Specificity and precision.
12.	Verification studies of the drug substance (Dextromethorphan HBr) performed by the drug product manufacturer shall be submitted.	Firm has submitted verification studies for the drug substance including Accuracy, Specificity and precision.

13.	Verification studies of the drug substance (Phenylephrine hydrochloride) performed by the drug product manufacturer shall be submitted.	Firm has submitted verification studies for the drug substance including Accuracy, Specificity and precision.
14.	Submission of results of analysis of relevant batch(es) of all the three Drug Substances (Paracetamol, Dextromethorphan HBr & Phenylephrine hydrochloride) performed by Drug Product manufacturer used during product development and stability studies, along with Certificate of Analysis (CoA) of the same batch from Drug Substance /Active Pharmaceutical Ingredient manufacture.	Firm has submitted COA's for all the three drug substances used in the trial batches both from the drug substance manufacturer and the finished product manufacturer with same batch numbers.
15.	Submission of stability study data for the drug substance (Phenylephrine hydrochloride) from concerned manufacturer shall be submitted.	Submitted.
16.	Reference of previous approval of applications with stability study data of the firm shall be submitted.	Firm has submitted that no application of powder for oral solution (Sachet) was submitted with stability studies to DRAP.
Decision: Deferred for deliberation regaring approval of applied formulation by reference regulatory authorities.		

b. Deferred cases of Human imported drugs of Form 5F.

449.	Name, address of Applicant / Importer	M/s Al Habib Pharmaceuticals, Plot No. 81-B Block B, S.M.C.H.S, Karachi.
	Details of Drug Sale License of importer	License No: 1245. Address: 81-B Block B, S.M.C.H.S, Karachi. Address of Godown: 1. Plot No. 10 sector 25 KIA, Karachi. 2. HT – 8, Landhi Industrial Area, Karachi. Validity: 18-05-2022. Status: License to sell, stock & exhibit for sale, distribute and sell drugs by way of wholesale by of manufacturer, importer or indenter.
	Name and address of marketing authorization holder (abroad)	Hebei Dawn Pharmaceuticals Co., Ltd., Block 3 No. 51, Xingye Road, Economic Development Zone, Cangzhou China.
	Name, address of manufacturer(s)	Hebei Dawn Pharmaceuticals Co., Ltd., Block 3 No. 51, Xingye Road, Economic Development Zone, Cangzhou China.
	Name of exporting country	China.
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original legalized CoPP certificate No. 202103082 dated 12-08-2021 issued by Hebei Province Drug Administration, No. 391 Hongqi Street, Shi Jiazhuang P.R. of China for Paclitaxel for injection (albumen bound). CoPP has mentioned Hebei Dawn Pharmaceuticals Co., Ltd., Block 3 No. 51, Xingye Road, Economic Development Zone, Cangzhou China as the manufacturer. The name of importing country on CoPP is mentioned as Pakistan. Furthermore, the CoPP was valid for one till 11-08-2023. *However, the certificate has mentioned that the above product is not registered in China and authorized to be placed in china. The exportation of the product is not restricted.* *The product has been reformulated with a view to improving its stability under specific conditions outside of china.* **GMP:** Firm has submitted copy of GMP certificate No. FT070/MH/001/2019 in the name of M/s Hebei Dawn Pharmaceuticals Co., Ltd., Block 3 No. 51, Xingye Road, Economic Development Zone, Cangzhou China issued by the National Authority of Medicines and Health Products, Portugal. Latest inspection was conducted on 20-07-2018 and the certificate reflects that the principles and guidelines of Good Manufacturing Practice laid down in the Directive 2003/94/EC are complied. The certificate is valid for three years. Furthermore, the certificate has mentioned that this certificate only covers the manufacturing activities

		in the building No. 1 (Injection workshop)
	Details of letter of authorization / sole agency agreement	**Letter of Authorization:** Firm has submitted original legalized and notarized letter of Authorization dated 11-04-2022 from Hebei Dawn Pharmaceuticals Co., Ltd., Block 3 No. 51, Xingye Road, Economic Development Zone, Cangzhou City, Hebei province China for Paclitaxel (Albumen bound) Injection 100mg wherein M/s Al Habib Pharmaceuticals, Plot No. 81-B Block B, S.M.C.H.S, Karachi is authorized as sole agent and distributor for the above said product.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 11265: 11-05-2022.
	Details of fee submitted	PKR 150,000/-: 13-04-2022.
	The proposed proprietary name / brand name	Albino 100 mg Lyophilized powder for injection.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains; Paclitaxel as albumen bound nanoparticles ……. 100mg
	Pharmaceutical form of applied drug	Lyophilized powder for injection.
	Pharmacotherapeutic Group of (API)	L01CD01 Antineoplastic Agents.
	Reference to Finished product specifications	In house specifications.
	Proposed Pack size	As per Policy.
	Proposed unit price	As per Policy.
	The status in reference regulatory authorities	Abraxane 100mg vial (paclitaxel protein-bound particles for injectable suspension) (albumin-bound)), USFDA Approved.
	For generic drugs (me-too status)	Nab-Xelpac Injection 100mg (Lyophilized powder), Himmel Pharmaceuticals, Reg. No. 106640.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information

		related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Fujian South Pharmaceutical Co. Ltd. No.98, Dongxin Road, Xuefeng Town, Mingxi Country, Fuijian Province, China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data for both sources related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated for 06 months as well as real time conditions for 36 months. The real time stability data is conducted at 25 ^{o}C ± 2^{o}C, RH 60% ± 5% and accelerated stability data is conducted at 40^{o}C ± 2^{o}C, RH 75% ± 5%. (Batch No. 902-1612411, 902-1701401, 902-1701402)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established against the reference product Abraxane 100mg (Paclitaxel Albumin Bound) by Abraxis Biosciences for the quality test i.e. Identification, pH, Water content, Particulate matter, Particle size & particle size distribution, Related substances, Human albumen content, Paclitaxel binding rate, sterility, Bacterial endotoxin and assay.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Borosilicate glass vial 50ml. Brominated butyl rubber stopper Aluminum plastic combination caps for injection vial.

	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 40°C ±2°C / 75% ± 5% RH for 6 months both upright and inverted orientation (Batch No. 1210101, 1210102 & 1210103). The real time stability study data is conducted at 30°C ±2°C / 75% ± 5% RH for 24 months (Batch No. 1210101, 1210102 & 1210103).

Evaluation by PEC:

Sr. No.	Section	Observation	Response by the firm
1	1.3.4	Valid and notarized copy of Drug Sale License of the applicant shall be submitted.	Attested copy of Drug Sale License No. 0230 dated 18-05-2022 in the name of Al Habib Pharmaceuticals 81-B Block B, S.M.C.H.S, Karachi is submitted by the firm. Validity is 18-05-2024. *However, the address of the Godown mentioned on the DSL is changed from the previously submitted.* *Plot no. 393/7 & 393/8 Sector 7A KIA, Karachi.*
2		Justification shall be submitted regarding the statement on the CoPP certificate that the product is not registered in China and not authorized to be placed in china.	Firm has submitted a document from M/s Hebei Dawn Pharmaceutical wherein they have declared the following; "We, Hebei Dawn Pharmaceutical Co., Ltd., hereby state that we are exporting Paclitaxel for injection (albumin bound) to following countries as our Plant is exclusively for export to Foreign Countries and EU GMP Certified. i. Austria. ii. Norway. iii. Iran. iv. South Korea. v. Vietnam *However, the firm has not produced any evidence of registration of their applied formulation in any of the Reference Regulatory Authorities as defined by the Registration Board.*
3		Valid, Notarized and legalized GMP certificate of the finished product manufacturer issued by the relevant regulatory authority shall be submitted.	Firm has submitted a copy of GMP certificate No. HE20170084 in the name of M/s Hebei Dawn Pharmaceutical Co., Ltd., Block 3 No. 51, Xingye Road, Economic Development Zone, Cangzhou China issued by the Hebei Drug Administration China dated 25-12-2017 valid till 24-12-2022.

4	3.2.P.1.1	• Innovator product has mentioned approximately 900 mg of human albumin while the applied formulation has mentioned 800 mg of Albumen. Justification shall be submitted. • Qualitative composition of the drug product is changed from the innovator product. Innovator product has used sodium caprylate and sodium acetyl tryptophanate while the applied formulation has chloroform, anhydrous ethanol and WFI. Compatibility studies shall be submitted.	Firm has submitted composition of formulation in different RRA as follows; • FDA 900 mg of Human Albumin. • NMPA 900 mg of Human Albumin. • PMDA 800mg of human albumin. • EMEA 800mg of human albumin. Firm has submitted that applied medicine is developed as per the innovator product following the PMDA and EMEA Abraxane and both are included in RRA. *However, the review report approved by Japan (Clinical Summary 2.7) has the following description;* *The dosage ratio of paclitaxel and human albumin in the original commercial batch prescription is 1:8 but due to the influence of the sterilization filtration process, the ratio of paclitaxel and human albumin become 1:9.* *While EPAR has not mentioned any ratio of paclitaxel and Albumin in the public assessment report.* Firm has submitted that other excipients used in the manufacturing of Paclitaxel albumin bound i.e. chloroform, anhydrous ethanol, WFI will be removed finally and the finished product does not contain these excipients that why the end product is same as reference product. Firm has also submitted new composition for the applied formulation wherein they have included sodium caprylate and sodium acetyl tryptophanate in the composition. *However, these excipients are not mentioned in the original submitted CoPP nor in original dossier submitted.*
5	3.2.P.1.3	Since the final product is lyophilized preparation, therefor, submit the details of reconstitution diluent along with the compatibility studies for the dry powder for injection.	Firm has submitted the following; "Aseptically, reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection, USP. Slowly inject the 20 mL of 0.9% Sodium Chloride Injection, USP, over a minimum of 1 minute, using the sterile syringe to direct the solution flow onto the inside wall of the Vial. The reconstituted suspension should be milky and homogenous without visible particulates. If particulates or settling

			are visible, the vial should be gently inverted again to ensure complete resuspension prior to use. Discard the reconstituted suspension if precipitates are observed. Discard any unused portion".
	3.2.P.2.2.1	Details of the innovator product including batch number, manufacturing date & Expiry date shall be submitted.	Firm has submitted the following; Batch No. 0F028C Exp. Date. 06-2023.
	3.2.P.8	Submit in use stability studies for drug product along with proposed in -use storage statement and in-use shelf life.	***Not submitted.*** Firm has submitted again the real time and accelerated stability studies that were submitted in the original dossier.

Decision of 320th meeting:

The Board deferred the case for clarification of the following points;

- The applied product is not present in the market of exporting country for free sale.
- The qualitative composition of the applied product is different from the innovator's product.
- In-use stability of the applied product is not submitted.

Reply by the firm;

Firm has submitted their reply vide reference no. nil dated 08-09-2022 wherein they have submitted new composition for the applied formulation which is similar to the innovator's product. They have also provided in use stability studies for the applied formulation.

Furthermore, they also provided copy of CoPP certificate for the applied formulation wherein it is confirmed that ***"this is to certify that the above product(s) is registered in china and authorized to be placed in china. The exportation of the product is not restricted."***

However, upon evaluation of the CoPP document following is revealed.

- **Submitted CoPP is neither notarized nor countersigned by the embassy of Pakistan.**
- **CoPP certificate is not as per format of WHO CoPP.**
- **New CoPP certificate submitted by the firm has same certificate number and same date of issuance, as that of the previously submitted CoPP in which following was mentioned**

  "That the above product is not registered in China and authorized to be placed in china. The exportation of the product is not restricted.

  The product has been reformulated with a view to improving its stability under specific conditions outside of china".
- **However, status of the applied formulation is only changed from the previously submitted certificate.**
- **Online data of the newly submitted CoPP is not available on the official website of China.**

Decision: Registration Board decided to send an email to NMPA China for confirmation of free sale status of applied formulation in China.

Case No. 05. Deferred application of Human Drugs Form 5.

450.	Name and address of manufacturer/ Applicant	M/s Wimits Pharmaceuticals (Pvt.) Ltd, Plot No. 129, Sundar Industrial Estate, Raiwind Road, Lahore.
	Brand Name + Dosage Form + Strength	Levocard tablet
	Composition	Each film- coated tablet contains: Levodopa……100mg Carbidopa……..……25mg

		Entacapone…….200mg
	Diary No. Date of R & I & fee	Dy.No.29712; 05-09-2018; Rs.20,000 (05-09-2018)
	Pharmacological Group	Anti-parkinson dopaminergic agent
	Type of Form	Form- 5
	Finished product Specification	Manufacturers
	Pack size & Demanded Price	14's, 20's & as per SRO
	Approval status of product in Reference Regulatory Authorities	Approved in MHRA
	Me-too status	Obsonerv 25/100/200mg tablet of M/s OBS Pakistan (Reg. # 070444)
	GMP status	Last GMP inspection was conducted on 03-11-2017 and the report concludes satisfactory GMP compliance.
	Remarks of the Evaluator	Salt is not complete because Carbidopa as monohydrate will come. No official monograph is available for the applied formulation. Methylene Chloride is added in the coating solution of the formulation. General tablet section is available in the firm as mentioned in the submitted section approval letter.
	Previous decision.	Deferred in 293rd DRB meeting for the following reasons: • Applied composition is not complete because Carbidopa "as Monohydrate" is approved in reference regulatory authority. • Applying a banned excipient "Methylene Chloride" in the coating solution of the applied formulation.
	Evaluation by PEC- XIII	• Firm has revised its Form- 5 and master formulation as "Carbidopa as Monohydrate" • Firm has again mentioned methylene chloride in the applied formulation.
	Decision of 296th meeting of Registration Board.	Deferred for clarification for using Methylene Chloride which is a banned excipient.
	Reply by the firm.	Firm has submitted new master formula for the applied formulation wherein they have removed/excluded the banned excipient from their formulation.
	Evaluation by PEC- XIII	• Firm has revised their formulation in 296th meeting as per reference product without submission of applicable fee. • Current GMP status could not be confirmed.
	Decision: Approved with innovator's specifications and following label claim; **Each film- coated tablet contains:** **Levodopa……100mg** **Carbidopa as monohydrate.……25mg** **Entacapone…….200mg** • **Registration letter will be issued after submission of fee of Rs. 30,000/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 and latest GMP certificate/last inspection report conducted within last three years.**	
451.	Name and address of manufacturer/ Applicant	M/s Genesis Pharmaceuticals, Plot # 25, Sunder Industrial Estate, Lahore.

	Brand Name + Dosage Form + Strength	Irosak tablet 150mg
	Composition	Each film-coated tablet contains: Elemental iron as iron polymaltose complex ….150mg
	Diary No. Date of R & I & fee	Dy.No.17064; 04-10-2017; Rs.20,000/- (04-10-2017)
	Pharmacological Group	Anti- Anemic.
	Type of Form	Form-5
	Finished product Specification	Manufacturers
	Pack size & Demanded Price	2x 10's & s per SRO
	Approval status of product in Reference Regulatory Authorities	Not applicable
	Me-too status	Could not be confirmed in the applied formulation as 100mg is available.
	GMP status	Last GMP inspection was conducted on 15-07-2016 and the report concludes: "A detailed re-inspection would be conducted in operational mode. At the time of inspection unit was found non-operational."
	Remarks of the Evaluator	The evidence of applied strength of me-too status could not be verified. GMP status could not be confirmed by the report.
	Previous decision	Deferred in 290th DRB meeting for evidence of applied formulation/ drug already approved by DRAP (generic /me-too status) along with registration number, brand name and name of firm. Further, Registration Board referred the case to QA & LT Division to update GMP status of Firm on priority.
	Evaluation by PEC- XIII	Firm has submitted wrong me- too status as Ferricure Capsule of M/s S.J. & G Fazul Ellahie, Karachi 050637 while tablets are applied. Firm has submitted its latest GMP inspection report which was conducted on 03-02-2020 and the report concludes satisfactory level of GMP compliance.
	Decision of 296th meeting.	Deferred for evidence of applied formulation/drug already approved by DRAP (generic / me too status) along with registration number, brand name and name of firm.
	Submission of the firm:	Firm has submitted their reply wherein they have requested to change their formulation of IROSAK tablet 150mg (Iron polysaccharide complex) from tablets to capsules and submitted fee of 5000/- vide deposit slip No. 1910045 dated 31-12-2020.
	Evaluation by PEC- XIII	For change of formulation, requisite fee is 30,000/-.
	Decision of 307th meeting.	Deferred for submission of fee applicable to the change of formulation.
	Reply by the firm.	Firm has submitted a differential fee of 25000/- vide slip No. 2045102990 dated 27-09-2022.
	Evaluation by PEC- XIII	**Revised formulation is as under;** **Each capsule contains:** **Elemental iron as iron polymaltose complex….150mg**

		• Capsule (General) section approved vide letter No. F. 6-3/2014-Lic (M-234) dated 04-04-2014. • Copy of GMP certificate No. 114/2020-DRAP (AD-1910741-175) dated 22-07-2020 issued on the basis of inspection conducted on 03-02-2020 is submitted.
	Decision: Approved with innovator's specifications. Registration letter will be issued after submission of fee of Rs. 7500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021. Years	
452.	Name and address of manufacturer/ Applicant	M/s Inventor Pharma, Plot # K/196, S.I.T.E., (SHW) Phase –II, Karachi.
	Brand Name + Dosage Form + Strength	Lactol syrup 3.35gm/ 5ml
	Composition	Each 5ml contains: Lactitol Monohydrate…….3.35gm
	Diary No. Date of R & I & fee	Dy. No. 25410; 21-12-2017; Rs.1,00,000/- (21-12-2017)
	Pharmacological Group	To treat constipation and chronic encephalopathy
	Type of Form	Form- 5
	Finished product Specification	Not claimed
	Pack size & Demanded Price	120ml & As per DRAP policy
	Approval status of product in Reference Regulatory Authorities	Lactitol Monohydrate by M/s Zambon Schweiz AG (Swiss Medica) Switzerland Approved
	Me-too status	Lacasil syrup 3.35gm/ 5ml of Sami Pharmaceuticals (Reg. # 070552)
	GMP status	Last GMP inspection was conducted on 05-07-2018 and the report concludes good level of GMP compliance.
	Remarks of the Evaluator	Evidence of availability of RI detector needs to be confirmed by the firm. • Source of lactitol, along with stability studies data, GMP certificate of supplier needs to be submitted. • Firm has oral Liquid General section. • Letter was issued to the firm on 3rd Dec., 2018 but still no reply has been received.
	Decision of 288th meeting of Registration Board.	Deferred for following: • Evidence of availability of RI detector is needed • Source of lactitol, along with stability studies data, GMP certificate of supplier needs to be submitted.
	Submission of the firm:	Firm has submitted a picture of Shimadzu RID-10A Refractive index detector. Stability data sheets for the drug substance is submitted for three batches. Firm has submitted copy of verification of compliance certificate for Shandong Lujian Biological Technology Co., Ltd. National High-tech Industrial Development Zone, Dezhou (Yucheng), Shandong Province, P.R. China. Scope of the audit is "Production of Food additives, including Xylitol, Lactitol, Malitol, Sorbitol" and the certificate is issued by SGS.

	Evaluation by PEC- XIII	• *However, no invoice nor any other document confirming the authenticity of the instrument is submitted.* • *However, name of the company and specifications are not mentioned in the stability data summary sheets.* • *GMP certificate issued by the relevant /concerned regulatory authority shall be submitted.* • *Fee of import for the imported source of drug substance shall be submitted.*
	Decision: Approved with USP specifications. The firm shall submit differential fee for import of bulk solution of Lactitol as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021. Registration Board further decided that firm shall submit GMP certificate for the drug substance manufacturer before issuance of registration letter.	
453.	Name and address of manufacturer/ Applicant	M/s Winilton Pharmaceuticals (Pvt.) Ltd., Plot # 45, Street # S-5, National Industrial Zone, Rawat, Islamabad (Contract giver) M/s Vision Pharmaceuticals, Plot # 22,23, Industrial Triangle, Kahuta Road, Islamabad (Contract acceptor) (Liquid vial general)
	Brand Name + Dosage Form + Strength	Win D3 5mg Injection.
	Composition	Each Ampoule Contains: Cholecalciferol …… 5mg
	Diary No. Date of R & I & fee	Dy. No 10124 dated 04-03-2019; Rs.50,000/- dated 01-03-2019.
	Pharmacological Group	Vitamin D and analogue.
	Type of Form	Form-5.
	Finished product Specification	BP specifications.
	Pack size & Demanded Price	1ml x 1's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	Vitamin D3 Good 200,000 IU / 1 ml IM solution for injection of (ANSM France approved)
	Me-too status	Cara-IN-D, Caraway Pharmaceuticals, Reg. No. 052731.
	GMP status	Same as above.
	Remarks of the Evaluator	• Firm has submitted that we cannot perform terminal sterilization of Cholecalciferol injection because crodamol oil is used in the manufacturing of it and have oily phase. • Firm has provided section approval letter wherein they have three approved sections and they also submitted that no product is registered on contract basis. • *Firm has claimed BP specifications. However, BP has the strength of 7.5 mg and Ethyl Oleate as vehicle.*
	Decision of 316th meeting of Registration Board.	Deferred for justification of claiming BP specifications for applied product, since the applied strength and composition is different form that specified by BP monograph of cholecalciferol injection.
	Submission of the firm:	In response of the decision of the Registration Board, M/s Vision Pharma has submitted the reply wherein they have informed that the product specification is as

		per innovator's specification and we are claiming innovator's specification. The API Cholecalciferol is on BP specifications. They also provided their registration letter wherein they have BP specifications and applied for change of specifications dated 10-02-2022.
	Evaluation by PEC- XIII	***In the submitted dossier BP specification are claimed by the applicant and no fee has been submitted for change of specifications.*** ***Documents are submitted by M/s Vision Pharma instead of the applicant.***
	Decision: Approved with Innovators specifcations along with revised drug product specifcations and fee of Rs. 7,500 for correction/revision of drug product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021	
454.	Name and address of manufacturer/ Applicant	M/s Winilton Pharmaceuticals (Pvt.) Ltd., Plot # 45, Street # S-5, National Industrial Zone, Rawat, Islamabad (Contract giver) M/s Vision Pharmaceuticals, Plot # 22,23, Industrial Triangle, Kahuta Road, Islamabad (Contract acceptor) (Liquid vial general)
	Brand Name + Dosage Form + Strength	Ketroq 30mg Injection.
	Composition	Each Ampoule Contains: Ketorolac Tromethamine ……..… 30mg
	Diary No. Date of R & I & fee	Dy. No 10122 dated 04-03-2019; Rs.50,000/- dated 01-03-2019.
	Pharmacological Group	Anti-inflammatory and Antirheumatic Products, Non-Steroids
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	1ml x 5's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	Toradol Injection 30mg/ampoule of 1ml by M/s Atnahs Pharma, UK (MHRA Approved)
	Me-too status	Tromit Injection 30mg/ml, Standpharm Pakistan, Reg. No. 049958.
	GMP status	Same as above.
	Remarks of the Evaluator	• Firm has revised their manufacturing outline wherein they have added terminal sterilization with submission of fee of 7500/- vide slip no. 51343740442 dated 12-11-2021. • Firm has provided section approval letter wherein they have three approved sections and they also submitted that no product is registered on contract basis.
	Decision of 316th meeting of Registration Board.	Deferred for scientific rationale of performing terminal sterilization, with reference to the innovator product.
	Submission of the firm:	Firm has submitted that Ketroq 30mg injection is not terminally sterilized. For sterilization initially the solution is first passed through 0.45-micron filter before filling on machine passed through 0.2-micron filter. Sterilization is assured by performing the sterility test of the product.

	Evaluation by PEC- XIII	• *Firm in initial reply revised their manufacturing outline wherein they have added terminal sterilization with submission of fee of 7500/- vide slip no. 51343740442 dated 12-11-2021.* • *Documents are submitted by M/s Vision Pharma instead of the applicant.*
	Decision: Deferred for for further deliberation regarding the sterilization method of the applied formulation.	
455.	Name and address of manufacturer/ Applicant	M/s Maxitech Pharma (Pvt.) Ltd., Plot No. E-178, S.I.T.E. Super Highway, Phase II, Karachi (Contract giver). M/s Safe Pharmaceuticals (Pvt.) Ltd., Plot No. C.I-20, Sector 6-B, Industrial Area, North Karachi (Contract acceptor).
	Brand Name + Dosage Form + Strength	Colymax 200,000 IU/100ml Injection.
	Composition	Each 100ml vial Contains: Colistimethate Sodium ……200,000 IU
	Diary No. Date of R & I & fee	Dy. No 30852 dated 13-09-2018 Rs.50,000/- dated 12-09-2018 (Duplicate).
	Pharmacological Group	Polymixin.
	Type of Form.	Form-5.
	Finished product Specification.	USP specifications.
	Pack size & Demanded Price	As per DRAP policy.
	Approval status of product in Reference Regulatory Authorities.	
	Me-too status.	Could not be confirmed.
	GMP status.	Same as above.
	Remarks of the Evaluator XIII	• Manufacturing facility/section approval of contact acceptor could not be confirmed. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • M/s Maxitech has 09 approved sections as per section approval letter. They further submitted that no product is registered in contract manufacturing. • They also clarified thay their product Colymax 200,000 IU/100ml Injection is ready to fill lyophilized powder. • M/s safe pharma is having sterile dry powder Injection (Lyophilized) section.
	Decision of 308th meeting of Registration Board.	Deferred for following: • Manufacturing facility/section approval of contact acceptor could not be confirmed. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.

		• Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Submission by the firm.	Firm has submitted that same product is registered in SRA as sterile powder for injection and for this no lyophilize section is required. They have also submitted reference of "*COLOMYCIN 2 million International Units (IU) Powder for solution for injection, infusion or inhalation*" with market authorization holder Teva UK Limited, Brampton Road, Hampden Park, Eastbourne, East Sussex, BN22 9AG, United Kingdom, with marketing authorization No. PL 00289/2256.
	Evaluation by PEC- XIII	• Evidence of reference provided by the firm could not be verified. Only 1MIU strength with marketing authorization No. PL 00289/2255 is confirmed. • Me too is not provided by the firm. • Stability study data as per the guidelines approved in 293rd meeting of Registration Board shall be submitted.
	Decision: Deferred for following: • **Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.** • **Submission of stability study data as per the guidelines approved in 293rd meeting of Registration Board.**	

Case No. 06. Deferred application of Veterinary Drugs Form 5.

456.	Name and address of manufacturer/ Applicant	M/s Elko Organization Pvt Ltd, Plot No.27 & 28, Sector 12-B, North Karachi, Industrial Area, Karachi
	Brand Name + Dosage Form + Strength	X20 Injection 20IU/ml
	Composition	Each ml contains: Oxytocin ……..…20IU
	Diary No. Date of R & I & fee	Dy. No 1876 dated 15-01-2019 Rs. 20,000/- Dated 14-01-2019.
	Pharmacological Group	Peptide hormone
	Type of Form	Form-5
	Finished product Specification	Manufacturers
	Pack size & Demanded Price	250ml & Decontrolled
	Me-too status	X20 Injection 100ml of M/s Elko 085466.
	GMP status	Last GMP inspection was conducted on 06-07-2017 and the report concludes good level of GMP compliance with advice of some improvements of some minor observations.
	Remarks of the Evaluator	Firm has General vial/ ampoule liquid vet section as mentioned in the submitted GMP inspection report.
	Decision of 295th meeting of registration Board.	Deferred for confirmation of manufacturing facility.

	Submission by the firm.	Firm has submitted that they have already registrations of Hormonal drugs namely; 1. Oxytocin 5 IU injection, Reg. No. 011121 with pack size of 1ml ampoule. 2. Oxytocin 10 IU injection, Reg. No. 011122 with pack size of 1ml ampoule, 50ml, 100ml & 250ml. 3. X20 injection (Oxytocin 20 IU), Reg. No. 085466 with pack size of 100ml. Furthermore, firm has submitted copy of DML renewal report conducted on 22-08-2022 wherein the panel unanimously recommends the grant of renewal of DML (000245) (Formulation) for the next five years for following sections and also recommends the regularization of existing layout plan. Report has also mentioned liquid injection Ampoule/vial (Hormone) Veterinary.
	Evaluation by PEC- XIII	• Submitted DML renewal report has only first page and last page. • Furthermore, the me too mentioned has not the same fill volume as that of the applied formulation.
	Decision: Deferred for Submission of evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm with same fill volume.	
457.	Name and address of manufacturer / Applicant	M/s Selmore Pharmaceuticals Pvt Ltd. 36-Km, Multan Road Lahore.
	Brand Name +Dosage Form + Strength	Vital 4 Solution
	Composition	Each 1000ml Contains: Vitamin A……..…30,000,000 IU Vitamin D3……..…1,000,000 IU Vitamin E……..…5,000mg Vitamin K3……6,000mg
	Diary No. Date of R& I & fee	Dy. No. 12782 dated 06.03.2019 Rs. 20,000/- dated 06.03.2019
	Pharmacological Group	Multivitamins
	Type of Form	Form 5
	Finished Product Specification	The firm has claimed in-house specifications.
	Pack size & Demanded Price	500ml, 1000ml, 5000ml; decontrolled.
	Reference / Me-too status	Adekbar Oral Liquid. Reg. No. 73950
	GMP status	The firm was inspected on 05-03-2018,17-08-2018 & 16-10-2018, where renewal of DML was recommended.
	Remarks of the Evaluator.	• The drug product specifications have not been evaluated.
		• Justify the capacity of one-liter water to accommodate Vitamin A…30,000,000 IU, Vitamin D3…1,000,000 IU, Vitamin E…5,000mg and Vitamin K3…6,000mg. the firm submitted the quantity to be Vitamin A…17.64g, Vitamin D3…25mg, Vitamin E…5,000mg and Vitamin K3…6,000mg

		• You have applied for solution. Justify the solubility of water insoluble vitamins in water. The firm submitted that these are emulsified with tween-80. • The quantity of APIs in master formula are not in line with the label claim. The firm revised the master formula accordingly. • Submitted Rs. (challan-70559611534)
	Decision of 321st meeting of Registration Board.	Deferred for following; • Justification of applied strength of formulation considering the solubility of each drug substance in terms of mg/ml. • Justification for the proposing formulation of water insoluble vitamins in water.
	Submission by the firm.	Firm has submitted master formulation and batch formula for the applied formulation wherein they have shown that total of 1.764 Kg of Vitamin A will be used in 100 Liter. 2.5Gm of Vitamin Din 100 liter, 0.5Kg of Vitamin E and 1.85kg of Vitamin K3 in 100 liters. They further showed the inactive ingredients of the formulation which contain tween 80 as emulsifying agent, Isopropyl alcohol as solubilizing agent, Propylene glycol as solubilizing agent, sorbitol as sweetening agent and purified water as vehicle.
	Evaluation by PEC- XIII	• ***However, upon evaluation of the initial dossier, Inactive mentioned are benzyle alcohol as preservative, Polysorbate 80 as solubilizing agent, Sodium metabisulphate as anti-oxidant, Sorbitol and purified water as solvent.*** • ***Furthermore, initial applied formulation is solution while after submission of reply it becomes as emulsion.*** • ***Also the quantities mentioned in the initially submitted dossier and in reply for batch are different from each other.***
	Decision: Deferred for following claridications: • **Change of formulation from solution to emulsion.** • **Change of inactive in the applied formulation.** • **Change of quantities of the active ingredients mentioned in the initially submitted dossier and in reply.**	

Case No. 07. Registration Applications awaiting reply from the applicants.

a. Registration Application for locally manufactured Human Drugs on Form 5F.

458.	Name, address of Applicant / Marketing Authorization Holder	M/s Cherwel Pharmaceuticals (Pvt.) Ltd., Plot # 20, Phase 4, Hattar Industrial Estate, Hattar KPK.
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt.) Ltd., Plot No. 145 Industrial Triangle, Kahuta Road, Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 11387; dated 14-4-2021.
	Details of fee submitted	PKR 50,000/-: dated 24-02-2021.
	The proposed proprietary name / brand name	Ketora 30mg Injection IM/IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1ml ampoule contains: Ketorolac Tromethamine …….. 30mg
	Pharmaceutical form of applied drug	Clear colorless liquid filled in glass ampoule
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	Innovator's Specifications.
	Proposed Pack size	1ml x 5's
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	US FDA approved.
	For generic drugs (me-too status)	Tekac 30mg/ml Injection, Sami Pharmaceuticals, Reg. No. 092855.
	GMP status of the Applicant.	GMP certificate issued on 26-03-2019 on the basis of inspection conduct 04-02-2019.
	GMP status of the Finished product manufacturer	GMP certificate issued on 21-05-2019 on the basis of inspection conduct 23-4-2019, valid up to 22-04-2022.
	Evidence of section approval of the Finished product manufacturer.	Liquid ampoule (from GMP certificate.) Ampoule general vide letter No. F. 1-12/89-Lic (Vol-II) dated 23-07-2012.
	Name and address of API manufacturer.	M/s. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India. Manufacturing site address: M/s. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including

		its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for both drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 60 months. (Batch No. KTM06130016, KTM06130017 & KTM06130018)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Toradol Ampoule 30mg, B. No. C2436, Mfg. date 01, 2020 by Barrett Hodgson by performing quality tests (Description, Identification, pH, Assay, Sterility, Bacterial endotoxin.)
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India. Manufacturing site address: M/s. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab India
API Lot No.	KM-0100918, KTM-180015 & KTM180015.
Description of Pack (Container closure system)	Glass ampoule
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months Accelerated: 6 months

Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)		
Batch No.	A-439	A-596	A-611
Batch Size	46,200 Ampoules	16,000 Ampoules	33,000 Ampoules
Manufacturing Date	05-2018	03-2019	03-2019
Date of Initiation	25-06-2018	22-04-2019	20-05-2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India valid upto 11-6-2021
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice# SCL/2020-21/111)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:
Letter was issued on 14-10-2021 with following observations and no reply received till date;

Section Number	Observations	Firm's Response
	Fee of 50,000/- is submitted. Differential of 25,000/- shall be submitted.	
1.5.6	Official monograph is available in USP. Firm has claimed innovator's specifications in "1.5.6" section of form 5F.	
1.4.3	Number of approved sections of the applicant and total number of approved registered products on contract basis could not be confirmed.	

1.6.5	Valid GMP certificate of API manufacturer issued by regulatory body of country shall be submitted.	
3.2. S.4	• Results of analysis of relevant batch(es) of drug substance performed by drug product manufacturer used during product development and stability studies along with COA of the same batch from drug substance/Active Pharmaceutical ingredient manufacturer. • Detailed analytical procedure for the drug substance by the drug product manufacturer shall be provided. • Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the drug product manufacturer shall be submitted.	
3.2. P.8.3	ADC attested invoices of the drug substance used during product development and stability studies shall be submitted.	
3.2. P.2.3	Justification of not performing terminal sterilization of the drug product.	
3.2. P.5.2	Detailed analytical procedure for the drug product by the drug product manufacturer shall be provided.	
3.2. P.5.3	In process validation protocol 30.45mg of ketorolac Tromethamine is used. Justification is required whether overage or potency adjustment?	
3.2. P.8.3	Submit raw data sheets for stability studies, reflecting the details of Standard weight, Sample dilution preparation, Potency of Reference standard and Calculation formula applied for the Assay test.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

459.	Name, address of Applicant / Marketing Authorization Holder	M/s Alliance Pharmaceuticals (Pvt.) Ltd., 112-A Industrial area, Hayatabad, Peshawar.
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt.) Ltd., Plot No 145 Industrial Triangle, Kahuta Road, Islamabad.
	Status of the applicant	☐ Manufacturer ☐ Importer

		☒ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13166; dated 06-05-2021
	Details of fee submitted	PKR 50,000/-: dated 07-04-2021.
	The proposed proprietary name / brand name	Ketolance Injection 30mg IM/IV
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1ml ampoule contains: Ketorolac Tromethamine …….. 30mg
	Pharmaceutical form of applied drug	Clear colorless liquid filled in glass ampoule
	Pharmacotherapeutic Group of (API)	NSAID
	Reference to Finished product specifications	Innovator's specifications.
	Proposed Pack size	1ml x 5's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	US FDA approved
	For generic drugs (me-too status)	Tekac 30mg/ml Injection, Sami Pharmaceuticals, Reg. No. 092855.
	GMP status of the Finished product manufacturer	GMP certificate issued on 21-05-2019 on the basis of inspection conduct 23-4-2019, valid upto 22-4-2022.
	Evidence of section approval.	Liquid ampoule (from GMP certificate.) Ampoule general vide letter No. F. 1-12/89-Lic (Vol-II) dated 23-07-2012.
	Name and address of API manufacturer.	M/s. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India. Manufacturing site address: M/s. Saurav Chemicals Limited, Bhagwanpura, Derabassi – Barwala Road, Mohali District Punjab India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized

		information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation/verification of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module III (Drug Substance)	Firm has submitted detailed data for drug substance related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies (Drug substance)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at $40^{O} \pm 2^{O}$ C /75% ± 5% RH for 6 months. The real time stability data is conducted at 30^{O}C ± 2^{O} C / 65% ± 5% RH for 60 months. (Batch No. KTM06130016, KTM06130017 & KTM06130018)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has performed pharmaceutical equivalence against the product Toradol Ampoule 30mg, B. No. C2436, Mfg. date 01, 2020 by Barrett Hodgson by performing quality tests (Description, Identification, pH, Assay, Sterility, Bacterial endotoxin.)
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India
API Lot No.	KM-0100918, KTM-180015 & KTM180015
Description of Pack (Container closure system)	Glass ampoule
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 24 months Accelerated: 6 months
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18 & 24 (Months)

Batch No.	A-439	A-596	A-611
Batch Size	46,200 Ampoules	16,000 Ampoules	33,000 Ampoules
Manufacturing Date	05-2018	03-2019	03-2019
Date of Initiation	25-06-2018	22-04-2019	20-05-2019
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	GMP certificate of M/s. Saurav Chemicals Limited 370 Industrial Area, Phase II Panchkula, Haryana, 134109 – India valid upto 11-6-2021
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has submitted attested copy of invoice (invoice# SCL/2020-21/111)
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	N/A
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Remarks of Evaluator:
Letter was issued on 14-10-2021 with following observations and no reply received till date;

Section Number	Observations	Firm's Response
	Fee of 50,000/- is submitted. Differential of 25,000/- shall be submitted.	
1.5.6	Official monograph is available in USP. Firm has claimed innovator's specifications in "1.5.6" section of form 5F.	
1.4.3	Number of approved sections of the applicant and total number of approved registered products on contract basis could not be confirmed. GMP status of the applicant could not be confirmed.	

2.3	Documents of Cherwel pharma are placed in QOS instead of the applicant. Justification is required.	
1.6.5	Valid GMP certificate of API manufacturer issued by regulatory body of country shall be submitted.	
3.2. S.4	• Results of analysis of relevant batch(es) of drug substance performed by drug product manufacturer used during product development and stability studies along with COA of the same batch from drug substance/Active Pharmaceutical ingredient manufacturer. • Detailed analytical procedure for the drug substance by the drug product manufacturer shall be provided. • Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the drug product manufacturer shall be submitted.	
3.2. P.8.3	ADC attested invoices of the drug substance used during product development and stability studies shall be submitted.	
3.2. P.2.3	Justification of not performing terminal sterilization of the drug product.	
3.2. P.5.2	Detailed analytical procedure for the drug product by the drug product manufacturer shall be provided.	
3.2. P.5.3	In process validation protocol 30.45mg of ketorolac tromethamine is used. Justification is required whether overage or potency adjustment?	
3.2. P.8.3	Submit raw data sheets for stability studies, reflecting the details of Standard weight, Sample dilution preparation, Potency of Reference standard and Calculation formula applied for the Assay test.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

b. Registration Application of Imported Human Drugs on Form 5F.

460.	Name, address of Applicant / Importer	M/s Genome Pharma, House no. 166-A St. # 9, Chaklala Scheme III, Rawalpindi-PAKISTAN.

	Details of Drug Sale License of importer	DSL NO. 01-374-0176-035673D. Address: M/s Genome Pharma, House No. 166-A, Street No. 09, Chaklala Scheme III, District Rawalpindi. Go-down address: C-19, Main commercial access road, RCCI Industrial Estate Rawat, Rawalpindi.
	Name and address of marketing authorization holder (abroad)	M/s Republican Unitary Production Enterprise "Belmedpreparaty", 220007, Minsk, 30 Fabritsius St., Belarus.
	Name, address of manufacturer(s)	M/s Republican Unitary Production Enterprise "Belmedpreparaty", 220007, Minsk, 30 Fabritsius St., Belarus. Manufacturing activities: 1/5, 1/22 Mayakovsky st., 7 Betonnyi Passage, Minsk, Republic of Belarus.
	Name of exporting country	Belarus.
	Detail of certificates attached (CoPP, Free sale certificate, GMP certificate)	Detail of certificates attached (CoPP, GMP certificate) • Original legalized CoPP (certificate No. 106-2019/CPP/PK) issued by Ministry of Health of the Republic of Belarus on 17/09/2019. The applied product is present in the market of exporting country for free sale. The facilities and operations conform to WHO-GMP. • Original legalized GMP certificate No. 073/2018/GMP valid till 28/05/2021 issued by Ministry of Health of the republic of Belarus. • Not valid
	Details of letter of authorization / sole agency agreement	Notarized copy of product specific sole agency agreement is submitted.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 11131: dated 12-04-2021.
	Details of fee submitted	PKR 100,000/-: dated 11-06-2020.
	The proposed proprietary name / brand name	Calfoli lyophilized powder for Injection 100mg
	Strength / concentration of drug of Active Pharmaceutical ingredient	Each vial contains: Calcium folinate as folinic acid ……. 100mg

	(API) per unit	
	Pharmaceutical form of applied drug	Lyophilized powder for solution for IM/IV injection.
	Pharmacotherapeutic Group of (API)	Detoxifying agents for antineoplastic treatment.
	Reference to Finished product specifications	EP
	Proposed Pack size	1's
	Proposed unit price	As per SRO.
	The status in reference regulatory authorities	Fusilev (leuovorin as calcium 50mg) lyophilized powder for solution for injection, USFDA Approved.
	For generic drugs (me-too status)	TETRAFOLIN-50 INJECTION (lyophilized powder), Reg. No. 4753800000000000
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Name, address of drug substance manufacturer	Manufacturing and quality control: M/s Cerbios-Pharma SA via Figino 6 CH-6917 Barbengo/Lugano, Switzerland. Heavy metals analysis: M/s Robertson Microlit Laboratories, Inc. 1705 US Highway 46 Suit 1D Ledgewood, New Jersey 9NJ) 07852 United States (USA).
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	• 24 months real time stability data at 25°C / 60% RH of 03 batches (B00089, B00094 & B00110) • 06 month accelerated stability data 40°C / 75% RH of 03 batches (B00089, B00094 & B00110)
	Module-III Drug Product:	Firm has submitted data of drug product including its

		description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has been established against Leucovorin-Lans, Lyophilsate for solution for injection 50mg, approved by Russia.
	Analytical method validation/verification of product	Submitted.
	Container closure system of the drug product	Glass vial with nominal capacity of 10ml seal with rubber stopper along with aluminium caps packed in a unit carton.
	Stability study data of drug product, shelf life and storage conditions	• 24 months real time stability data at 30°C ± 2°C / 65% ± 5% RH of 03 batches (280918, 020119 & 030119) • 06 month accelerated stability data 40°C ± 2°C / 75% ± 5% RH of 03 batches (010110, 020110 & 030110)

Evaluation by PEC:

Letter was issued to the firm dated 21-10-2021 with following observations and no reply received till date.

Section number	Observation	Response by the firm
1.3	Details of applicants are not mentioned. Provided form 5F is from the manufacturer/Marketing authorization holder side while it should be from the applicant holding the Drug sale license.	
1.5.6	Form 5F has mentioned EP reference for the product under section 1.5.6. However, official monograph is not available in pharmacopoeias. Justification is required.	
1.5.8	Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm shall be submitted.	
1.5.9	Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting shall be submitted.	
	Valid & legalized copy of GMP certificate of drug product manufacturer shall be submitted.	
	Notarized product specific sole agency agreement is required.	
3.2 S.4	Analytical method verification studies for drug substance performed by the Drug product manufacturer shall be provided.	

3.2 P.2.2	Pharmaceutical equivalence of the applied drug shall be established with the innovator /reference/comparator product and results of all the quality tests of the developed formulation and the innovator /reference/comparator product shall be submitted.	
3.2 P.7	Details of container closure system, description of the primary container closure system, including material of construction, unit count or fill size, container size or volume shall be provided.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

461.	Name, address of Applicant / Importer	M/s Medinet Pharmaceuticals, Building No. 601, Lane No. 5, Main Peshawar Road, Rawalpindi.
	Details of Drug Sale License of importer	License No: 01-374-0176-022646D. Address: Building No. 601, Lane No. 5, Main Peshawar Road, Rawalpindi. Address of Godown: N/A. Validity: 13-12-2021. Status: License to sell drugs as distributor.
	Name and address of marketing authorization holder (abroad)	Laboratorio Varifarma S.A. Ernesto De Las Carreras 2469 at the corner of Uruguay Nº 3698 of the city of Beccar, District of San Isidro, Province of Buenos Aires, Argentina Republic.
	Name, address of manufacturer(s)	Laboratorio Varifarma S.A. Ernesto De Las Carreras, No. Beccar, Buenos Aires, Argentina.
	Name of exporting country	Argentina.
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted copy of CoPP dated 17-04-2020 issued by National Institute of Drugs Avenida Caseros 2161 City of Buenos Aires Argentina Republic for PEMETREXED Varifarma 500 lyophilized powder for injection (Pemetrexed as disodium hemi pentahydrate 500mg) in the name of *Laboratorio Varifarma S.A. Ernesto De Las Carreras 2469 at the corner of Uruguay Nº 3698 of the city of Beccar, District of San Isidro, Province of Buenos Aires, Argentina Republic*. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through periodic inspection every two year. The name of importing country on CoPP is mentioned as Pakistan. Furthermore, the CoPP was valid for one year. **GMP:** Firm has submitted original, legalized copy of GMP certificate in the name of Laboratorio *Varifarma S.A. Ernesto De Las Carreras 2469 at the corner of Uruguay Nº 3698 of the city of*

		Beccar, District of San Isidro, Province of Buenos Aires, Argentina Republic issued by the National Administration of Drugs, Food and medical Devices (ANMAT) through the National Institute of Drugs (INAME) issued on 09-12-2020 which states that the manufacturing facility of the above said manufacturer is subject to regular inspection to verify compliance with the Good Manufacturing practices according to the regulation in force in the Argentina Republic. Valid for 12 months. However, status of the finished product manufacturer has not been revealed whether compliant Good Manufacturing practices according to the regulation in force or otherwise.
	Details of letter of authorization / sole agency agreement	**Letter of Authorization:** Firm has submitted copy of letter of Authorization from M/s Laboratorio Varifarma S.A. Ernesto De Las Carreras 2469 at the corner of Uruguay Nº 3698 of the city of Beccar, District of San Isidro, Province of Buenos Aires, Argentina Republic for 21 products which does not contain pemetrexed 500mg injection. The said agreement was made on March, 2009. However, firm has also submitted an addendum dated 30-09-2020 wherein the list of products in the agreement is replaced with PEMETREXED Varifarma 500 lyophilized powder for injection 500mg.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only
	Dy. No. and date of submission	Dy. No. 26030: 20-09-2021.
	Details of fee submitted	PKR 100,000/-: 15-04-2021.
	The proposed proprietary name / brand name	Pemetrexed Varifarma lyophilized Powder for Injection 500mg.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains; Pemetrexed as disodium hemi pentahydrate ……. 500mg

	Pharmaceutical form of applied drug	Lyophilized powder for injection.
	Pharmacotherapeutic Group of (API)	Antineoplastic Agents ATC code: L01BA04
	Reference to Finished product specifications	USP specifications.
	Proposed Pack size	1's.
	Proposed unit price	As per Policy.
	The status in reference regulatory authorities	ALIMTA (pemetrexed disodium heptahydrate for injection) 500mg, USFDA Approved. Pemetrexed Accord 25 mg/ml (pemetrexed disodium hemi pentahydrate equivalent to 500 mg pemetrexed.) concentrate for solution for infusion, Netherland approved.
	For generic drugs (me-too status)	Almita 500mg injection, Eli Lilly Pakistan, Reg. No. 043068.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	Shandong Boyuan Pharmaceutical Co. Ltd., Qingjin Street, Jibei Economic Development Zone, Jinan City, Shandong Province, China.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated for 06 months as well as real time conditions for 24 months. The real time stability data is conducted at 5 ^{o}C ± 3^{o}C, and accelerated stability data is conducted at 25^{o}C ± 2^{o}C, RH 60% ± 5%. (Batch No. 141201PN, 141202PN & 141203PN)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of

		analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Pharmaceutical equivalence has not been established. Firm has submitted that products intended to be administered parenterally (for example: Intravenous lines, intramuscular or intrathecal) in aqueous solutions containing the same principle (s) active in the same concentrations (s) WHO, 1996 do not require equivalence studies.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type I colourless glass vial x 50ml with rubber stopper sealed with flip flop cap colour magenta.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted only real time stability study data of 3 batches. The real time stability study data is conducted at $30^oC \pm 2^oC$ / 65% ± 5% RH for 24 months (Batch No. BK172, DG136 & EE070). Firm has not submitted accelerated stability data and stated that it was not carried out because their regulatory authority, ANMAT, does not require it.

Evaluation by PEC:
Letter was issued to the firm dated 07-07-2022 with following observations and no reply received till date.

Sr. No.	Section	Observation	Response by the firm
1.	1.3.4	Valid copy of Drug Sale License of the applicant shall be submitted.	
2.		• Valid and notarized GMP certificate of the finished product manufacturer shall be submitted. • Notarized copy of agreement shall be submitted. • Notarized copy of sole agency agreement shall be submitted.	
3.	3.2.S	Drug substance document has mentioned pemetrexed disodium hemi penta hydrate while the official monograph of USP has mentioned pemetrexed disodium heptahydrate. Clarification is required.	
4.	3.2.S.4.1	Water content mentioned in the specifications of the drug substance is 7.0% - 11% while the monograph has mentioned 19.5 to 22.1%. Clarification is required.	

5.	3.2.S.4.2	Flow rate in assay test of the drug substance is 2ml/min while official monograph has mentioned 1ml/min. Clarification is required.	
6.	3.2.S.7.3	Specifications mentioned in the stability data of the drug substance are Ph. Eur. While all the other data is as per USP. Clarification is required.	
7.	3.2.P.2.2.1	The comparison of the developed formulation and the innovator product including the results of all the quality tests shall be submitted and discussed.	
8.	3.2.P.5	• Specification of the finished product are not mentioned whether USP specifications or in-house specifications. • If in-house specifications are applied then justification shall be submitted that why in-house specifications are applied while the official monograph is available in USP. • If USP specifications are applied then justification shall be submitted regarding Chromatographic conditions in the assay test of the finished product as conditions are completely different from USP monograph.	
9.	3.2.P.8	Accelerated stability study data of the finished product as per zone IV-a, shall be submitted.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

462.	Name, address of Applicant / Importer	M/s Servier Research & Pharmaceutical Pakistan (Pvt.) Ltd, 9-KM, Lahore – Sheikhupura Road Near Dosaco Chowk Kot Abdul Malik Tehsil Ferozwala District Sheikhupura.
	Details of Drug Sale License of importer	License No: 05-354-0078-033161D. Address: 9-KM, Lahore – Sheikhupura Road Near Dosaco Chowk Kot Abdul Malik Tehsil Ferozwala District Sheikhupura. Address of Godown: Same. Validity: 28-06-2022. Status: License to sell drugs as distributor.
	Name and address of marketing authorization holder (abroad)	Les Laboratories Servier, 50, rue Carnot, 92284 Suresnes Cedex, France.

	Name, address of manufacturer(s)	• Ispen Biosciences Inc., 1 Kendall Square Suite B7401 Cambridge, Massachusetts 02139-1670 USA, (Also responsible for quality control) and • Ajinomoto Althea Inc., 11040 Roselle Street, San Diego, California 92121-1205, USA, (Also responsible for quality control and primary packaging) • Les Laboratories Servier Industrie, 905, Route de Saran, 45520 Gidy, France (responsible for Batch release in EU).
	Name of exporting country	France.
	Detail of certificates attached (CoPP, Freesale certificate, GMP certificate)	**CoPP:** Firm has submitted original legalized CoPP No. 04/19/140340 dated 28-11-2019 issued by European Medicine Agency Domenico Scarlattilaan 6, 1083 HS Amsterdam, the Netherlands for Onivyde Pegylated Liposomal concentrate for solution for infusion (Irinotecan anhydrous free base 4.3mg/ml 10ml vial). The CoPP confirms that the product is actually on the market in the exporting region. It also confirms that the facility and operation conform to GMP as recommended by WHO. The name of importing country on CoPP is mentioned as Pakistan. Status of the community marketing authorization holder is **"C"** which means that community marketing authorization is neither manufacturer nor packages and /or labels a pharmaceutical product form manufactured by an independent company.
	Details as per CoPP.	• Ipsen Biosciences Inc., 1 Kendall Square Suite B7401 Cambridge, Massachusetts 02139-1670 USA, (Also responsible for quality control) and • Ajinomoto Althea Inc., 11040 Roselle Street, San Diego, California 92121-1205, USA, (Also responsible for quality control and primary packaging) **Site responsible for Batch release in EU;** • Les Laboratories Servier Industrie, 905, Route de Saran, 45520 Gidy, France. **Site responsible for quality control;** • Quality Chemical Laboratories, 3400 Enterprise Drive, Wilmington, North Carolina 28405, USA • Avista Pharma Solutions, 104 Gold Street, Agawam, Massachusetts 01001, USA • Associates of Cape Cod, 124 Bernard E. Saint Jean Drive, East Falmouth, Massachusetts 02536, USA. • SGS Institute Fresenius Berlin GmbH and Co. KG, Tegeler Weg 33, Berlin D-10589 Germany • SGS Institute Fresenius GmbH, Im Maisel 14, Taunusstein D-65232, Germany. **Site responsible for secondary packaging;**

		• Baxter Oncology GmbH, Kantstrasse 2, 33790 Halle/Westfalen, Germany.
	GMP status;	**Ajinomoto Althea Inc., USA.** Firm has submitted copy of Eudra GMP certificate No. 17482 issued on the basis of inspection conducted on 22-09-2017 issued by the HPRA in the name of Ajinomoto Althea Inc., 11040 Roselle Street, San Diego, California 92121-1205, USA. Validity is for three years. **Baxter Oncology GmbH;** Firm has submitted copy of Eudra GMP certificate No. DE-NW-02-GMP-2018-0022 issued on the basis of inspection conducted on 18-01-2017 in the name of Baxter Oncology GmbH, Kantstrasse 2, Halle/Westfalen, Germany valid for three years. **Les Laboratories Servier, France.** Firm has submitted copy of Eudra GMP certificate No. 2018/HPF/FR/235 issued on the basis of inspection conducted on 27-11-2015 in the name of Les Laboratories Servier Industrie, 905, Route de Saran, 45520 Gidy, France valid for three years. **SGS Institute Fresenius GmbH, Germany;** Firm has submitted copy of Eudra GMP certificate No. DE-HE-01-GMP-2017-1082 issued on the basis of inspection conducted on 04-12-2017 in the name of SGS Institute Fresenius GmbH, Im Maisel 14, Taunusstein D-65232, Germany valid for three years.
	Details of letter of authorization / sole agency agreement	**Letter of Authorization:** Firm has submitted letter of Authorization from M/s Les Laboratories Servier, France for Onivyde Pegylated Liposomal 4.3mg/ml concentrate for solution for infusion (Irinotecan anhydrous free base). The letter authorizes/confirms exclusively M/s Servier Research and Pharmaceuticals Pakistan (Pvt) Ltd., 65 main Boulevard Gulberg Lahore to act in their name and on their behalf for the registration of the above said product.
	Status of the applicant	☐ Manufacturer ☒ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☒ New Drug Product (NDP) ☐ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	For imported products, specify one the these	☒ Finished Pharmaceutical product import ☐ Buk import and local repackaging ☐ Buk import and local repackaging for export purpose only

	Dy. No. and date of submission	Dy. No. 31738: 28-01-2020.
	Details of fee submitted	PKR 50,000/- vide slip No. 0776629 dated 31-12-2019: & 25,000/- vide slip No. 1333549855 dated 21-07-2021.
	The proposed proprietary name / brand name	Onivyde Pegylated Liposomal 4.3mg/ml concentrate for solution for infusion.
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 10ml vial contains; Irinotecan anhydrous free base as Irinotecan sucrosofate in PEGylated liposomes …. 43mg
	Pharmaceutical form of applied drug	Powder for solution for injection/ infusion.
	Pharmacotherapeutic Group of (API)	Antineoplastic and Immunomodulating Agents.
	Reference to Finished product specifications	Innovator's specifications.
	Proposed Pack size	Not provided.
	Proposed unit price	As per DPC.
	The status in reference regulatory authorities	ONIVYDE (Each 10 mL single-dose vial contains 43 mg irinotecan free base at a concentration of 4.3 mg/mL), IPSEN INC, USFDA Approved.
	For generic drugs (me-too status)	N/A.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Name, address of drug substance manufacturer	ScinoPharm Taiwan, Ltd., No. 1, Nan-Ke 8th Road Shan-Hua, Tainan 74144 Taiwan.
	Module-III Drug Substance:	Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of API at accelerated for 06 months as well as real time conditions for 24 months. The real time stability data is conducted at 5 ^{o}C ± 3^{o}C, and accelerated stability data is conducted at 25^{o}C ± 2^{o}C, RH 60% ± 5%. (Batch No. 70495AA284, 70495AA285, 70495AA286)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process

		and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence and Comparative Dissolution Profile	Onivyde Pegylated Liposomal 4.3mg/ml concentrate for solution for infusion is an Innovator product.
	Analytical method validation/verification of product	Firm has submitted analytical method validation studies for the applied product.
	Container closure system of the drug product	Type I glass vial with rubber stopper and a flip off seal.
	Stability study data of drug product, shelf life and storage conditions	Firm has submitted stability study data of 3 batches. The accelerated stability study data is conducted at 25°C / 60% RH for 6 months (Batch No. 3-FIN-1780, 3-FIN-1781 & 3-FIN-1782). The real time stability study data is conducted at 05°C ±3°C for 36 months (Batch No. 3-FIN-1780, 3-FIN-1781 & 3-FIN-1782).

Evaluation by PEC:

Letter was issued to the firm dated 19-07-2022 with following observations and no reply received till date.

Sr. No.	Section	Observation	Response by the firm.
1.		Legalized copy of the agreement shall be submitted.	
2.		Valid, notarized and legalized copies of GMP certificates of all the manufacturer shall be submitted.	
3.		In submitted CoPP, different manufacturers are mentioned. Please specify the facility which will manufacture the finished product.	
4.	1.3.4	Valid copy of DSL of the applicant shall be submitted.	
5.	1.5.4	Details of proposed pack size shall be submitted.	
6.	1.5.10	Justify the applied dosage form i.e. powder for solution for injection/infusion since the standard manufacturing procedure of the drug product shows concentrate for of drug substance equivalent to 5mg/ml expressed as irinotecan as HCl.	
7.	3.2.S.4.3	• Drug substance method verification report is for Merrimack pharmaceutical. Clarification is required.	

		• Also, the method verification report is against USP monograph while the specifications of the drug substance are Eu. Phr. Clarification is required.	
8.	3.2.S.4.4	Batch analysis of the drug substance by the finished product manufacturer shall be submitted.	
9.	3.2.P.5.4	The copies of complete analysis (COA's) of at least two batches of the finished product by the finished product manufacturer shall be submitted.	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

c. Registration Application of Imported Human Drugs on Form 5A.

463.	Name and address of Applicant	Pharmatec Pakistan (Pvt.) Ltd., D-86/A, Manghopir Road, S.I.T.E., Karachi.
	Detail of Drug Sale License	Name: M/s Pharmatec Pakistan (Pvt.) Limited. Address: D-86/A Site Manghopir Road Karachi. Address of Godown: Plot No. D-81 Site Manghopir Road Karachi. Validity: 22-02-2023. Status: License to sell drugs by way of whole sale (Form No.7).
	Name and address of manufacturer	PHARMIDEA SIA 4 Rupnicu Street, Olaine, Olaine district, LV-2114 Latvia.
	Name and address of marketing authorization holder	STRAGEN FRANCE, 52 RUE DE LA REPUBLIQUE 69002 LYON.
	Name of exporting country	France.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No 11395 dated 05-03-2019.
	Fee including differential fee	Rs50,000/- dated 01-03-2019.
	Brand Name +Dosage Form + Strength	Atosiban Stragen 6.75mg/0.9ml concentration for solution for infusion.
	Composition	Each 0.9ml vial Contains: Atosiban as acetate ……6.75mg
	Finished Product Specification	Manufacturer's Specifications.
	Pharmacological Group	Other Gynaecological (G02CX). Atosiban is indicated to delay imminent pre-term birth in pregnant adult women with: - • Regular uterine contractions of at least 30 seconds duration at a rate of ≥ 4 per 30 minutes. • a cervical dilation of 1 to 3 cm (0-3 for nulliparas) and effacement of ≥ 50%. • a gestational age from 24 until 33 completed weeks - a normal foetal heart rate.
	Shelf life	30 months

	Demanded Price	Rs. 13,000/0.9ml x 1's vial.
	Pack size	1's x 0.9ml. (2ml colorless glass vial (Type I) sealed with grey Bromo butyl rubber stoppers with fluoropolymer coating and aluminum flip-off seal with plastic button.)
	International availability	Atosiban 6.75 mg/0.9 ml solution for injection, MHRA approved.
	Me-too status	Could not be confirmed.
	Stability studies	Firm has provided real time stability study data sheets conducted at 2-8ºC of three batches for 36 months and accelerated stability data sheet conducted at 30 ± 2 ºC and 65 ± 5%RH of three batches for six months. Batch No. NP140413, NP150413, NP160513.
	Detail of certificates attached	**GMP certificate (Copy and not notarized)** Certificate No: ZVA/LV/2018/012H. Certifying Authority: State agency of Medicines of the Republic of Latvia. Date: 10/08/2018. Complies with the principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC. Validity: Valid for three years. **Certificate of Medicinal Product.** Certificate No: 023665. Certifying Authority: Chamber de commerce et d'Industrie de Region Paris Ile-de-France. Date**:** 26/11/2018. Status of the marketing authorization holder: C Free Sale Certificate Confirms the free sale of the product in exporting country. **Letter of Authorization** Name: Pharmatec Pakistan (Private) Ltd., D-86/A, S.I.T.E., Karachi. Date of Agreement: 04-07-2018. Stragen Pharma S.A Chemin du Pre-Fleuri 3, 1228 Plan-les Ouates, Switzerland.
	Remark of the Evaluator [XIII]	**Deficiency letter was issued on 15-07-2021 with following observation but no reply received till to date.** • Submit valid legalized GMP certificate of the manufacturer issued by concerned regulatory authority. • Agency agreement provided is with Stragen Pharma Switzerland while the marketing authorization holder is STRAGEN FRANCE. Submit notarized Agency agreement with the marketing authorization holder. • Storage condition of the product mentioned on SMPC is 2-8 ºC.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
464.	Name and address of Applicant	Pharmatec Pakistan (Pvt.) Ltd., D-86/A, Manghopir Road, S.I.T.E., Karachi.
	Detail of Drug Sale License	Name: M/s Pharmatec Pakistan (Pvt.) Limited. Address: D-86/A Site Manghopir Road Karachi. Address of Godown: Plot No. D-81 Site Manghopir Road Karachi.

		Validity: 22-02-2023. Status: License to sell drugs by way of whole sale (Form No.7).
	Name and address of manufacturer	PHARMIDEA SIA 4 Rupnicu Street, Olaine, Olaine district, LV-2114 Latvia.
	Name and address of marketing authorization holder	STRAGEN FRANCE, 52 RUE DE LA REPUBLIQUE 69002 LYON.
	Name of exporting country	France.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No. 11394 dated 05-03-2019.
	Fee including differential fee	Rs50,000/- dated 01-03-2019.
	Brand Name +Dosage Form + Strength	Atosiban Stragen 37.5mg/5ml concentration for solution for infusion.
	Composition	Each 5ml vial Contains: Atosiban as acetate …… 37.5mg
	Finished Product Specification	Manufacturer's Specifications.
	Pharmacological Group	Other Gynaecological (G02CX). Atosiban is indicated to delay imminent pre-term birth in pregnant adult women with: - • Regular uterine contractions of at least 30 seconds duration at a rate of ≥ 4 per 30 minutes. • a cervical dilation of 1 to 3 cm (0-3 for nulliparas) and effacement of ≥ 50%. • a gestational age from 24 until 33 completed weeks - a normal foetal heart rate.
	Shelf life	30 months.
	Demanded Price	Rs. 33,000/1 x 5ml vial.
	Pack size	1 vial. (6ml colorless glass vial (Type I) sealed with grey Bromo butyl rubber stoppers with fluoropolymer coating and aluminum flip-off seal with plastic button.)
	International availability	Atosiban EVER Pharma 37.5 mg/5 ml concentrate for solution for infusion.
	Me-too status	Could not be confirmed.
	Stability studies	Firm has provided real time stability study data sheets conducted at 2-8 ºC of three batches for 36 months and accelerated stability data sheet conducted at 30 ± 2 ºC and 65 ± 5%RH of three batches for six months. Batch No. NP140413, NP150413, NP160513.
	Detail of certificates attached	**GMP certificate (copy and not legalized)** Certificate No: ZVA/LV/2018/012H. Certifying Authority: State agency of Medicines of the Republic of Latvia. Date: 10/08/2018. Complies with the principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC. Validity: Valid for three years. **Certificate of Medicinal Product.** Certificate No: 023666.

		Certifying Authority: Chamber de commerce et d'Industrie de Region Paris Ile-de-France. Date**:** 26/11/2018. Status of the marketing authorization holder: C Free Sale Certificate Confirms the free sale of the product in exporting country. **Letter of Authorization** Name: Pharmatec Pakistan (Private) Ltd., D-86/A, S.I.T.E., Karachi. Date of Agreement: 04-07-2018. Stragen Pharma S.A Chemin du Pre-Fleuri 3, 1228 Plan-les Ouates, Switzerland.
	Remark of the Evaluator [XIII]	• Submit valid legalized GMP certificate of the manufacturer issued by concerned regulatory authority. • Agency agreement provided is with Stragen Pharma Switzerland while the marketing authorization holder is STRAGEN FRANCE. Submit notarized Agency agreement with the marketing authorization holder. • Storage condition of the product mentioned on SMPC is 2-8 ^{o}C.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
465.	Name and address of Applicant	Qasim Traders, Shop No. 7 Medicine Centre Kutchi Gali No. 1, Marriot Road, Karachi.
	Detail of Drug Sale License	Name: M/s Qasim Traders. Address: Shop No. 7 Medicine Centre Kutchi Gali No. 1, Marriot Road, Karachi. Validity: 23rd November, 2019. Status: License by the way of whole sale.
	Name and address of manufacturer	Shandong Shenglu Pharmaceutical Co., Ltd. North of Sihe Road, Sishui Country, Shandong, China.
	Name and address of marketing authorization holder	Shandong Shenglu Pharmaceutical Co., Ltd. North of Sihe Road, Sishui Country, Shandong, China.
	Name of exporting country	China.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No 11462 dated 05-03-2019.
	Fee including differential fee	Rs100,000/- dated 04-03-2019.
	Brand Name +Dosage Form + Strength	Benzyl Penicillin Injection 500,000 IU per Vial.
	Composition	Each vial Contains: Benzyl Penicillin …… 500,000 IU
	Finished Product Specification	Manufacturer's Specifications.
	Pharmacological Group	Antibiotic.
	Shelf life	03 years under routine storage conditions.
	Demanded Price	As per pricing committee.
	Pack size	Not mentioned.
	International availability	Not provided.
	Me-too status	Could not be confirmed.
	Stability studies	Firm has submitted real-time stability data sheet conducted at 30 ± 2ºC and **75%** ± 5% RH of three batches for 36 months and accelerated stability data sheet conducted at 40 ± 2 ºC and

		75 ± 5%RH of three batches for six months.
	Detail of certificates attached	**GMP certificate.** Certificate No: SD20130162. Certifying Authority: Sishui Food and Drug Administration People's Republic of China. Date: 25-08-2015. Complies with the requirements of Chinese Good Manufacturing Practice. Validity: Valid until 25-08-2020. **Certificate of Pharmaceutical Product.** Certificate No: SI-P201708002. Certifying Authority: Sishui Food and Drug Administration People's Republic of China. Date**:** Not mentioned. The certificate conforms to the format recommended by the WHO. Validity: This certificate is valid for five years from issuing date. **Free Sale Certificate:** Certificate No: 2017-10-16. Certifying Authority: Sishui Food and Drug Administration People's Republic of China. The certificate conforms that the product is freely sold on the market of China. Validity: This certificate is valid for two years. **Letter of Authorization (copy without legalization)** Name: Qasim Traders, Shop No. 7 Medicine Centre Kutchi Gali No. 1, Marriot Road, Karachi. Date of Agreement: 13-11-2018. Shandong Shenglu Pharmaceutical Co., Ltd. North of Sihe Road, Sishui Country, Shandong, China.
	Remark of the Evaluator [XIII]	Deficiency letter was issued on 16-08-2021 with following observation but no reply received till to date. • Submit applied pack size and details of packaging material. • Submit valid copy of Drug sale license. • In form 5A benzyl penicillin is mentioned while free sale certificate and CoPP both has mentioned Benzyl Penicillin sodium. Clarification is required. • Submit Original valid legalized GMP certificate of manufacturer issued by concerned regulatory Authority. • Submit Original valid legalized CoPP or free sale certificate issued by concerned regulatory Authority. • Agency agreement is neither notarized nor signed & stamped by the second party i.e. Qasim traders. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
466.	Name and address of Applicant	Qasim Traders, Shop No. 7 Medicine Centre Kutchi Gali No. 1, Marriot Road, Karachi.
	Detail of Drug Sale License	Name: M/s Qasim Traders.

		Address: Shop No. 7 Medicine Centre Kutchi Gali No. 1, Marriot Road, Karachi. Validity: 23rd November, 2019. Status: License by the way of whole sale.
	Name and address of manufacturer	Bicon Pharmaceutical Xinyi Group Holding Co., Ltd. No. 46 Anqing Road, Xinyi, Jiangsu.
	Name and address of marketing authorization holder	Bicon Pharmaceutical Xinyi Group Holding Co., Ltd. No. 46 Anqing Road, Xinyi, Jiangsu.
	Name of exporting country	China.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No 11461 dated 05-03-2019.
	Fee including differential fee	Rs100,000/- dated 04-03-2019.
	Brand Name +Dosage Form + Strength	Normal Saline (0.9% NaCl)
	Composition	Each 100ml contains: Sodium Chloride (NaCl) ……. 0.9 gm
	Finished Product Specification	BP specifications.
	Pharmacological Group	Electrolyte solution.
	Shelf life	03 years under routine storage conditions.
	Demanded Price	As per pricing committee.
	Pack size	Not mentioned.
	International availability	Not provided.
	Me-too status	Sodium Chloride Injection 0.9%, Getz Pharma, Reg. No. 067418.
	Stability studies	Firm has submitted real-time stability data sheet conducted at 30 ± 2ºC and **75%** ± 5% RH of three batches for 36 months and accelerated stability data sheet conducted at 40 ± 2 ºC and 75 ± 5%RH of three batches for six months.
	Detail of certificates attached	**GMP certificate.** Certificate No: CN20150130. Certifying Authority: China Food and Drug Administration. Date: 11-08-2015. Certificate conforms that the manufacturer complies with the requirements of Chinese Good Manufacturing Practices for pharmaceutical products. Validity: Valid until 10-08-2020. **Certificate of Pharmaceutical Product.** Certificate No: XZ2017036. Certifying Authority: Jiangsu Food and Drug Administration No. 5 Gulou Street, Nanjing City China. Date**:** 04-08-2017. The certificate conforms to the format recommended by the WHO. Validity: This certificate remains valid for two years. **Free Sale Certificate:** Certificate No: XZ2017039. Certifying Authority: Jiangsu Food and Drug Administration People's Republic of China. The certificate conforms that the product is freely sold on the market of China. Date: 31-08-2017.

		Validity: This certificate is valid for two years. **Letter of Authorization (copy without legalization)** Name: Qasim Traders, Shop No. 7 Medicine Centre Kutchi Gali No. 1, Marriot Road, Karachi. Date of Agreement: 13-11-2018. Bicon Pharmaceutical Xinyi Group Holding Co., Ltd. No. 46 Anqing Road, Xinyi, Jiangsu.
	Remark of the Evaluator [XIII]	• Submit applied pack size and details of packaging material. • Submit valid copy of Drug sale license. • Submit Original valid legalized GMP certificate of manufacturer issued by concerned regulatory Authority. • Submit Original valid legalized CoPP or free sale certificate issued by concerned regulatory Authority. • Agency agreement is neither notarized nor signed & stamped by the second party i.e. Qasim traders. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
467.	Name and address of Applicant	M/s Revive Healthcare. Office 503, 5th Floor, 6 Main Gulberg, Jail Road, Lahore, Pakistan.
	Detail of Drug Sale License	Name: M/s Revive Healthcare. Address: Office 503, 5th Floor, Eden Heights, 6 Main Gulberg, Jail Road, District Lahore. Validity: 21st May, 2020 Status: License to sell drugs as a distributor (Form No.11)
	Name and address of manufacturer	M/s Emcure Pharmaceuticals Limited, Plot No. P1 & P2 I.T.B.T Park, Phase II, M.I.D.C. Hinjawadi Pune 411057 Maharashtra State, India.
	Name and address of marketing authorization holder	M/s Emcure Pharmaceuticals Limited, Plot No. P1 & P2 I.T.B.T Park, Phase II, M.I.D.C. Hinjawadi Pune 411057 Maharashtra State, India.
	Name of exporting country	India.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No 11418-B dated 05-03-2019.
	Fee including differential fee	Rs.50,000/- dated 05-03-2019.
	Brand Name +Dosage Form + Strength	Atazor-R Tablet.
	Composition	Each Tablet Contains: Atazanavir ……300mg Ritonavir ……..…100mg
	Finished Product Specification	Manufacturer specifications.
	Pharmacological Group	Antivirals for treatment of HIV infections, combinations.
	Shelf life	24 months
	Demanded Price	As per SRO.
	Pack size	30's
	International availability	WHO pre-qualified formulation (Ref. No. NDA 205508)/ USFDA approved.
	Me-too status	Could not be confirmed.
	Stability studies	

	Detail of certificates attached	**Letter of authorization: - (Copy submitted)** M/s Revive Healthcare. Office 503, 5th Floor, Eden Heights 6 Main Gulberg, Jail Road, Lahore, Pakistan Dated: 24-08-2017. Validity: not mentioned. Letter of authorization has neither product list nor it has any sole distribution details. **Certificate of Pharmaceutical Product (Copy submitted).** Certificate No: COPP/CERT/PD/79590/2018/11/25928/134892. Certifying Authority: Food & Drug Administration, M.S. Bandra-Kurla complex, Bandra (E), Mumbai-400 051 Maharashtra, India. Date**:** 24-11-2018. The certificate conforms to the format recommended by the WHO. Validity: 02-11-2021. Certificate also confirms that this product is also actually on the market in the exporting country. **GMP certificate (Copy submitted).** Certificate No: NEW-WHO-GMP/CERT/PD/74276/2018/11/25582. Certifying Authority: Food & Drug Administration, M.S. Bandra-Kurla complex, Bandra (E), Mumbai-400051 Maharashtra, India. Date: 03-11-2018. Complies with the Good Manufacturing Practice for the dosage forms categories and activities listed in Table 1. Validity: Valid until 02-11-2021.
	Remark of the Evaluator [XIII]	**Deficiency letter was issued on 05-10-2021 with following observation but no reply received till to date.** • Form 5A has neither mentioned film coated tablets nor salt form of the active ingredients. Label claim in form 5 needs revision with submission of applicable fee. • Submit Original, valid & legalized COPP issued by concerned regulatory Authority • Submit Original, valid & legalized GMP certificate of manufacturer issued by concerned regulatory Authority • Submit Original and complete Letter of Authorization from Product License Holder • Submission of stability studies data of three batches as per zone IV-A as per Requirements of Registration Board decision of 293rd meeting.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
468.	Name and address of Applicant	M/s Revive Healthcare. Office 503, 5th Floor, 6 Main Gulberg, Jail Road, Lahore, Pakistan.
	Detail of Drug Sale License	Name: M/s Revive Healthcare. Address: Office 503, 5th Floor, Eden Heights, 6 Main Gulberg, Jail Road, District Lahore.

		Validity: 21st May, 2020 Status: License to sell drugs as a distributor (Form No.11)
	Name and address of manufacturer	M/s Emcure Pharmaceuticals Limited, Plot No. P1 & P2 I.T.B.T Park, Phase II, M.I.D.C. Hinjawadi Pune 411057 Maharashtra State, India.
	Name and address of marketing authorization holder	M/s Emcure Pharmaceuticals Limited, Plot No. P1 & P2 I.T.B.T Park, Phase II, M.I.D.C. Hinjawadi Pune 411057 Maharashtra State, India.
	Name of exporting country	India.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No 11419-B dated 05-03-2019.
	Fee including differential fee	Rs.50,000/- dated 05-03-2019.
	Brand Name +Dosage Form + Strength	Viropil tablet.
	Composition	Each Tablet Contains: Dolutegravir Sodium ……50mg Tenofovir Disoproxil ……..…300mg Lamivudine ……300mg
	Finished Product Specification	Manufacturer specifications.
	Pharmacological Group	Antivirals for treatment of HIV infections, combinations.
	Shelf life	24 months
	Demanded Price	As per SRO.
	Pack size	30's
	International availability	WHO pre-qualified formulation (Ref. No. HA722-0)/ USFDA approved.
	Me-too status	Could not be confirmed.
	Stability studies	Not provided.
	Detail of certificates attached	**Letter of authorization: - (Copy submitted)** M/s Revive Healthcare. Office 503, 5th Floor, Eden Heights 6 Main Gulberg, Jail Road, Lahore, Pakistan Dated: 24-08-2017. Validity: not mentioned. Letter of authorization has neither product list nor it has any sole distribution details. **Certificate of Pharmaceutical Product (Copy submitted).** Certificate No: COPP/CERT/PD/80502/2018/11/26370/136689. Certifying Authority: Food & Drug Administration, M.S. Bandra-Kurla complex, Bandra (E), Mumbai-400 051 Maharashtra, India. Date**:** 29-12-2018. The certificate conforms to the format recommended by the WHO. Validity: 02-11-2021. Certificate confirms that this product is also actually on the market in the exporting country. **GMP certificate (Copy submitted).** Certificate No: NEW-WHO-GMP/CERT/PD/74276/2018/11/25582.

		Certifying Authority: Food & Drug Administration, M.S. Bandra-Kurla complex, Bandra (E), Mumbai-400051 Maharashtra, India. Date: 03-11-2018. Complies with the Good Manufacturing Practice for the dosage forms categories and activities listed in Table 1. Validity: Valid until 02-11-2021.
	Remark of the Evaluator [XIII]	• Form 5A has neither mentioned film coated tablets nor salt form of the active ingredients. Label claim in form 5 needs revision with submission of applicable fee. • Submit Original, valid & legalized COPP issued by concerned regulatory Authority • Submit Original, valid & legalized GMP certificate of manufacturer issued by concerned regulatory Authority • Submit Original and complete Letter of Authorization/Agency agreement from Product License Holder. • Submission of stability studies data of three batches as per zone IV-A as per Requirements of Registration Board decision of 293rd meeting.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
469.	Name and address of Applicant	M/s Revive Healthcare. Office 503, 5th Floor, 6 Main Gulberg, Jail Road, Lahore, Pakistan.
	Detail of Drug Sale License	Name: M/s Revive Healthcare. Address: Office 503, 5th Floor, Eden Heights, 6 Main Gulberg, Jail Road, District Lahore. Validity: 21st May, 2020 Status: License to sell drugs as a distributor (Form No.11)
	Name and address of manufacturer	M/s Emcure Pharmaceuticals Limited, Plot No. P1 & P2 I.T.B.T Park, Phase II, M.I.D.C. Hinjawadi Pune 411057 Maharashtra State, India.
	Name and address of marketing authorization holder	M/s Emcure Pharmaceuticals Limited, Plot No. P1 & P2 I.T.B.T Park, Phase II, M.I.D.C. Hinjawadi Pune 411057 Maharashtra State, India.
	Name of exporting country	India.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No 11418-A dated 05-03-2019.
	Fee including differential fee	Rs.50,000/- dated 05-03-2019.
	Brand Name +Dosage Form + Strength	Tavin-Em Tablets
	Composition	Each Tablet Contains: Tenofovir Disoproxil Fumarate ……..…300mg Emtricitabine ……..…200mg
	Finished Product Specification	Manufacturer specifications.
	Pharmacological Group	Antivirals for treatment of HIV infections, combinations.
	Shelf life	24 months
	Demanded Price	As per SRO.
	Pack size	30’s.

	International availability	WHO pre-qualified formulation (Ref. No. HA726-0)/ TRUVADA® (emtricitabine and tenofovir disoproxil fumarate) USFDA approved.
	Me-too status	Could not be confirmed.
	Stability studies	Not provided.
	Detail of certificates attached	**Letter of authorization: - (Copy submitted)** M/s Revive Healthcare. Office 503, 5th Floor, Eden Heights 6 Main Gulberg, Jail Road, Lahore, Pakistan Dated: 24-08-2017. Validity: not mentioned. Letter of authorization has neither product list nor it has any sole distribution details. **Certificate of Pharmaceutical Product (Copy submitted).** Certificate No: COPP/CERT/PD/79590/2018/11/25928/134886. Certifying Authority: Food & Drug Administration, M.S. Bandra-Kurla complex, Bandra (E), Mumbai-400 051 Maharashtra, India. Date**:** 24-11-2018. The certificate conforms to the format recommended by the WHO. Validity: 02-11-2021. Certificate confirms that this product is also actually on the market in the exporting country. **GMP certificate (Copy submitted).** Certificate No: NEW-WHO-GMP/CERT/PD/74276/2018/11/25582. Certifying Authority: Food & Drug Administration, M.S. Bandra-Kurla complex, Bandra (E), Mumbai-400051 Maharashtra, India. Date: 03-11-2018. Complies with the Good Manufacturing Practice for the dosage forms categories and activities listed in Table 1. Validity: Valid until 02-11-2021.
	Remark of the Evaluator [XIII]	• Form 5A has not mentioned film coated tablets. Label claim in form 5 needs revision with submission of applicable fee. • Submit Original, Valid & legalized COPP issued by concerned regulatory Authority • Submit Original, valid & legalized GMP certificate of manufacturer issued by concerned regulatory Authority • Submit Original and complete Letter of Authorization/Agency agreement from Product License Holder. • Submission of stability studies data of three batches as per zone IV-A as per Requirements of Registration Board decision of 293rd meeting.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
470.	Name and address of Applicant	M/s Revive Healthcare. Office 503, 5th Floor, 6 Main Gulberg, Jail Road, Lahore, Pakistan.
	Detail of Drug Sale License	Name: M/s Revive Healthcare.

		Address: Office 503, 5th Floor, Eden Heights, 6 Main Gulberg, Jail Road, District Lahore. Validity: 21st May, 2020 Status: License to sell drugs as a distributor (Form No.11)
	Name and address of manufacturer	M/s Emcure Pharmaceuticals Limited, Plot No. P1 & P2 I.T.B.T Park, Phase II, M.I.D.C. Hinjawadi Pune 411057 Maharashtra State, India.
	Name and address of marketing authorization holder	M/s Emcure Pharmaceuticals Limited, Plot No. P1 & P2 I.T.B.T Park, Phase II, M.I.D.C. Hinjawadi Pune 411057 Maharashtra State, India.
	Name of exporting country	India.
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy. No 11419-A dated 05-03-2019.
	Fee including differential fee	Rs.50,000/- dated 05-03-2019.
	Brand Name +Dosage Form + Strength	Instgra 50mg Tablet.
	Composition	Each Tablet Contains: Dolutegravir …… 50mg
	Finished Product Specification	Manufacturer specifications.
	Pharmacological Group	Direct Acting Antivirals.
	Shelf life	24 months
	Demanded Price	As per SRO.
	Pack size	30's.
	International availability	WHO pre-qualified formulation (Ref. No. HA701-0)/ TIVICAY (dolutegravir) film coated tablets USFDA approved.
	Me-too status	Could not be confirmed.
	Stability studies	Not provided.
	Detail of certificates attached	**Letter of authorization: - (Copy submitted)** M/s Revive Healthcare. Office 503, 5th Floor, Eden Heights 6 Main Gulberg, Jail Road, Lahore, Pakistan Dated: 24-08-2017. Validity: not mentioned. Letter of authorization has neither product list nor it has any sole distribution details. **Certificate of Pharmaceutical Product (Copy submitted).** Certificate No: COPP/CERT/PD/79590/2018/11/25928/134887. Certifying Authority: Food & Drug Administration, M.S. Bandra-Kurla complex, Bandra (E), Mumbai-400 051 Maharashtra, India. Date**:** 24-11-2018. The certificate conforms to the format recommended by the WHO. Validity: 02-11-2021. Certificate also conforms that this product is also actually on the market in the exporting country. **GMP certificate (Copy submitted).** Certificate No: NEW-WHO-GMP/CERT/PD/74276/2018/11/25582.

		Certifying Authority: Food & Drug Administration, M.S. Bandra-Kurla complex, Bandra (E), Mumbai-400051 Maharashtra, India. Date: 03-11-2018. Complies with the Good Manufacturing Practice for the dosage forms categories and activities listed in Table 1. Validity: Valid until 02-11-2021.
	Remark of the Evaluator [XIII]	• Form 5A has neither mentioned film coated tablets nor salt form of active ingredient. Label claim in form 5 needs revision with submission of applicable fee. • Submit Original, valid & legalized COPP issued by concerned regulatory Authority • Submit Original, valid & legalized GMP certificate of manufacturer issued by concerned regulatory Authority • Submit Original and complete Letter of Authorization/Agency agreement from Product License Holder. • Submission of stability studies data of three batches as per zone IV-A as per Requirements of Registration Board decision of 293rd meeting.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	

d. Registration Application of locally manufactured Human Drugs on Form 5.

471.	Name and address of manufacturer/ Applicant	M/s Adamjee Pharmaceuticals (Pvt.) Ltd., Plot 39, Sector 15, Korangi Industrial Area, Karachi (contract giver). M/s Safe Pharmaceuticals (Pvt.) Ltd., Plot No. C.I-20, Sector 6-B, Industrial Area, North Karachi (Contract acceptor).
	Brand Name + Dosage Form + Strength	Mobidol 150mg/3ml Injection.
	Composition	Each 3ml Contains: Aceclofenac (B.P) …….. 150m
	Diary No. Date of R & I & fee	Dy. No 10703 dated 05-03-2019 Rs.50,000 dated 04-03-2019.
	Pharmacological Group	Anti-inflammatory and Antirheumatic Products, Non-Steroids.
	Type of Form.	Form-5.
	Finished product Specification.	Not provided.
	Pack size & Demanded Price	5 x 3ml ampoule & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Could not be confirmed.
	Me-too status.	Could not be confirmed.
	GMP status.	Conclusion Safe pharmaceuticals (04-03-2019): All the observations pointed out during inspection were discussed with the management of the firm and they were committed to overcome before next periodic inspection. Based on the above observations and keeping in view their attitude for better compliance, their current compliance level is rated as Good.

	Remarks of the Evaluator.	Deficiency letter was issued on 17-03-2021 but no reply received till to date. • Copy of contract agreement is missing. • Finished product specification not provided. • Manufacturing facility/section approval of contract acceptor is missing. • GMP certificate or latest inspection report of the contract giver is missing. • Number of approved sections and total number of registered products on contract manufacturing of the applicant is missing. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting. • Me too status of the product could not be confirmed.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
472.	Name and address of manufacturer/ Applicant	M/s Adamjee Pharmaceuticals (Pvt.) Ltd., Plot 39, Sector 15, Korangi Industrial Area, Karachi (contract giver). M/s Safe Pharmaceuticals (Pvt.) Ltd., Plot No. C.I-20, Sector 6-B, Industrial Area, North Karachi (Contract acceptor).
	Brand Name + Dosage Form + Strength	Clamycin 500mg / vial Injection.
	Composition	Each Vial of Dry Substance Contains: Clarithromycin …….…. 500mg
	Diary No. Date of R & I & fee	Dy. No 10704 dated 05-03-2019 Rs.50,000 dated 04-03-2019.
	Pharmacological Group	Macrolides.
	Type of Form.	Form-5.
	Finished product Specification.	Not provided.
	Pack size & Demanded Price	& as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Clarithromycin 500 mg (as clarithromycin lactobionate) Powder for concentrate for solution for infusion, MHRA approved.
	Me-too status.	Clariset 500mg Injection, Mediate Pharmaceutical, Reg. No. 061952.
	GMP status.	Conclusion Safe pharmaceuticals (04-03-2019): All the observations pointed out during inspection were discussed with the management of the firm and they were committed to overcome before next periodic inspection. Based on the above observations and keeping in view their attitude for better compliance, their current compliance level is rated as Good.
	Remarks of the Evaluator.	• Copy of contract agreement is missing. • Finished product specification not provided. • Manufacturing facility/section approval of contract acceptor is missing.

		• GMP certificate or latest inspection report of the contract giver is missing. • Number of approved sections and total number of registered products on contract manufacturing of the applicant is missing. • In RRA each vial contains clarithromycin lactobionate, corresponding to 500 mg in lyophilized form clarithromycin but the applied formulation has not mentioned its salt form.
	Decision: Registration Board decided to deferred the case for the reply of aove cited observations within six months.	
473.	Name and address of manufacturer/ Applicant	M/s Eros Pharmaceuticals (Pvt.) Ltd., 94-95/23 Korangi Industrial Area, Karachi. (Contract giver). M/s Mediate Pharmaceuticals (Pvt.) Ltd., Plot No. 150-151, Sector 24 Korangi Industrial Area, Karachi. (Contract acceptor) (Dry powder general injection).
	Brand Name + Dosage Form + Strength	Ezac 40mg injection.
	Composition	Each vial contains: Omeprazole ……..40mg.
	Diary No. Date of R & I & fee	Dy. No. 10983 dated: 05-03-2019 Rs.50,000/- Dated 04-03-2019.
	Pharmacological Group	Proton pump inhibitor.
	Type of Form.	Form 5-A
	Finished product Specification.	Not provided.
	Pack size & Demanded Price	1 x 1 & as per DRAP policy.
	Approval status of product in Reference Regulatory Authorities.	Omeprazole 40 mg Powder for Solution for Infusion, MHRA approved.
	Me-too status.	Risek 40mg Infusion, Getz Pharma, Reg. No. 024170
	GMP status.	Mediate Pharmaceuticals (Conclusion 02-04-2019): Keeping in view the areas inspected, people met, documents reviewed and the considering findings of the inspection M/s Mediate Karachi was considered to be operating at an acceptable level of good compliance with GMP guidelines.
	Remarks of the Evaluator.	• M/s Eros Pharmaceuticals has submitted that they have three products registered on contract basis. • Firm has revised their label claim as per reference product without submission of applicable fee. **Revised label claim is as under:** **Each vial contains:** **Omeprazole as sodium ……..40mg.** • Firm has submitted that their manufacturing is through dry powder vial filling. • GMP certificate / latest inspection report conducted within last three years of the contract giver is missing. • Number of approved sections and total number of registered products on contract manufacturing of the applicant is missing.

	Decision: Approved with innovator specifications and following label claim; **Revised label claim is as under:** **Each vial contains:** **Omeprazole as sodium ……..40mg.** • **Registration letter will be issued after submission of fee of Rs. 75,000/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Applicant will also submit latest copies of GMP certificate/last inspection report conducted within last three years of both the contract giver and acceptor.**	
474.	Name and address of manufacturer/ Applicant	M/s Invictus Pharmaceuticals, Plot No. 21, 26, Street No.NS-2, National Industrial Zone, Rawat, Islamabad.
	Brand Name + Dosage Form + Strength	Aclofen 100mg Tablets.
	Composition	Each Tablet Contains: Aceclofenac ……100mg
	Diary No. Date of R & I & fee	Dy. No. 10363 dated 05-03-2019; Rs.20,000/- dated 05-02-2019.
	Pharmacological Group	NSAID's.
	Type of Form.	Form-5
	Finished product Specification.	Manufacturer specifications.
	Pack size & Demanded Price	3 x 10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Aceclofenac 100 mg Film-coated Tablets, MHRA approved.
	Me-too status.	Acenac 100Mg Tablets, S.J & G. Fazul Ellahie, Reg. No. 039336.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	**Deficiency letter was issued on 16-04-2021 but no reply received till to date.** • First page of form-5 is not signed by the authorized person. Annexures of form-5 are not signed by the technical persons. • Section approval/manufacturing facility could not be confirmed. • GMP status could not be confirmed. • Reference product is film coated while the applied formulation is uncoated. Label claim needs revision in line with reference product with requisite fee.
	Decision: Approved with innovator's specifications and following label claim; **Each film coated tablet Contains:** **Aceclofenac ……100mg** • **Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.** • **Firm will also submit first page of form-5 signed by the authorized person, Latest GMP certificate/last inspection report conducted within last three years, Section approval letter and revised label claim as per reference product.**	

	Name and address of manufacturer/ Applicant	M/s Invictus Pharmaceuticals, Plot No. 21, 26, Street No.NS-2, National Industrial Zone, Rawat, Islamabad.
	Brand Name + Dosage Form + Strength	Aclofen 200mg Tablets.
	Composition	Each Tablet Contains: Aceclofenac ……200mg
	Diary No. Date of R & I & fee	Dy. No. 10364 dated 05-03-2019; Rs.20,000/- dated 05-02-2019.
	Pharmacological Group	NSAID's.
	Type of Form.	Form-5
	Finished product Specification.	Manufacturer specifications.
	Pack size & Demanded Price	3 x 10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Could not be confirmed.
	Me-too status.	Could not be confirmed.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• First page of form-5 is not signed by the authorized person. Annexures of form-5 are not signed by the technical persons. • Section approval/manufacturing facility could not be confirmed. • GMP status could not be confirmed. • Reference product is film coated while the applied formulation is uncoated. Label claim needs revision in line with reference product with requisite fee. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Decision: Registration Board decided to deferred the case for the reply of aove cited observations within six months.	
475.	Name and address of manufacturer/ Applicant	M/s ISIS Pharmaceuticals & Chemical Works, 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi.
	Brand Name + Dosage Form + Strength	Impride 1mg Tablet.
	Composition	Each Tablet Contains: Glimepride ……1mg
	Diary No. Date of R & I & fee	Dy. No. 11269 dated 05-03-2019 Rs.20,000/- dated 05-03-2019.
	Pharmacological Group	Sulfonylureas.
	Type of Form.	Form-5
	Finished product Specification.	Manufacturer's specifications.
	Pack size & Demanded Price	1 x10's, 10 x10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	AMARYL (glimepiride) 1mg tablets, USFDA approved.

	Me-too status.	Pamaryl Tab 1mg, Himont Pharmaceuticals, Reg. No. 030499.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	Deficiency letter was issued on 30-04-2021 but no reply received till to date. • First page of form-5 is not signed by the authorized person. • Manufacturing facility/section approval could not be confirmed. • GMP status of the firm could not be confirmed. • Strength of the applied formulation is not mentioned on fee slip. • Official monograph of the applied formulation is available in USP & BP.
	Decision: Approved with USP specifications. Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021. • **Firm will also submit first page of form-5 signed by the authorized person, Latest GMP certificate/last inspection report conducted within last three years, Section approval letter.**	
476.	Name and address of manufacturer/ Applicant	M/s ISIS Pharmaceuticals & Chemical Works, 25/1-3, Sector 12-C, North Karachi Industrial Area, Karachi.
	Brand Name + Dosage Form + Strength	Ismolium 10mg Tablet.
	Composition	Each Film Coated Tablet Contains: Domperidone ……..…10mg
	Diary No. Date of R & I & fee	Dy. No. 11220 dated 05-03-2019 Rs.20,000/- dated 05-03-2019.
	Pharmacological Group	Anti-emetic.
	Type of Form.	Form-5
	Finished product Specification.	BP specifications.
	Pack size & Demanded Price	1 x10's, 10 x10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Motilium 10 mg Film Coated Tablets, TGA Approved.
	Me-too status.	Medidome Tablets, Medicon Pharmaceuticals, Reg. No. 070307.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• First page of form-5 is not signed by the authorized person. • Manufacturing facility/section approval could not be confirmed. • GMP status of the firm could not be confirmed.
	Decision: Approved. Registration letter will be issued after submission of first page of form-5 signed by the authorized person along with applicable fee for revision/correction in Form 5 as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021 and latest GMP certificate/last inspection report conducted within last three years	
477.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Binafin 125mg Tablet

	Composition	Each Tablet Contains: Terbinafine As HCl ……125mg
	Diary No. Date of R & I & fee	Dy. No 12989 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Antifungal.
	Type of Form.	Form-5.
	Finished product Specification.	USP specifications.
	Pack size & Demanded Price	10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Terbinafine 125mg tablets MHRA Approved.
	Me-too status.	Lamisil 125mg Tablet, Novartis pharma, Reg. No. 013208.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed.
	Decision: Approved. Registration letter will be issued after submission of signed annexures of form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years	
478.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Binafin 250mg Tablet
	Composition	Each Tablet Contains: Terbinafine As HCl ……250mg
	Diary No. Date of R & I & fee	Dy. No 12990 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Antifungal.
	Type of Form.	Form-5.
	Finished product Specification.	USP specifications.
	Pack size & Demanded Price	10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Terbinafine 250mg tablets, MHRA Approved.
	Me-too status.	Lamisil 250mg Tablet, Sandoz, Reg. No. 013209.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed.
	Decision: Approved. Registration letter will be issued after submission of signed annexures of form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years	
479.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.

	Brand Name + Dosage Form + Strength	Lasamide 50mg Tablet.
	Composition	Each Film Coated Tablet Contains: Lacosamide ……50mg
	Diary No. Date of R & I & fee	Dy. No 12992 dated 05-03-2019 Rs.20,000/- dated 04-03-2019
	Pharmacological Group	Antiepileptic.
	Type of Form.	Form-5
	Finished product Specification.	Manufacturer specifications.
	Pack size & Demanded Price	14's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Trelema 50 mg film-coated tablets, MHRA approved.
	Me-too status.	Lalap 50mg Tablets, Genix Pharma, Reg. No. 070470.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed.
	Decision: Approved with innovator's specifications. Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021. • **Firm will also submit signed annexures of form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years.**	
480.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Lasamide 100mg Tablet.
	Composition	Each Film Coated Tablet Contains: Lacosamide ……100mg
	Diary No. Date of R & I & fee	Dy.No 12993 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Antiepileptic.
	Type of Form.	Form-5
	Finished product Specification.	Manufacturer specifications.
	Pack size & Demanded Price	14's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Trelema 100 mg film-coated tablets, MHRA approved.
	Me-too status.	Lalap 100mg Tablets, Genix Pharma, Reg. No. 070471.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed.

		• GMP status could not be confirmed.
	Decision: Approved with innovator's specifications. Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021. • **Firm will also submit signed annexures of Form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years**	
481.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Lizo 600mg Tablet.
	Composition	Each Film Coated Tablet Contains: Linezolid ……..…600mg
	Diary No. Date of R & I & fee	Dy. No 12991 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Antibacterial.
	Type of Form.	Form-5
	Finished product Specification.	USP specifications.
	Pack size & Demanded Price	12's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	ZYVOX 600 mg film-coated, USFDA approved.
	Me-too status.	Zolrest 600mg Tablets, Bosch Pharmaceuticals, Reg. No. 048509.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed. • Firm has claimed USP specifications. However, official monograph of the applied formulation is not available In USP.
	Decision: Approved with innovator's specifications. Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021. • **Firm will also submit signed annexures of form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years.**	
482.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Lezole 2.5mg Tablet.
	Composition	Each Film Coated Tablet Contains: Letrozole ……..…2.5mg
	Diary No. Date of R & I & fee	Dy. No 12988 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Aromatase inhibitor (L02BG).
	Type of Form.	Form-5
	Finished product Specification.	USP specifications.

	Pack size & Demanded Price	10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Femara 2.5mg (letrozole) film coated tablets, USFDA approved.
	Me-too status.	Letzole 2.5mg Tablet, Opal Labs, Reg. No. 075805.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed.
	Decision: Approved. Registration letter will be issued after submission of signed annexures of form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years	
483.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Febux 80mg Tablet.
	Composition	Each Film Coated Tablet Contains: Febuxostat ……..…80mg
	Diary No. Date of R & I & fee	Dy. No 12996 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Preparations inhibiting uric acid production.
	Type of Form.	Form-5
	Finished product Specification.	Manufacturer specifications.
	Pack size & Demanded Price	20's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	ULORIC 80mg (febuxostat) coated tablets, USFDA approved.
	Me-too status.	Zurig 80mg Tablet, Getz Pharma, Reg. No. 067291
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed.
	Decision: Approved with innovator's specifications. Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021. • **Firm will also submit signed annexures of form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years**	
484.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Dexipro 300mg Tablet.
	Composition	Each Film Coated Tablet Contains: Dexibuprofen ……..…300mg

	Diary No. Date of R & I & fee	Dy. No. 12987 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Anti-inflammatory and anti-rheumatic products, non-steroids.
	Type of Form.	Form-5.
	Finished product Specification.	Manufacturer specifications.
	Pack size & Demanded Price	30's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Seractil 300 mg film-coated tablets, MHRA approved.
	Me-too status.	Dofen 300mg Tablet, Maple pharma, Reg. No. 058490.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed.
	Decision: Approved with innovator's specifications. Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021. • **Firm will also submit signed annexures of form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years**	
485.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Anazole 1mg Tablet.
	Composition	Each Film Coated Tablet Contains: Anastrozole ……1mg
	Diary No. Date of R & I & fee	Dy. No. 12994 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Aromatase inhibitor (L02BG).
	Type of Form.	Form-5.
	Finished product Specification.	USP specifications.
	Pack size & Demanded Price	10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	ARIMIDEX anastrozole 1mg film coated tablets, TGA approved.
	Me-too status.	Arimisol 1mg Tablet, Swiss Pharmaceuticals, Reg. No. 091125.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed.

	Decision: Approved. Registration letter will be issued after submission of signed annexures of form-5 signed by the technical persons and latest GMP certificate/last inspection report conducted within last three years	
486.	Name and address of manufacturer/ Applicant	M/s Qintar Pharmaceuticals 14-A, P.I.S.E Lahore Road Sargodha.
	Brand Name + Dosage Form + Strength	Fovir D 300mg Tablet.
	Composition	Each Film Coated Tablet Contains: Tenofovir Disoproxil Fumarate 300mg Eq. To Tenofovir Disoproxil ……245mg
	Diary No. Date of R & I & fee	Dy. No. 12995 dated 05-03-2019; Rs.20,000/- dated 04-03-2019.
	Pharmacological Group	Direct acting antiviral.
	Type of Form.	Form-5.
	Finished product Specification.	IP specifications.
	Pack size & Demanded Price	30's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	VIREAD® (tenofovir disoproxil fumarate) film coated tablets, USFDA approved.
	Me-too status.	Tenastra 300mg Tablets, Hamaz Pharmaceuticals, Reg. No. 085023.
	GMP status.	Could not be confirmed.
	Remarks of the Evaluator.	• Annexures of form-5 are not signed by technical persons. • Brand name on fee challan and form-5 is different. • Manufacturing facility/section approval could not be confirmed. • GMP status could not be confirmed.
	Decision: Approved. Registration letter will be issued after submission of signed annexures of Form-5 signed by the technical persons, Latest GMP certificate/last inspection report conducted within last three years.	
487.	Name and address of manufacturer/ Applicant	M/s SPL Pharmaceutical, Plot No 4, Phase III, Hattar Industrial Estate, Hattar.
	Brand Name + Dosage Form + Strength	Splopram 10mg Tablet.
	Composition	Each Film Coated Tablet Contains: Escitalopram as Oxalate ……10mg
	Diary No. Date of R & I & fee	Dy. No. 8158 dated 26-02-2019; Rs. 20,000/- dated **08-07-2019.** Firm Submitted application on 25th Feb without fee. Fee was submitted on 8th of July 2019 and attached in the dossier
	Pharmacological Group	Selective serotonin reuptake inhibitors.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	Lexapro® (escitalopram) film coated tablets, USFDA approved.
	Me-too status	Param 10mg Tablets, Saydon Pharmaceuticals, Reg. No. 064052.
	GMP status	Could not be confirmed.

	Remarks of the Evaluator	Deficiency letter was issued on 24-08-2021 but no reply received till to date. • Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed.
	Decision: Registration Board deliberated that since firm has submitted fee for the applied application after the cut off date for submission of Form 5 i.e., 07-03-2019, hence Board deferred the case for submission of application on Form 5F.	
488.	Name and address of manufacturer/ Applicant	M/s SPL Pharmaceutical, Plot No 4, Phase III, Hattar Industrial Estate, Hattar.
	Brand Name + Dosage Form + Strength	Spline 50mg Tablet.
	Composition	Each Film Coated Tablet Contains: Sertraline as HCl ……..…50mg
	Diary No. Date of R & I & fee	Dy. No. 8152 dated 25-02-2019; Rs. 20,000/- dated **08-07-2019.** Firm Submitted application 0n 25th Feb without fee. Fee was submitted on 8th of July 2019 and attached in the dossier.
	Pharmacological Group	Selective serotonin reuptake inhibitors.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	14's, 20's, 30's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	ZOLOFT 50mg, 100mg (sertraline hydrochloride) film coated tablets, USFDA approved.
	Me-too status	Ertalin 50mg tablet, Genome Pharmaceuticals, Reg. No. 076844.
	GMP status	Could not be confirmed.
	Remarks of the Evaluator	• Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed.
	Decision: Registration Board deliberated that since firm has submitted fee for the applied application after the cut off date for submission of Form 5 i.e., 07-03-2019, hence Board deferred the case for submission of application on Form 5F.	
489.	Name and address of manufacturer/ Applicant	M/s SPL Pharmaceutical, Plot No 4, Phase III, Hattar Industrial Estate, Hattar.
	Brand Name + Dosage Form + Strength	Spline 100mg Tablet.
	Composition	Each Film Coated Tablet Contains: Sertraline as HCl ……..…100mg
	Diary No. Date of R & I & fee	Dy. No. 8153 dated 25-02-2019; Rs. 20,000/- dated **08-07-2019.** Firm Submitted application 0n 25th Feb without fee. Fee was submitted on 8th of July 2019 and attached in the dossier.
	Pharmacological Group	Selective serotonin reuptake inhibitors.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.

	Pack size & Demanded Price	14's, 20's, 30's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	ZOLOFT 50mg, 100mg (sertraline hydrochloride) film coated tablets, USFDA approved.
	Me-too status	Ertalin 100mg tablet, Genome Pharmaceuticals, Reg. No. 076845.
	GMP status	Could not be confirmed.
	Remarks of the Evaluator	• Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed.
	Decision: Registration Board deliberated that since firm has submitted fee for the applied application after the cut off date for submission of Form 5 i.e., 07-03-2019, hence Board deferred the case for submission of application on Form 5F.	
490.	Name and address of manufacturer/ Applicant	M/s SPL Pharmaceutical, Plot No 4, Phase III, Hattar Industrial Estate, Hattar.
	Brand Name + Dosage Form + Strength	SPLDS 50mg Delayed Release Tablet.
	Composition	Each Enteric Coated Tablet Contains: Diclofenac as Sodium ……50mg
	Diary No. Date of R & I & fee	Dy. No. 8151 dated 25-02-2019; Rs. 20,000/- dated 08-07-2019. Firm Submitted application 0n 25th Feb without fee. Fee was submitted on 8th of July 2019 and attached in the dossier.
	Pharmacological Group	Anti-inflammatory and Antirheumatic Products, Non-Steroids.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	2 x 10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	VOLTAREN 50 (diclofenac sodium) enteric coated tablets, TGA approved.
	Me-too status	Diclopal Tablet (delayed released) 50mg, Palpex Pharmaceuticals, Reg. No. 82298.
	GMP status	Could not be confirmed.
	Remarks of the Evaluator	• Label claim of reference product diclofenac sodium while the applied formulation has diclofenac as sodium. Label claim needs revision as per reference product with applicable fee. • Recommended dose is 40mg in form-5. Clarification/justification is required. • Justification of 5% overage. • Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed.
	Decision: Registration Board deliberated that since firm has submitted fee for the applied application after the cut off date for submission of Form 5 i.e., 07-03-2019, hence Board deferred the case for submission of application on Form 5F.	
491.	Name and address of manufacturer/ Applicant	M/s SPL Pharmaceutical, Plot No 4, Phase III, Hattar Industrial Estate, Hattar.

	Brand Name + Dosage Form + Strength	SPLDS 100mg Delayed Release Tablet.
	Composition	Each Enteric Coated Tablet Contains: Diclofenac as Sodium ……100mg
	Diary No. Date of R & I & fee	Dy. No. 8156 dated 25-02-2019; Rs. 20,000/- dated 08-07-2019. Firm Submitted application 0n 25th Feb without fee. Fee was submitted on 8th of July 2019 and attached in the dossier.
	Pharmacological Group	Anti-inflammatory and Antirheumatic Products, Non-Steroids.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	2 x 10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	Could not be confirmed.
	Me-too status	Could not be confirmed.
	GMP status	Could not be confirmed.
	Remarks of the Evaluator	• Recommended dose is 40mg in form-5. Clarification/justification is required. • Justification of 5% overage. • Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Decision: Registration Board deliberated that since firm has submitted fee for the applied application after the cut off date for submission of Form 5 i.e., 07-03-2019, hence Board deferred the case for submission of application on Form 5F.	
492.	Name and address of manufacturer/ Applicant	M/s SPL Pharmaceutical, Plot No 4, Phase III, Hattar Industrial Estate, Hattar.
	Brand Name + Dosage Form + Strength	Splopot 75mg Tablet.
	Composition	Each Film Coated Tablet Contains: Diclofenac Potassium ……75mg
	Diary No. Date of R & I & fee	Dy. No. 8155 dated 25-02-2019; Rs. 20,000/- dated 08-07-2019. Firm Submitted application on 25th Feb without fee. Fee was submitted on 8th of July 2019 and attached in the dossier.
	Pharmacological Group	Anti-inflammatory and Antirheumatic Products, Non-Steroids.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.

	Pack size & Demanded Price	2 x 10's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	Not provided.
	Me-too status	Maxit 75 mg Tablet, Hilton Pharma, Reg. No. 022543.
	GMP status	Could not be confirmed.
	Remarks of the Evaluator	• Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.
	Decision: Registration Board deliberated that since firm has submitted fee for the applied application after the cut off date for submission of Form 5 i.e., 07-03-2019, hence Board deferred the case for submission of application on Form 5F.	
493.	Name and address of manufacturer/ Applicant	M/s SPL Pharmaceutical, Plot No 4, Phase III, Hattar Industrial Estate, Hattar.
	Brand Name + Dosage Form + Strength	Splozole 40mg Delayed Release Tablet.
	Composition	Each Enteric Coated Tablet Contains: Pantoprazole as Sodium Sesquihydrate …….40mg
	Diary No. Date of R & I & fee	Dy. No. 8157 dated 25-02-2019; Rs. 20,000/- dated 08-07-2019. Firm Submitted application on 25th Feb without fee. Fee was submitted on 8th of July 2019 and attached in the dossier.
	Pharmacological Group	Proton pump inhibitor.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	14's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	PROTONIX (pantoprazole sodium) delayed-release tablets, USFDA approved.
	Me-too status	Protonix tablet 40mg, Wilshire Laboratories, Reg. No. 030041.
	GMP status	Could not be confirmed.
	Remarks of the Evaluator	• Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed.
	Decision: Registration Board deliberated that since firm has submitted fee for the applied application after the cut off date for submission of Form 5 i.e., 07-03-2019, hence Board deferred the case for submission of application on Form 5F.	
494.	Name and address of manufacturer/ Applicant	M/s SPL Pharmaceutical, Plot No 4, Phase III, Hattar Industrial Estate, Hattar.
	Brand Name + Dosage Form + Strength	Splecoxib 200mg Capsule.
	Composition	Each Hard Gelatin Capsule Contains: Celecoxib ……200mg

	Diary No. Date of R & I & fee	Dy. No. 8154 dated 25-02-2019; Rs. 20,000/- dated 08-07-2019. Firm Submitted application on 25th Feb without fee. Fee was submitted on 8th of July 2019 and attached in the dossier.
	Pharmacological Group	Anti-inflammatory and antirheumatic products, non-steroids
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	As per SRO.
	Approval status of product in Reference Regulatory Authorities	CELEBREX ® (celecoxib) capsules, USFDA approved.
	Me-too status	Bexicox 200 Capsule, Medipak Pharma, Reg. No. 23947
	GMP status	Could not be confirmed.
	Remarks of the Evaluator	• Fee for tablet formulation. Clarification/justification is required. • Geneome specification are mentioned in finished product specifications. Clarification is required. Needs revision with applicable fee. • Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed.
	Decision: Registration Board deliberated that since firm has submitted fee for the applied application after the cut off date for submission of Form 5 i.e., 07-03-2019, hence Board deferred the case for submission of application on Form 5F.	
495.	Name and address of manufacturer/ Applicant	M/s Rogen Pharmaceuticals Plot No.30, S-4, National Industrial Zone Rawat, Islamabad.
	Brand Name + Dosage Form + Strength	Monosen Lotion
	Composition	Each ml Contains: Minoxidil ……..…500mg
	Diary No. Date of R & I & fee	Dy. No. 20885 dated 11-06-2018; Rs. 20,000/- dated 11-06-2018. Duplicate File Bearing Dy. No. 7998 Dated 11-03-2021.
	Pharmacological Group	Potassium channel opener/Other Dermatological Preparations.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	25ml, 60ml & As per SRO.
	Approval status of product in Reference Regulatory Authorities	Could not be confirmed.
	Me-too status	Minoxin Plus Solution, Brookes Pharmaceuticals, Reg. No. 034492.
	GMP status	11-11-2019 Show Cause Notice / Suspension of production in All sections.
	Remarks of the Evaluator	• Wrong Pharmacological group is mentioned.

		• Latest GMP certificate/Inspection report conducted within last three years could not be confirmed. • Section approval/manufacturing facility could not be confirmed. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.
	Decision: Deferred for submission of reply of above cited obsevations within six months	
496.	Name and address of manufacturer/ Applicant	M/s Horizon Healthcare (Pvt.) Ltd., Plot No. 33, Sundar Industrial Estate, Lahore (Tablet general).
	Brand Name + Dosage Form + Strength	Ermect 3mg Tablet.
	Composition	Each Tablet Contains: Ivermectin ……3mg
	Diary No. Date of R & I & fee	Dy. No. 3221 dated 19-02-2018; Rs. 20,000/- dated 19-02-2018. Duplicate File Bearing Dy. No 6447 Dated 26th Feb, 2021 Verification from R & I section on the file. change Of Company Name.
	Pharmacological Group	Anthelmintic.
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications.
	Pack size & Demanded Price	10's, 30's & as per SRO.
	Approval status of product in Reference Regulatory Authorities	STROMECTOL® 3mg Uncoated tablets, TGA approved.
	Me-too status	Mectimite 3mg tablets, Mass pharma, Reg. No. 057558
	GMP status	GMP certificate issued on 06-07-2020 on the basis of inspection conducted on 18-06-2020.
	Remarks of the Evaluator	• First page of form 5 is not signed by authorized person. • Firm has claimed innovator's specification. However, the official monograph of the applied formulation is available in USP. Finished product specifications needs revision with applicable fee. • Both uncoated and film coated tablets are mentioned in different parts of the dossier. Clarification is required.
	Decision: Approved with USP specifications. Registration letter will be issued after submission of fee of Rs. 7,500/- for correction/pre-approval change in the method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with first page of form 5 signed by authorized person.	
497.	Name and address of manufacturer/ Applicant	M/s Horizon Healthcare (Pvt.) Ltd., Plot No. 33, Sundar Industrial Estate, Lahore (Oral liquid).

	Brand Name + Dosage Form + Strength	Sevosetron 250ml Solution (External liquid).
	Composition	Each 250ml Contains: Sevoflurane ……..…99.9%
	Diary No. Date of R & I & fee	Dy. No. 6126 dated 19-02-2018; Rs. 20,000/- dated 19-02-2018 Duplicate File Bearing Dy. No 6448 Dated 26th Feb, 2021 Verification from R & I section on the file.
	Pharmacological Group	Anesthetics, General.
	Type of Form	Form-5
	Finished product Specification	Innovator's specifications.
	Pack size & Demanded Price	250ml & as per SRO.
	Approval status of product in Reference Regulatory Authorities	ULTANE® (sevoflurane) volatile liquid for inhalation, USFDA approved.
	Me-too status	Sojourn Inhalational Liquid, imported by Allied Distributors, Reg. No. 088891. Sevorance Volatile Liquid For Inhalation, Imported by Getz pharma, Reg. No. 027374.
	GMP status	GMP certificate issued on 06-07-2020 on the basis of inspection conducted on 18-06-2020.
	Remarks of the Evaluator	• Reference product contains 100% Sevoflurane while the applied formulation has 99.9%. Clarification is required. • Master formula is having 150mg/250ml sevoflurane. Clarification is required. Master formula has also mentioned tablet formulation. • Reference product is volatile liquid for inhalation, while the applied formulation by the firm is Liquid/external liquid. • Section approval/manufacturing facility could not be confirmed.
	Decision: Registration Board decided to reject the application since firm does not have approval of required manufacturing facility for the applied fromulation.	
498.	Name and address of manufacturer/ Applicant	M/s Care Pharmaceuticals, 8-Km, Thokar Raiwind Road, Lahore (Oral liquid).
	Brand Name + Dosage Form + Strength	Simithon suspension.
	Composition	Each 5ml contains: Aluminium hydroxide ……200mg Magnesium hydroxide ……200mg Simethicon ……..20mg
	Diary No. Date of R & I & fee	Dy. No. 633 dated 07-04-2014; Rs. 20,000/- dated 04-04-2014. Duplicate File Bearing Dy. No. 30475 dated 16-11-2020.
	Pharmacological Group	Antacid/Anti flatulent.
	Type of Form	Form-5.
	Finished product Specification	Manufacturer specifications.
	Pack size & Demanded Price	As per SRO.
	Approval status of product in Reference Regulatory Authorities	Could not be confirmed.
	Me-too status	Could not be confirmed.

	GMP status	GMP certificate issued on 12-06-2019 on the basis of inspection conducted on 13-03-2019.
	Remarks of the Evaluator	Deficiency letter was issued on 03-09-2021 but no reply received till to date. • Composition mentioned in form 5 is completely different from master formulation. Clarification is required. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting. Provided evidence is discontinued.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
499.	Name and address of manufacturer/ Applicant	M/s Care Pharmaceuticals, 8-Km, Thokar Raiwind Road, Lahore (Oral liquid).
	Brand Name + Dosage Form + Strength	Furol suspension.
	Composition	Each 15ml contains: Furazolidone ……. 50mg
	Diary No. Date of R & I & fee	Dy. No. 631 dated 07-04-2014; Rs. 20,000/- dated 04-04-2014. Duplicate File Bearing Dy. No. 30475 dated 16-11-2020.
	Pharmacological Group	Other anti-infective and antiseptics.
	Type of Form	Form-5.
	Finished product Specification	Manufacturer specifications.
	Pack size & Demanded Price	As per SRO.
	Approval status of product in Reference Regulatory Authorities	Furoxone suspension 50mg/15ml, USFDA Current status is discontinued.
	Me-too status	Colud not be confirmed.
	GMP status	GMP certificate issued on 12-06-2019 on the basis of inspection conducted on 13-03-2019.
	Remarks of the Evaluator	• Composition mentioned in form 5 is completely different from master formulation. Clarification is required. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting. Provided evidence is discontinued.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	

500.	Name and address of manufacturer/ Applicant	Vega pharmaceuticals (Pvt.) Ltd., Plot. No. 4 pharma city, 30 KM, Multan Road, Lahore (Dry powder for injectable cephalosporin).
	Brand Name + Dosage Form + Strength	Cefopraz 250mg Dry injection IM/IV.
	Composition	Each vial contains: Cefoperazone as sodium …….. 250mg
	Diary No. Date of R & I & fee	Dy. No 128 dated 09-09-2013; Rs. 20,000/- dated 09-09-2013. Duplicate File Bearing Dy No. 15176 dated 01-06-2021.
	Pharmacological Group	Third-generation cephalosporins.
	Type of Form	Form-5.
	Finished product Specification	USP specifications.
	Pack size & Demanded Price	100 per vial.
	Approval status of product in Reference Regulatory Authorities	Could not be confirmed.
	Me-too status	Hicoject 250mg Injection, Himont Pharmaceuticals, Reg. No. 031026
	GMP status	21-03-2019. Panel concluded that M/s Vega pharmaceuticals (Pvt.) Ltd., Plot. No. 4 pharma city, 30 KM, Multan Road, Lahore was considered to be operating at a fair level of cGMP compliance at time of inspection.
	Remarks of the Evaluator	**Deficiency letter was issued on 03-09-2021 but no reply received till to date.** • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting.
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
501.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	Semet Tablet 50/1000mg
	Composition	Each Tablet Contains: Sitagliptin……...50mg Metformin HCL……..…1000mg
	Diary No. Date of R & I & fee	Dy. No 10024 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Antidiabetic.
	Type of Form.	Form-5.
	Finished product Specification.	Innovator's Specifications.
	Pack size & Demanded Price	10's, 14's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Janumet 50/1000mg film coated tablets (USFDA approved)
	Me-too status.	Duvel plus 50/1000mg tablets, Martin Dow, reg. no. 075895.
	GMP status.	The firm was inspected by the panel on 17-01-2019 and the panel concluded that during review of

		approval of above-mentioned sections/manufacturing facilities, it was assessed that following two sections needs regularization from Licensing Division: 1- Cream/Ointment 2- Tablet (General) The firm has applied for the regularization of same in Licensing Division. Keeping in view the observations noticed during inspection as narrated above, the panel is of the opinion that the firm may be allowed to start manufacturing in the light of GMP guidelines. The panel further recommended granting the GMP certificate for export purpose**.**
	Remarks of the Evaluator.	**Deficiency letter was issued on 07-01-2021 but no reply received till to date.** • Reference product is film coated tablet and contain Sitagliptin as phosphate monohydrate while the firm has applied for plain tablet in enclosures of Form-5 without sitagliptin as phosphate monohydrate. However, in master formulation they have showed sitagliptin as phosphate monohydrate and in manufacturing process they have showed coating of tablets. • The firm has provided Setal tablet & Lowsemet tablets as proposed brand names also. • Official monograph of applied formulation is not available in available pharmacopoeias (USP, BP, IP, JP)
	Decision: Approved with following label claim; **Each film coated tablet Contains:** **Sitagliptin as phosphate monohydrate…...50mg** **Metformin HCL……1000mg** • **Registration letter will be issued after submission of fee of Rs. 30,000/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with current GMP certificate/last inspection report conducted within last three years.**	
502.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	Semet Tablet 50/500mg
	Composition	Each Tablet Contains: Sitagliptin……...50mg Metformin HCL……500mg
	Diary No. Date of R & I & fee	Dy. No 10025 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Antidiabetic.
	Type of Form.	Form-5.
	Finished product Specification.	Innovator's Specifications.
	Pack size & Demanded Price	10's, 14's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Janumet 50/500mg film coated tablets (USFDA approved)

	Me-too status.	Neoglip 50/500mg Tablets, Atco Laboratories, Reg. No. 053099
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Reference product is film coated tablet and contain Sitagliptin as phosphate monohydrate while the firm has applied for plain tablet in enclosures of Form-5 without sitagliptin as phosphate monohydrate. However, in master formulation they have showed sitagliptin as phosphate monohydrate and in manufacturing process they have showed coating of tablets. • The firm has provided Setal tablet & Lowsemet tablets as proposed brand names also. • Official monograph of applied formulation is not available in available pharmacopoeias (USP, BP, IP, JP)
	Decision: Approved with following label claim; **Each film coated tablet Contains:** **Sitagliptin as phosphate monohydrate…...50mg** **Metformin HCL……..…500mg** • **Registration letter will be issued after submission of fee of Rs. 30,000/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with current GMP certificate/last inspection report conducted within last three years.**	
503.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	Vilmat Tablet 50mg/1000mg.
	Composition	Each Tablet Contains: Vildagliptin…….50mg Metformin HCl…….1000mg
	Diary No. Date of R & I & fee	Dy. No 10028 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Antidiabetic.
	Type of Form.	Form-5.
	Finished product Specification.	Innovator's Specifications.
	Pack size & Demanded Price	14's, 30's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Each film-coated tablet contains 50 mg of vildagliptin and 1000 mg of metformin HCl MHRA approved.
	Me-too status.	GALVUS MET 50mg/1000mg, Novartis pharma, Reg. No. 066107
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Reference product is film coated tablet while the firm has applied for plain tablet in enclosures of Form-5. However, in manufacturing process they have showed coating of tablets. • The firm has provided Vilmet, Fortin and Vildor tablets as proposed brand names also.

		• Official monograph of applied formulation is not available in available pharmacopoeias (USP, BP, IP, JP)
	Decision: Approved with following label claim; **Each film coated tablet Contains:** **Vildagliptin…….50mg** **Metformin HCl…….1000mg** • **Registration letter will be issued after submission of fee of Rs. 7500/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with current GMP certificate/last inspection report conducted within last three years.**	
504.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	Bisolol 2.5mg Tablet.
	Composition	Each Tablet Contains: Bisoprolol fumarate……2.5mg
	Diary No. Date of R & I & fee	Dy. No 10029 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Beta blocking agents, selective (C07AB)
	Type of Form.	Form-5.
	Finished product Specification.	USP specifications.
	Pack size & Demanded Price	14's, 20's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Each tablet contains 2.5 mg of bisoprolol fumarate, MHRA approved.
	Me-too status.	Barilol 2.5mg Tablet, Barrett Hodgson Pakistan, Reg. No. 075860
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Firm has applied for plain tablet on form-5 while in manufacturing process and master formulation, they have showed coating of the tablets. Clarification is required.
	Decision: Approved. Registration letter will be issued after submission of fee of Rs. 7500/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with current GMP certificate/last inspection report conducted within last three years and revised master formulation and manufacturing method.	
505.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	De Flozin 5mg Tablets.
	Composition	Each Tablet Contains: Dapagliflozin propanediol monohydrate eq to Dapagliflozin…….5mg
	Diary No. Date of R & I & fee	Dy. No 10022 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Drugs Used in Diabetes
	Type of Form.	Form-5.
	Finished product Specification.	Innovator's Specification.

	Pack size & Demanded Price	14's, 28's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	FARXIGA (dapagliflozin) film coated tablets, USFDA approved.
	Me-too status.	Xiga Tablets, CCL Pharmaceuticals, Reg. No. 090504
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Reference product is film coated tablet while the firm has applied for plain tablet in enclosures of Form-5. However, in manufacturing process they have showed coating of tablets. • Form-5 needs to be resubmitted with applicable fee. • The firm has provided Dapalow and Lowset Tablets as proposed brand names also.
	Decision: Decision: Registration Board deferred the case for submission o stability studies data as per checklist of 293rd meeting of DRB, in light of the Notifdication No. 320-DRB/ 2022(PE&R) dated 17th October 2022.	
506.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	Quetil 100mg Tablet.
	Composition	Each Tablet Contains: Quetiapine fumarate…….100mg
	Diary No. Date of R & I & fee	Dy. No 10023 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Antipsychotics.
	Type of Form.	Form-5.
	Finished product Specification.	USP Specifications.
	Pack size & Demanded Price	10's, 20's, 30's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	SEROQUEL® (quetiapine) film coated tablets, USFDA approved.
	Me-too status.	Evokalm 100mg Tablet, Pharm-Evo, Karachi, Reg. No. 042222
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Reference product is film coated tablet while the firm has applied for plain tablet in enclosures of Form-5. However, in manufacturing process they have showed coating of tablets. • Reference product has label claim of Each 100 mg tablet contains 115.13 mg of quetiapine fumarate equivalent to 100 mg quetiapine while the applied formulation has label claim of Each Tablet Contains Quetiapine fumarate 100mg. • Enclosure of Form-5 are not signed by the technical persons. • The firm has provided Paraquit, Shiizpine, Mount-Pine and Q-pine Tablets as proposed brand names also.
	Decision: Approved with following label claim; **Each film coated tablet Contains:** **Quetiapine as fumarate…….100mg**	

	• **Registration letter will be issued after submission of fee of Rs. 30,000/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with revised label claim and current GMP certificate/last inspection report conducted within last three years.**	
507.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	Quetil 200mg Tablet.
	Composition	Each Tablet Contains: Quetiapine fumarate…….200mg
	Diary No. Date of R & I & fee	Dy. No 10037 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Antipsychotics.
	Type of Form.	Form-5.
	Finished product Specification.	USP Specifications.
	Pack size & Demanded Price	10's, 20's, 30's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	SEROQUEL® (quetiapine) film coated tablets, USFDA approved.
	Me-too status.	Quziq 200mg Tablet, Wilshire Laboratories, Reg. No. 062824
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Reference product is film coated tablet while the firm has applied for plain tablet in enclosures of Form-5. However, in manufacturing process they have showed coating of tablets. • Reference product has label claim of Each 200 mg tablet contains 230.26 mg of quetiapine fumarate equivalent to 200 mg quetiapine while the applied formulation has label claim of Each Tablet Contains Quetiapine fumarate 200mg. • Enclosure of Form-5 are not signed by the technical persons. • The firm has provided Paraquit, Shiizpine, Mount-Pine and Q-pine Tablets as proposed brand names also.
	Decision: Approved with following label claim; **Each film coated tablet Contains:** **Quetiapine as fumarate…….200mg** **Registration letter will be issued after submission of fee of Rs. 30,000/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with revised label claim and current GMP certificate/last inspection report conducted within last three years.**	
508.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	Ropin 1mg Tablet.
	Composition	Each Tablet Contains: Ropinirole HCl…….1mg

	Diary No. Date of R & I & fee	Dy. No 10030 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Anti-Parkinson Drugs.
	Type of Form.	Form-5.
	Finished product Specification.	USP Specifications.
	Pack size & Demanded Price	10's, 21's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	REQUIP (ropinirole) film coated tablets, USFDA approved.
	Me-too status.	Reol Tablet 1mg, Genome Pharmaceuticals, Reg No. 063098
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Reference product is film coated tablet while the firm has applied for plain tablet in enclosures of Form-5. However, in manufacturing process they have showed coating of tablets. • Reference product has label claim of Each 1 mg film-coated tablet contains 1.14mg of ropinirole hydrochloride equivalent to ropinirole 1mg while the applied formulation has label claim of Each Tablet Contains Ropinirole HCl 1mg. • The firm has provided Inrol, Ropsin and Parol Tablets as proposed brand names also.
	Decision: Approved with following label claim; **Each film coated tablet Contains:** **Ropinirole HCl…….1mg** • **Registration letter will be issued after submission of fee of Rs. 30,000/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with revised label claim and current GMP certificate/last inspection report conducted within last three years.**	
509.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Tablet General**).
	Brand Name + Dosage Form + Strength	Leptic 500mg Tablet.
	Composition	Each Tablet Contains: Sodium valproate ……500mg
	Diary No. Date of R & I & fee	Dy. No 10036 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Antiepileptic.
	Type of Form.	Form-5.
	Finished product Specification.	BP Specifications.
	Pack size & Demanded Price	20's, 30's, 100's & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Orlept 500mg Gastro-Resistant Tablets, MHRA approved
	Me-too status.	Valep Tablet, Geofman Pharmaceuticals, Reg. No. 024793
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Reference product is enteric coated (Gastro resistant) tablet while the firm has applied for plain tablet in enclosures of Form-5. In master formulation the firm has shown enteric coated

		granules of sodium valproate and in manufacturing process they have showed film coating of tablets. • Enclosures of Form-5 are not signed by the technical persons. • The firm has provided Naval, Valpro Tablets as proposed brand names also.
	Decision: Approved with following label claim; **Each enteric coated tablet Contains:** **Sodium valproate ……500mg** **Registration letter will be issued after submission of fee of Rs. 30,000/- for correction/pre-approval change in the label claim, method of manufacture/specifications, as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021 along with revised label claim and current GMP certificate/last inspection report conducted within last three years.**	
510.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Cream/Ointment**).
	Brand Name + Dosage Form + Strength	Clindox 40mg Cream.
	Composition	Each cream contains: Clindamycin phosphate 2%.....40g
	Diary No. Date of R & I & fee	Dy. No 10035 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Anti-infectives for treatment of acne.
	Type of Form.	Form-5.
	Finished product Specification.	Innovator's Specifications.
	Pack size & Demanded Price	1's (40gm) & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	CLEOCIN Vaginal Cream 2%, which contains 2% clindamycin phosphate, USP, at a concentration equivalent to 20 mg clindamycin per gm, USFDA approved.
	Me-too status.	Acneris V Cream 2%, Global Pharmaceuticals, Reg. No. 085735
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Label claim of the formulation needs revision as the applied formulation has Clindamycin phosphate 2% while the reference product has clindamycin phosphate, USP, at a concentration equivalent to 20 mg clindamycin per gram. • Official monograph of applied formulation is available in USP. • The firm has provided Clindam, Clincin Cream as proposed brand names also.
	Decision: Deferred for revision of Label claim of the formulation as the applied formulation has Clindamycin phosphate 2% while the reference product has clindamycin phosphate, USP, at a concentration equivalent to 20 mg clindamycin per gram.	
511.	Name and address of manufacturer/ Applicant	M/s Paramount Pharmaceuticals, Plot No. 36, Industrial Triangle, Kahuta Road, Islamabad (**Cream/Ointment**).

	Brand Name + Dosage Form + Strength	Leptic 250mg/5ml Syrup.
	Composition	Each 5ml contains: Sodium valproate…….250mg
	Diary No. Date of R & I & fee	Dy. No 10026 dated 04-03-2019; Rs.20,000/- Dated 04-03-2019
	Pharmacological Group	Antiepileptic.
	Type of Form.	Form-5.
	Finished product Specification.	JP Specifications.
	Pack size & Demanded Price	1's (60ml, 120ml) & as per SRO.
	Approval status of product in Reference Regulatory Authorities.	Could not be confirmed.
	Me-too status.	Soparate Syrup 250mg/5ml, Alina Combine, Reg. No. 039616
	GMP status.	Same as above.
	Remarks of the Evaluator.	• Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting is not provided.
	Decision: Deferred for Evidence of approval of applied formulation in reference regulatory authorities/agencies which were adopted by the Registration Board in its 275th meeting is not provided.	

Item No. XIV: Agenda of Evaluator-VI (Mr. Ishtiaq Shafique)

Case No. 1: M/s Martin Dow Marker Limited, 7-Jail Road, Quetta

Assistant Director PR-I / EFD vide its letter No. F.1-6/2019-PR-I (EFD) dated 6th October 2022 informed that as per decision of 133rd meeting of DRAP Authority wherein it was decided to grant registration on priority basis to the pharmaceutical i.e. one molecule for each 100,000 USD worth of export of medicine (to a maximum of 15 such molecules) during a financial year.

In compliance to the above decision M/s Martin Dow Marker Limited, 7-Jail Road, Quetta have achieved benchmark of more than 100,000 USD and submitted their applications for priority consideration including following applications:

512.	Name, address of Applicant / Marketing Authorization Holder	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)	
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales	
	Dy. No. and date of submission	Dy. No. 3186 dated 02/02/2022	
	Details of fee submitted	PKR 75,000/-:	dated 01/11/2021(114414828)

		dated 23/11/2021(48350671821)
	The proposed proprietary name / brand name	Empaphage-M 12.5mg+1000mg Tablets
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…...12.5mg Metformin HCl. EP…...1000mg
	Pharmaceutical form of applied drug	Dark Grey Color, Biconvex, Oblong film coated engraved "C1" on one side and another side plain.
	Pharmacotherapeutic Group of (API)	**Empagliflozin:** Sodium-glucose co-transporter 2 (SGLT2) inhibitors **Metformin HCl:** Biguanides (Anti-Diabetic)
	Reference to Finished product specifications	Innovator's Specification
	Proposed Pack size	As per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy Tablets, USFDA Approved.
	For generic drugs (me-too status)	Empagen-M 12.5mg+1000mg Tablets by M/s Ferozsons Laboratories Limited, DRAP Approved.
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited, Xiaba Development Zone, Ruyuan Country, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** M/s Merck SanteM 5 rue Clement Ader, Calais, 62100, France.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance

	Stability studies	**Empagliflozin** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Accelerated Time:** ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Metformin HCl.** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: C17367, C17995, C19005. **Accelerated Time:** C13153, C13154, CC21674.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Synjardy® by M/s Boehringer Ingelheim Canada** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is **Synjardy® by M/s Boehringer Ingelheim Canada** in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited (China) **Metformin HCl:** M/s Merck Sante (France)		
API Lot No.	**Empagliflozin:** 2851ROC203000001 **Metformin HCl:** C23371		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03

Batch Size	6000 Tablets	6000 Tablets	6000 Tablets
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	06-2021	06-2021	06-2021
No. of Batches	03		

Administrative Portion		
7.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**M/s Ruyuan HEC Pharm, Company Limited (China):** GMP Certificate No DE_BE_01_GMP_2019_0042 issued by Germany valid till 29/Nov/2022 **M/s Merck Sante (France):** GMP Certificate No 21MPP078HFR01 issued by EUDRA valid till 17/11/2024.
9.	Documents for the procurement of API with approval from DRAP (in case of import).	**M/s Ruyuan HEC Pharm, Company Limited (China):** ADC Invoice No: WIS200249, 17-Nov-2020 is submitted wherein the permission to import API (Empagliflozin) for the purpose of test/analysis and stability studies is granted. **M/s Merck Sante (France):** ADC Invoice No: DE237881540, 1-Oct-2020 is submitted wherein the permission to import API (Metformin HCl) for the purpose of test/analysis and stability studies is granted.
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section#	Observation	Response of firm
1.	1.6.5	EMPAGLIFOZIN one of the following documents shall be submitted. i. Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. ii. Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin. iii. CEP certificate.	Firm has provided GMP certificate no. DE_BE_01_GMP_2019_0042, Valid till 28-11-2022. However, Empagliflozin is not present in scope.
2.	3.2.S.4	EMPAGLIFLOZIN • Method verification studies condition for testing on HPLC are not in accordance with analytical method of M/s M/s Martin Dow	Submitted method of analysis is based on HPLC method which was extracted from another API Manufacturer of Empagliflozin. Since this method is based on HPLC and stability indicating method,

		Marker Limited and Drug Substance manufacturer. Justification required. METFORMIN HCL • In Method verification studies method used is UV-Spectrophotometer. Whereas in official Pharmacopoeia (Eur. Ph.) and provided analytical method of M/s M/s Martin Dow Marker Limited method of assay is potentiometric titration. Justification required.	and method validation is also performed to ensure its suitability for intended use, therefore, this method is being used for testing of Empagliflozin. Although, titration method of assay is given in both Official Pharmacopoeia (Eur. Ph) and Martin Dow Marker method, however, an alternate method of assay of Metformin HCl is also given in testing method of Martin Dow Marker Which is based on UV-Visible spectrophotometric technique. This method is also based on BP Monograph of Metformin Tablets which is more sensitive than titration and method verification is also performed to authenticate it for intended use.
3.	3.2.P.8.3	Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated) shall be submitted for complete stability period.	Submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the performance of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter along with the submission of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

513.	Name, address of Applicant / Marketing Authorization Holder	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)	
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales	
	Dy. No. and date of submission	Dy. No. 569 dated 06/01/2022	
	Details of fee submitted	PKR 75,000/-:	dated 01/11/2021(59207791779) dated 23/11/2021(3099684301)
	The proposed proprietary name / brand	Empaphage-M 12.5mg+850mg Tablets	

	name	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…...12.5mg Metformin HCl. EP…...850mg
	Pharmaceutical form of applied drug	Light Pink Color, Biconvex, Oblong film coated, engraved "GL IG" with bisection line on one side and other side engraved bisection line.
	Pharmacotherapeutic Group of (API)	**Empagliflozin:** Sodium-glucose co-transporter 2 (SGLT2) inhibitors **Metformin HCl:** Biguanides (Anti-Diabetic)
	Reference to Finished product specifications	Innovator's Specification
	Proposed Pack size	7X2's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy 12.5 mg/850 mg film-coated tablets MHRA Approved.
	For generic drugs (me-too status)	Emsyn-Met Tablets 5/850mg Tablets by The Searle Company Limited, DRAP Approved.
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited, Xiaba Development Zone, Ruyuan Country, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** M/s Merck SanteM 5 rue Clement Ader, Calais, 62100, France.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin** Stability study conditions:

		Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Accelerated Time:** ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Metformin HCl.** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: C17367, C17995, C19005. **Accelerated Time:** C13153, C13154, CC21674.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Synjardy® by M/s Boehringer Ingelheim Canada** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is **Synjardy® by M/s Boehringer Ingelheim Canada** in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited (China) **Metformin HCl:** M/s Merck Sante (France)		
API Lot No.	**Empagliflozin:** EGLZ-RD202009001 **Metformin HCl:** C23371		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	6000 Tablets	6000 Tablets	6000 Tablets
Manufacturing Date	04-2021	04-2021	04-2021

Date of Initiation	04-2021	04-2021	04-2021
No. of Batches	03		
Administrative Portion			
	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted	
1.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**M/s Ruyuan HEC Pharm, Company Limited (China):** GMP Certificate No DE_BE_01_GMP_2019_0042 issued by Germany valid till 26/Nov/2022. However, API is not present in scope of certificate. **M/s Merck Sante (France):** GMP Certificate No 21MPP078HFR01 issued by EUDRA valid till 16/11/2024.	
2.	Documents for the procurement of API with approval from DRAP (in case of import).	**M/s Ruyuan HEC Pharm, Company Limited (China):** ADC Invoice No: WIS200249, 17-Nov-2020 is submitted wherein the permission to import API (Empagliflozin) for the purpose of test/analysis and stability studies is granted. **M/s Merck Sante (France):** ADC Invoice No: DE237881540, 1-Oct-2020 is submitted wherein the permission to import API (Metformin HCl) is granted.	
3.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted	
4.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted	
5.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted	

Remarks of Evaluator:

Sr.#	Section#	Observation	Reply
1.	**1.6.5**	**EMPAGLIFOZIN** one of the following documents shall be submitted. i. Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. ii. Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin. iii. CEP certificate.	Firm has provided GMP certificate no. DE_BE_01_GMP_2019_0042, Valid till 28-11-2022. However, Empagliflozin is not present in scope.
2.	**3.2.S.4**	**EMPAGLIFLOZIN** • Method verification studies condition for testing on HPLC are not in accordance with analytical method of M/s M/s Martin Dow Marker Limited and Drug Substance manufacturer. Justification required.	Submitted method of analysis is based on HPLC method which was extracted from another API Manufacturer of Empagliflozin. Since this method is based on HPLC and stability indicating method, and method validation is also performed to ensure its suitability for intended use,

		METFORMIN HCL • In Method verification studies method used is UV-Spectrophotometer. Whereas in official Pharmacopoeia (Eur. Ph.) and provided analytical method of M/s M/s Martin Dow Marker Limited method of assay is potentiometric titration. Justification required.	therefore, this method is being used for testing of Empagliflozin. Although, titration method of assay is given in both Official Pharmacopoeia (Eur. Ph) and Martin Dow Marker method, however, an alternate method of assay of Metformin HCl is also given in testing method of Martin Dow Marker Which is based on UV-Visible spectrophotometric technique. This method is also based on BP Monograph of Metformin Tablets which is more sensitive than titration and method verification is also performed to authenticate it for intended use.
3.	**3.2.P.8.3**	Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated) shall be submitted for complete stability period.	Submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the performance of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter along with the submission of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

514.	Name, address of Applicant / Marketing Authorization Holder	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)	
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales	
	Dy. No. and date of submission	Dy. No. 568 dated 06/01/2022	
	Details of fee submitted	PKR 75,000/-:	dated 01/11/2021(52442635) dated 23/11/2021(73863871012)
	The proposed proprietary name / brand name	Empaphage-M 12.5mg+500mg Tablets	

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…...12.5mg Metformin HCl. EP…...500mg
	Pharmaceutical form of applied drug	Dark Grey Color, Biconvex, Oblong film coated, plain on one side and engraved with bisection line on another side
	Pharmacotherapeutic Group of (API)	**Empagliflozin:** Sodium-glucose co-transporter 2 (SGLT2) inhibitors **Metformin HCl:** Biguanides (Anti-Diabetic)
	Reference to Finished product specifications	Innovator's Specification
	Proposed Pack size	As per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy Tablets, USFDA Approved.
	For generic drugs (me-too status)	Empagen-M 12.5mg+500mg Tablets by M/s Ferozsons Laboratories Limited, DRAP Approved.
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021. Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited, Xiaba Development Zone, Ruyuan Country, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** M/s Merck SanteM 5 rue Clement Ader, Calais, 62100, France.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months

		Batches: **Real Time**: ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Accelerated Time:** ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Metformin HCl.** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: C17367, C17995, C19005. **Accelerated Time:** C13153, C13154, CC21674.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Synjardy® by M/s Boehringer Ingelheim Canada** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is **Synjardy® by M/s Boehringer Ingelheim Canada** in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited (China) **Metformin HCl:** M/s Merck Sante (France)		
API Lot No.	**Empagliflozin:** EGLZ-RD202009001 **Metformin HCl:** C23371		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	6000 Tablets	6000 Tablets	6000 Tablets
Manufacturing Date	01-2021	01-2021	01-2021

Date of Initiation	03-2021	03-2021	03-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**M/s Ruyuan HEC Pharm, Company Limited (China):** GMP Certificate No DE_BE_01_GMP_2019_0042 issued by Germany valid till 28/Nov/2022 **M/s Merck Sante (France):** GMP Certificate No 21MPP078HFR01 issued by EUDRA valid till 16/11/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**M/s Ruyuan HEC Pharm, Company Limited (China):** ADC Invoice No: WIS200249, 17-Nov-2020 is submitted wherein the permission to import API (Empagliflozin) for the purpose of test/analysis and stability studies is granted. **M/s Merck Sante (France):** ADC Invoice No: DE237881540, 1-Oct-2020 is submitted wherein the permission to import API (Metformin HCl) is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section#	Observation	Reply
1.	**1.6.5**	**EMPAGLIFOZIN** one of the following documents shall be submitted. i. Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. ii. Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin. iii. CEP certificate.	Firm has provided GMP certificate no. DE_BE_01_GMP_2019_0042, Valid till 28-11-2022. However, Empagliflozin is not present in scope.
2.	**3.2.S.4**	**EMPAGLIFLOZIN** • Method verification studies condition for testing on HPLC are not in accordance with analytical method of M/s M/s Martin Dow Marker Limited and Drug Substance manufacturer. Justification required.	Submitted method of analysis is based on HPLC method which was extracted from another API Manufacturer of Empagliflozin. Since this method is based on HPLC and stability indicating method, and method validation is also performed to ensure its suitability for intended use, therefore, this method is being used for testing of Empagliflozin.

		METFORMIN HCL • In Method verification studies method used is UV-Spectrophotometer. Whereas in official Pharmacopoeia (Eur. Ph.) and provided analytical method of M/s M/s Martin Dow Marker Limited method of assay is potentiometric titration. Justification required.	Although, titration method of assay is given in both Official Pharmacopoeia (Eur. Ph) and Martin Dow Marker method, however, an alternate method of assay of Metformin HCl is also given in testing method of Martin Dow Marker Which is based on UV-Visible spectrophotometric technique. This method is also based on BP Monograph of Metformin Tablets which is more sensitive than titration and method verification is also performed to authenticate it for intended use.
3.	**3.2.P.8.3**	Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated) shall be submitted for complete stability period.	Submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the performance of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter along with the submission of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

515.	Name, address of Applicant / Marketing Authorization Holder	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)	
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales	
	Dy. No. and date of submission	Dy. No. 1302 dated 14/01/2022	
	Details of fee submitted	PKR 75,000/-:	dated 23/11/2021(5455039504)
	The proposed proprietary name / brand name	Empaphage-M 5mg+1000mg Tablets	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…...5mg Metformin HCl. EP…...1000mg	

	Pharmaceutical form of applied drug	Dark Yellow Color, Biconvex, Oblong film coated engraved "C1" on one side and another side plain.
	Pharmacotherapeutic Group of (API)	**Empagliflozin:** Sodium-glucose co-transporter 2 (SGLT2) inhibitors **Metformin HCl:** Biguanides (Anti-Diabetic)
	Reference to Finished product specifications	Innovator's Specification
	Proposed Pack size	7X2' s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy Tablets, USFDA Approved.
	For generic drugs (me-too status)	Empagen-M 5mg+1000mg Tablets by M/s Ferozsons Laboratories Limited, DRAP Approved.
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited, Xiaba Development Zone, Ruyuan Country, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** M/s Merck Sante 5 rue Clement Ader, Calais, 62100, France.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503.

		Accelerated Time: ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Metformin HCl.** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: C17367, C17995, C19005. **Accelerated Time:** C13153, C13154, CC21674.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Synjardy® by M/s Boehringer Ingelheim Canada** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is **Synjardy® by M/s Boehringer Ingelheim Canada** in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited (China) **Metformin HCl:** M/s Merck Sante (France)		
API Lot No.	**Empagliflozin:** 2851ROC203000001 **Metformin HCl:** FR21030170085		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	6000 Tablets	6000 Tablets	6000 Tablets
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	06-2021	06-2021	06-2021
No. of Batches	03		
Administrative Portion			

1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**M/s Ruyuan HEC Pharm, Company Limited (China):** GMP Certificate No DE_BE_01_GMP_2019_0042 issued by Germany valid till 28/Nov/2022 **M/s Merck Sante (France):** GMP Certificate No 21MPP078HFR01 issued by EUDRA valid till 16/11/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**M/s Ruyuan HEC Pharm, Company Limited (China):** ADC Invoice No: WIS200249, 17-Nov-2020 is submitted wherein the permission to import API (Empagliflozin) for the purpose of test/analysis and stability studies is granted. **M/s Merck Sante (France):** ADC Invoice No: DE237881540, 1-Oct-2020 is submitted wherein the permission to import API (Metformin HCl) is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.#	Section#	Observation	Reply
1.	**1.6.5**	**EMPAGLIFOZIN** one of the following documents shall be submitted. i. Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. ii. Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin. iii. CEP certificate.	Firm has provided GMP certificate no. DE_BE_01_GMP_2019_0042, Valid till 28-11-2022. However, Empagliflozin is not present in scope.
2.	**3.2.S.4**	**EMPAGLIFLOZIN** • Method verification studies condition for testing on HPLC are not in accordance with analytical method of M/s M/s Martin Dow Marker Limited and Drug Substance manufacturer. Justification required. **METFORMIN HCL**	Submitted method of analysis is based on HPLC method which was extracted from another API Manufacturer of Empagliflozin. Since this method is based on HPLC and stability indicating method, and method validation is also performed to ensure its suitability for intended use, therefore, this method is being used for testing of Empagliflozin.

		• In Method verification studies method used is UV-Spectrophotometer. Whereas in official Pharmacopoeia (Eur. Ph.) and provided analytical method of M/s M/s Martin Dow Marker Limited method of assay is potentiometric titration. Justification required.	Although, titration method of assay is given in both Official Pharmacopoeia (Eur. Ph) and Martin Dow Marker method, however, an alternate method of assay of Metformin HCl is also given in testing method of Martin Dow Marker Which is based on UV-Visible spectrophotometric technique. This method is also based on BP Monograph of Metformin Tablets which is more sensitive than titration and method verification is also performed to authenticate it for intended use.
3.	**3.2.P.8.3**	Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated) shall be submitted for complete stability period.	Submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the performance of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter along with the submission of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

516.	Name, address of Applicant / Marketing Authorization Holder	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)	
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales	
	Dy. No. and date of submission	Dy. No. 1301 dated 14/01/2022	
	Details of fee submitted	PKR 75,000/-:	dated 23/11/2021(0886311030)
	The proposed proprietary name / brand name	Empaphage-M 5mg+850mg Tablets	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…...5mg Metformin HCl. EP…...850mg	
	Pharmaceutical form of applied drug	Light Yellow Color, Biconvex, Oblong film coated engraved "GLIG" with bisection line on one side and bisection line on another side.	

	Pharmacotherapeutic Group of (API)	**Empagliflozin:** Sodium-glucose co-transporter 2 (SGLT2) inhibitors **Metformin HCl:** Biguanides (Anti-Diabetic)
	Reference to Finished product specifications	Innovator's Specification
	Proposed Pack size	7X2 s
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy 5 mg/850 mg film-coated tablets(MHRA Approved).
	For generic drugs (me-too status)	Empagen-M 5mg+850mg Tablets by M/s Ferozsons Laboratories Limited, DRAP Approved.
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited, Xiaba Development Zone, Ruyuan Country, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** M/s Merck SanteM 5 rue Clement Ader, Calais, 62100, France.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Accelerated Time:** ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Metformin HCl.**

		Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: C17367, C17995, C19005. **Accelerated Time:** C13153, C13154, CC21674.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Synjardy® by M/s Boehringer Ingelheim Canada** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is **Synjardy® by M/s Boehringer Ingelheim Canada** in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited (China) **Metformin HCl:** M/s Merck Sante (France)		
API Lot No.	**Empagliflozin:** EGLZ-RD202009001 **Metformin HCl:** C23371		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	6000 Tablets	6000 Tablets	6000 Tablets
Manufacturing Date	04-2021	04-2021	04-2021
Date of Initiation	04-2021	04-2021	04-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**M/s Ruyuan HEC Pharm, Company Limited (China):** GMP Certificate No DE_BE_01_GMP_2019_0042 issued by Germany valid till 28/Nov/2022 **M/s Merck Sante (France):** GMP Certificate No 21MPP078HFR01 issued by EUDRA valid till 16/11/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**M/s Ruyuan HEC Pharm, Company Limited (China):** ADC Invoice No: WIS200249, 17-Nov-2020 is submitted wherein the permission to import API (Empagliflozin) for the purpose of test/analysis and stability studies is granted. **M/s Merck Sante (France):** ADC Invoice No: DE237881540, 1-Oct-2020 is submitted wherein the permission to import API (Metformin HCl) is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.#	Section#	Observation	Reply
1.	**1.6.5**	**EMPAGLIFOZIN** one of the following documents shall be submitted. i. Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. ii. Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin. iii. CEP certificate.	Firm has provided GMP certificate no. DE_BE_01_GMP_2019_0042, Valid till 28-11-2022. However, Empagliflozin is not present in scope.
2.	**3.2.S.4**	**EMPAGLIFLOZIN** • Method verification studies condition for testing on HPLC are not in accordance with analytical method of M/s M/s Martin Dow Marker Limited and Drug Substance manufacturer. Justification required. **METFORMIN HCL** • In Method verification studies method used is UV-Spectrophotometer. Whereas in	Submitted method of analysis is based on HPLC method which was extracted from another API Manufacturer of Empagliflozin. Since this method is based on HPLC and stability indicating method, and method validation is also performed to ensure its suitability for intended use, therefore, this method is being used for testing of Empagliflozin. Although, titration method of assay is given in both Official Pharmacopoeia (Eur. Ph) and Martin Dow Marker method, however, an alternate method of assay of Metformin

		official Pharmacopoeia (Eur. Ph.) and provided analytical method of M/s M/s Martin Dow Marker Limited method of assay is potentiometric titration. Justification required.	HCl is also given in testing method of Martin Dow Marker Which is based on UV-Visible spectrophotometric technique. This method is also based on BP Monograph of Metformin Tablets which is more sensitive than titration and method verification is also performed to authenticate it for intended use.
3.	**3.2.P.8.3**	Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated) shall be submitted for complete stability period.	Submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the performance of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter along with the submission of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

517.	Name, address of Applicant / Marketing Authorization Holder	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Name, address of Manufacturing site.	M/s Martin Dow Marker Limited, 7-Jail Road, Quetta	
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)	
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)	
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales	
	Dy. No. and date of submission	Dy. No. 669 dated 07/01/2022	
	Details of fee submitted	PKR 75,000/-:	Dated 01/11/2021(2514616760) Dated 23/11/2021(131882637454)
	The proposed proprietary name / brand name	Empaphage-M 5mg+500mg Tablets	
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Empagliflozin…...5mg Metformin HCl. EP…...500mg	
	Pharmaceutical form of applied drug	Dark Yellow Color, Biconvex, Oblong film coated, plain on one side and engraved with bisection line on another side.	
	Pharmacotherapeutic Group of (API)	**Empagliflozin:** Sodium-glucose co-transporter 2 (SGLT2) inhibitors	

		Metformin HCl: Biguanides (Anti-Diabetic)
	Reference to Finished product specifications	Innovator's Specification
	Proposed Pack size	As per DPC
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Synjardy Tablets, USFDA Approved.
	For generic drugs (me-too status)	Empagen-M 5mg+500mg Tablets by M/s Ferozsons Laboratories Limited, DRAP Approved.
	GMP status of the Finished product manufacturer	Certificate No:015/2021-DRAP (Q)/K issued on 10th September 2021 Tablet (General & Psychotropic), Capsule (General), Oral Liquid Syrup (General), Sterile Liquid Injection/Ampoule, Ointment/Cream, Dry Powder Sachet (General), Dry Powder Suspension (General) section approved.
	Name and address of API manufacturer.	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited, Xiaba Development Zone, Ruyuan Country, Shaoguan City, Guangdong Province, P.R. China **Metformin HCl:** M/s Merck Sante 5 rue Clement Ader, Calais, 62100, France.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	**Empagliflozin** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Accelerated Time:** ENGLZ-20160501, ENGLZ-20160502, ENGLZ-20160503. **Metformin HCl.** Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months

		Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: **Real Time**: C17367, C17995, C19005. **Accelerated Time:** C13153, C13154, CC21674.
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is **Synjardy® by M/s Boehringer Ingelheim Canada** by performing quality tests (Identification, Assay, Dissolution). CDP has been performed against the same brand that is **Synjardy® by M/s Boehringer Ingelheim Canada** in Acid media (pH 1.2), Acetate Buffer (pH 4.5) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method validation studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	**Empagliflozin:** M/s Ruyuan HEC Pharm, Company Limited (China) **Metformin HCl:** M/s Merck Sante (France)		
API Lot No.	**Empagliflozin:** EGLZ-RD202009001 **Metformin HCl:** C23371		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-01	T-02	T-03
Batch Size	6000 Tablets	6000 Tablets	6000 Tablets
Manufacturing Date	01-2021	01-2021	01-2021
Date of Initiation	03-2021	03-2021	03-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Submitted

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**M/s Ruyuan HEC Pharm, Company Limited (China):** GMP Certificate No DE_BE_01_GMP_2019_0042 issued by Germany valid till 29/Nov/2022 **M/s Merck Sante (France):** GMP Certificate No 21MPP078HFR01 issued by EUDRA valid till 17/11/2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	**M/s Ruyuan HEC Pharm, Company Limited (China):** ADC Invoice No: WIS200249, 17-Nov-2020 is submitted wherein the permission to import API (Empagliflozin) for the purpose of test/analysis and stability studies is granted. **M/s Merck Sante (France):** ADC Invoice No: DE237881540, 1-Oct-2020 is submitted wherein the permission to import API (Metformin HCl) for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.#	Section#	Observation	Reply
1.	**1.6.5**	**EMPAGLIFOZIN** one of the following documents shall be submitted. i. Valid Drug Manufacturing License issued by the relevant regulatory authority of country of origin. ii. Valid Good Manufacturing Practice (GMP) certificate of the Drug Substance manufacturer issued by relevant regulatory authority of country of origin. iii. CEP certificate.	Firm has provided GMP certificate no. DE_BE_01_GMP_2019_0042, Valid till 28-11-2022. However, Empagliflozin is not present in scope.
2.	**3.2.S.4**	**EMPAGLIFLOZIN** • Method verification studies condition for testing on HPLC are not in accordance with analytical method of M/s M/s Martin Dow Marker Limited and Drug Substance manufacturer. Justification required. **METFORMIN HCL** • In Method verification studies method used is UV-	Submitted method of analysis is based on HPLC method which was extracted from another API Manufacturer of Empagliflozin. Since this method is based on HPLC and stability indicating method, and method validation is also performed to ensure its suitability for intended use, therefore, this method is being used for testing of Empagliflozin. Although, titration method of assay is given in both Official Pharmacopoeia (Eur. Ph) and Martin Dow Marker method, however,

		Spectrophotometer. Whereas in official Pharmacopoeia (Eur. Ph.) and provided analytical method of M/s M/s Martin Dow Marker Limited method of assay is potentiometric titration. Justification required.	an alternate method of assay of Metformin HCl is also given in testing method of Martin Dow Marker Which is based on UV-Visible spectrophotometric technique. This method is also based on BP Monograph of Metformin Tablets which is more sensitive than titration and method verification is also performed to authenticate it for intended use.
3.	**3.2.P.8.3**	Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated) shall be submitted for complete stability period.	Submitted.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit revised specifications of Metformin HCl drug substance according to latest edition of USP along with the performance of analytical method verifications studies (including specificity, accuracy and method precision) before the issuance of registration letter along with the submission of Rs. 7,500/- for as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.**

Case No. 02 Registration applications of local manufacturing of human drugs submitted on CTD format

518.	Name, address of Applicant / Marketing Authorization Holder	M/s Islam Pharmaceuticals, 7Km Pasrur Road, Sialkot.
	Name, address of Manufacturing site.	M/s Islam Pharmaceuticals, 7Km Pasrur Road, Sialkot.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 28730 dated: 20-10-2021
	Details of fee submitted	PKR 30,000/- dated: 06/10/2021
	The proposed proprietary name / brand name	Pregab 75mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule contains: Pregabalin …….75mg

	Pharmaceutical form of applied drug	White to Off-White color powder filled in EHGC shells of green cap and grey body
	Pharmacotherapeutic Group of (API)	Antiepiliptics
	Reference to Finished product specifications	In-house
	Proposed Pack size	2×7's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Pregabalin 75 mg capsules, PHARMATHEN S.A., Greece, MHRA Approved.
	For generic drugs (me-too status)	Gablin 75mg capsule, CCL Pharmaceuticals (Pvt) Limited
	GMP status of the Finished product manufacturer	Ref. No. 115/2020-DRAP (AD-1949403-534) Dated: 27/07/2020 valid till 09/07/2022 Applied for renewal of GMP certificate, challan Slip Number 65317072674
	Name and address of API manufacturer.	KOPRAN RESEARCH LABORATORIES LIMITED K4/4, Additional MIDC, At & Post Birwadi Taluka Mahad, District Raigad 402302 Maharashtra, INDIA
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Pregabalin is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for related substances (any individual impurity and total impurities), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:(PRG/P1208124, PRG/P1208125, PRG/P1208126)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.

	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against is Dologab 75mg Capsule by Martin Dow Marker Ltd, Pakistan by performing quality tests (Identification, Assay, Dissolution, Disintegration, Uniformity of dosage form). CDP has been performed against the same brand that is Dologab 75mg Capsule by Martin Dow Marker Ltd, Pakistan in Acid media (pH 1.0-1.2) & Acetate buffer 4.5pH and Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including accuracy, precision and specificity.

STABILITY STUDY DATA

Manufacturer of API	KOPRAN RESEARCH LABORATORIES LIMITED K4/4, Additional MIDC, At & Post Birwadi Taluka Mahad, District Raigad 402302 Maharashtra, INDIA		
API Lot No.	PRGH/P2003027		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 06 months Accelerated: 06 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	20CRn007	21CRn006	21CRn005
Batch Size	2000 capsule	2000 capsule	2000 capsule
Manufacturing Date	12-2020	04-2021	04-2021
Date of Initiation	29-05-2021	01-06-2021	01-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. NEW-WHO-GMP/CERT/KD/89275/2020/11/33788 issued by FDA valid till 19/10/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.12086/2020/DRAP-AD-G (I&E) dated 28/08/2020 is submitted wherein the permission to import different APIs including Pregabalin for the purpose of test/analysis and stability studies is granted. • Air Way Bill No. 157/BOM/65804675
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.#	Section#	Observation	Reply
1.	**1.3.5**	GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years is missing.	**1.3.5** GMP certificate of manufacturing unit based on evaluation 09-07-2020, issued within last three years is submitted
2.	**3.2.S.4.1**	Justification is required for import and usage of in-house specification drug substance. Whereas the API is present in the official monograph i.e. United States Pharmacopoeia(USP).	**3.2.S.4.1** Pregabalin was included in USP in 2020 and we imported drug substance in the same year so no drug substance manufacturer had complete long term stability studies (03 years) at the time of purchase of material of pregabalin as per USP specifications. Due to above reason we have to import and use in-house specification material. However we tested the drug substance as per USP method and specification and it complies the USP specifications as given in CoA of drug substance by Drug product manufacturer under batch analysis section
3.	**3.2.S.7.1**	In stability studies protocol of drug substance storage conditions for long term stability are 25 ±2 ^{o}C and relative humidity is 60±5%. Whereas in data sheets it is 30 ±2 ^{o}C and relative humidity is 65±5%	**3.2.S.7.1** Initially we received DMF with stability studies at 25±2^{o}C and relative humidity 60±5% which were also mentioned in stability protocols, we then requested Drug substance manufacturer to provide Zone-IVA stability studies (30±2^{o}C and relative humidity 65±5%) which were provided later and were added in section 3.2.S.7.3. Due to above reason the protocols contain different conditions from the stability sheets provided in section 3.2.S.7.3.
4.	**3.2.P.1**	In composition of The drug product quantity of claim / capsule is 75.240. Justification is required if any overage.	**3.2.P.1** Assay result of pregabalin drug substance was 99.67% on as is basis, so for 75mg pregabalin we required 75.24mg of pragabalin. The quantity is adjusted for achieve claimed amount (75mg) of pregabalin per capsule.
5.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies & CDP against the innovator product.	**3.2.P.2.2.1** Because innovator brand was not available and as per DRAP guidance Document# **PE&R/GL/AF/004**, Dated: 01-10-2020, pharmaceutical equivalence studies can be performed against innovator / reference / comparator product if the innovator brand is not available. Pharmaceutical equivalence and CDP was performed against Dologab capsule manufactured by Martin Dow Marker Ltd.

6.	**3.2.P.4.1**	Justification shall be submitted for not using Pharmacopeia specification for drug product. Whereas drug product is present in the BP. Furthermore justification also required for not using analytical condition as per Pharmacopeia and innovator.	**3.2.P.4.1** We developed and manufactured trial batches in December 2020 and April-2021 and at that time the drug product was not included in any of official monograph, we used in-house method and specifications which was validated and results are provided under section 3.2.P.5.3. As pregabalin capsule monograph is now available in BP we hereby undertake that we will adopt BP monograph for specification and testing of pregab capsule for commercial batches.
7.	**3.2.P.8.3**	• Documents confirming procurement of drug substance and COA shall be submitted. • Firm has manufactured 2 batches in Apr-2021 and 1 batch in December 2020. Whereas stability is started at May 2021. Justification is required. Furthermore, data for storage conditions of December 2020 batch is required. • Record of Digital data logger for temperature and humidity monitoring of stability chambers and audit trail reports on product testing for complete testing periods are missing.	• Submitted First stability batch was manufactured in December 2020, mix powder was tested 19-12-2020, it was then quarantined due to unavailability of required capsule shells. The batch was filled on 31-Mar-2021 and test for filled capsule performed on 09-Apr-2021, product was re-tested before starting of stability on 29-May-2021. Report is attached under section 3.2.P.5.4 batch analysis. Submitted.
Decision: Approved, with BP specifications. The Board further decided that the applicant will submit fee of Rs. 7,500/- for revision of specifications as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021. • **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.** • **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.** • **Firm will submit revised specifications and analytical procedure along with analytical method verifications studies (including specificity, accuracy and method precision) according to BP monograph for both drug susbtance and drug product before the issuance of registration letter.**			

519.	Name, address of Applicant / Marketing Authorization Holder	M/s Axis Pharmaceuticals 3-B Value Addition City, 1.5 Km Khurrianwala – Sahianwala Road, Faisalabad – Pakistan
	Name, address of Manufacturing site.	M/s Axis Pharmaceuticals 3-B Value Addition City, 1.5 Km Khurrianwala – Sahianwala Road, Faisalabad – Pakistan

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33459 (dated: 22-12-2021)
	Details of fee submitted	PKR 30,000/-: 18-11-21 (deposit slip# 170221961208)
	The proposed proprietary name / brand name	**Axopid Tablet 25mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contain: Levosulpiride … 25mg
	Pharmaceutical form of applied drug	Immediate Release Tablet (Uncoated).
	Pharmacotherapeutic Group of (API)	Neuroleptic agent
	Reference to Finished product specifications	In-house specification
	Proposed Pack size	30's, 20's, 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Levopraid Tablet by Teofarma (AiFa approved).
	For generic drugs (me-too status)	Sowel Tablet by Dyson RL. (Reg. # 049132).
	GMP status of the Finished product manufacturer	Firm has submitted GMP certificate issued on dated 06-07-2020.
	Name and address of API manufacturer.	Kimia Biosciences Limited Address: Village-Bhondsi, Tehsil-Sohna, Distt. Gurugram(Haryana)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph for drug is not present in any pharmacopoeia. Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.

	Stability studies	Firm has submitted stability study data of 3 batches of API as per zone IV-A conditions Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches:LA/LSD/SPP/18/004, LA/LSD/SPP/18/005, LA/LSD/SPP/18/006
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product as per specification and comparative study against the comparator product i.e. Sowel Tablet by Dyson RL. Pharmaceutical Equivalence have been conducted by performing quality tests (Friability, DT, Dissolution, Identification, Content Uniformity and Assay). CDP has been performed against the same brand in Acid media (pH 1.2), Acetate Buffer (pH 4.5), Phosphate Buffer (pH 6.8) & Water. The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted report of validation of analytical method for the drug product including system suitability, specificity, accuracy, spiking, repeatability, intermediate precision, linearity, range & robustness.

STABILITY STUDY DATA

Manufacturer of API	Kimia Biosciences Limited Address: Village-Bhondsi, Tehsil-Sohna, Distt. Gurugram(Haryana)		
API Lot No.	B#: KB/LSD/MC/21/003 (QC#: R-117/21)		
Description of Pack (Container closure system)	Alu – PVC Blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-002	T-003	T-004
Batch Size	2500 Tabs.	2500 Tabs.	2500 Tabs.
Manufacturing Date	05 – 2021	05 – 2021	05 – 2021
Date of Initiation	06-07-2021	06-07-2021	06-07-2021

No. of Batches	03	
Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Product approved in 316th Meeting of Registration Board. • Femecare – H Cream • Loxicaine Jelly • Lansix Capsule 30mg
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate of Kimia Biosciences Limited. The certificate is valid till 06-04-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of procurement invoice dated 22-02-2021 specifying import of 1.20Kg of API.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section#	Observation	
1.	**1.3.5**	Firm has provided GMP Certificate which is valid until 08-06-2022.GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted.	Copy of valid GMP Certificate submitted based on evaluation conducted on 13-06-2022.
2.	**3.2.S.4**	• Analytical Method drug substance manufacturer is missing. • Analytical Method validation studies for drug substance are missing.	Submitted
3.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies & CDP against the innovator product.	The pharmaceutical equivalence is submitted against comparator product as per DRAP's guidance document (FAQs about Form 5F), dated 28-01-2021. Copy of FAQs is presented herewith.
4.	**3.2.P.5.2**	In analytical procedure of drug product manufacturer, assay and content uniformity is performed by UV-spectrophotometer. Justification required.	As Levosulpiride is not available in any available pharmacopoeia nor any data is available in other SRA database. Drug substance manufacturer used titration method and other research articles showed quantitative analysis using UV spectrophotometer. Therefore, UV

			technique was adopted and appropriately validated for quantification.
5.	**3.2.P.8.**	In stability studies data of accelerated stability studies significant change in assay (i.e. from 100.74% to 93.98% in T-004 batch from initial to 6 months testing), Justification required.	The analytical method for the drug product states the use of sonication during sample preparation which was out of order during that time frame, due to which variation in the results may have occurred. However, it was allowed to continue based on dissolution results as they flawlessly complied the specification. The test results up to 12 months have been compiled and all the parameters meet the specification without any significant change. Therefore, it is requested to you to kindly consider the data up to 12 months.
6.	**3.2.P.8.3**	Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated) shall be submitted.	Submitted

Decision: Approved with innovator's specifications. The firm will submit fee of Rs. 7,500/- for revision of specifications as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

520.	Name, address of Applicant / Marketing Authorization Holder	M/s Axis Pharmaceuticals 3-B Value Addition City, 1.5 Km Khurrianwala – Sahianwala Road, Faisalabad – Pakistan
	Name, address of Manufacturing site.	M/s Axis Pharmaceuticals 3-B Value Addition City, 1.5 Km Khurrianwala – Sahianwala Road, Faisalabad – Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 33360 (dated: 22-12-2021)
	Details of fee submitted	PKR 30,000/-: 18-11-21 (deposit slip# 40994710)
	The proposed proprietary name / brand name	**Axopid Tablet 50mg**
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each tablet contains: Levosulpiride … 50mg

	Pharmaceutical form of applied drug	Immediate Release Tablet (Uncoated).
	Pharmacotherapeutic Group of (API)	Neuroleptic agent
	Reference to Finished product specifications	In-house specification
	Proposed Pack size	30's, 20's, 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Levopraid Tablet by Teofarma (AiFa approved).
	For generic drugs (me-too status)	Sowel Tablet by Dyson RL. (Reg. # 049133).
	GMP status of the Finished product manufacturer	Firm has submitted GMP certificate issued on dated 06-07-2020.
	Name and address of API manufacturer.	Kimia Biosciences Limited Address: Village-Bhondsi, Tehsil-Sohna, Distt. Gurugram(Haryana)
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph for drug is not present in any pharmacopoeia. Firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Firm has submitted stability study data of 3 batches of API as per zone IV-A conditions Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 60 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: LA/LSD/SPP/18/004, LA/LSD/SPP/18/005, LA/LSD/SPP/18/006
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Firm has submitted results of pharmaceutical equivalence for all the quality tests for their product

		as per specification and comparative study against the. Sowel Tablet by Dyson RL Pharmaceutical Equivalence have been conducted by performing quality tests (Friability, DT, Dissolution, Identification, Content Uniformity and Assay). CDP has been performed against the same brand in Acid media (pH 1.2), Acetate Buffer (pH 4.5), Phosphate Buffer (pH 6.8) & Water. The values for f2 are in the acceptable range.
	Analytical method validation/verification of product	Firm has submitted report of validation of analytical method for the drug product including system suitability, specificity, accuracy, spiking, repeatability, intermediate precision, linearity, range & robustness.

STABILITY STUDY DATA			
Manufacturer of API	Kimia Biosciences Limited Address: Village-Bhondsi, Tehsil-Sohna, Distt. Gurugram(Haryana)		
API Lot No.	B#: KB/LSD/MC/21/003 (QC#: R-117/21)		
Description of Pack (Container closure system)	Alu – PVC Blister		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-005	T-006	T-007
Batch Size	2500 Tabs.	2500 Tabs.	2500 Tabs.
Manufacturing Date	05 – 2021	05 – 2021	05 – 2021
Date of Initiation	07-06-2021	07-06-2021	07-06-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Product approved in 316th Meeting of Registration Board. • Femecare – H Cream • Loxicaine Jelly • Lansix Capsule 30mg
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP Certificate of Kimia Biosciences Limited. The certificate is valid till 06-04-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of procurement invoice dated 22-02-2021 specifying import of 1.20Kg of API.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not Submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section#	Observation	Response of firm
1.	**1.3.5**	Firm has provided GMP Certificate which is valid until 08-06-2022.GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted.	Copy of valid GMP Certificate submitted based on evaluation conducted on 13-06-2022.
2.	**3.2.S.4**	• Analytical Method drug substance manufacturer is missing. • Analytical Method validation studies for drug substance are missing.	Submitted
3.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies & CDP against the innovator product.	The pharmaceutical equivalence is submitted against comparator product as per DRAP's guidance document (FAQs about Form 5F), dated 28-01-2021. Copy of FAQs is presented herewith.
4.	**3.2.P.5.2**	In analytical procedure of drug product manufacturer, assay and content uniformity is performed by UV-spectrophotometer. Justification required.	As Levosulpiride is not available in any available pharmacopoeia nor any data is available in other SRA database. Drug substance manufacturer used titration method and other research articles showed quantitative analysis using UV spectrophotometer. Therefore, UV technique was adopted and appropriately validated for quantification.
5.	**3.2.P.8.**	In stability studies data of accelerated and real time stability studies significant change in assay (i.e. from 99.99% to 93.69% in T005 batch,99.47% to 95.59% in T-006 batch in interval of initial to 06 months testing), Justification required.	Only T-005 shows a significant change at accelerated condition. The analytical method for the drug product states the use of sonication during sample preparation which was out of order during that time frame, due to which variation in the results may have occurred. However, it was allowed to continue based on dissolution results as they flawlessly complied the specification. The test results up to 12 months have been compiled and all the parameters meet the specification without any significant change. Therefore, it is requested to you to kindly consider the data up to 12 months.
6.	**3.2.P.8.3**	Record of Digital data logger for temperature and humidity monitoring of stability chambers (accelerated) shall be submitted.	Submitted.

Decision: Approved with innovator's specifications. The firm will submit fee of Rs. 7,500/- for revision of specifications as pre-registration variation fee as per notification No.F.7-11/2021-B&A/DRAP dated 07-05-2021.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

521.	Name, address of Applicant / Marketing Authorization Holder	M/s Vision Pharmaceuticals (Pvt) Ltd Plot No 22-23, Industrial Triangle kahuta road Islamabad
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt) Ltd Plot No 22-23, Industrial Triangle kahuta road Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.27311 dated 04/10/2021
	Details of fee submitted	PKR 30,000/-: dated 29/08/2021 (#94527609874)
	The proposed proprietary name / brand name	Lurasidone HCl 80mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Lurasidone HCl……80mg
	Pharmaceutical form of applied drug	Yellow color, round shaped film coated tablet
	Pharmacotherapeutic Group of (API)	Atypical Anti- Psychotics
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	2 ×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lurasidone HCl 80mg Tablet by M/s Sunovion Pharma Inc, USFDA Approved.
	For generic drugs (me-too status)	Lurisa Tablet 40mg (Lurasidone HCl) tablet by Helix Pharma, Reg. No. 089359
	GMP status of the Finished product manufacturer	license granted on 25/02/2019 Tablet (General) section approved.
	Name and address of API manufacturer.	M/s Solara Active Pharma Sciences Limited R. S. No. 33 & 34, Mathur Road, Periyakalapet Puducherry -605 014, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Paroxetine Hydrochloride is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (LDH-P 20001, LDH-P 20002, LDH-P 20003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is LURISA 40mg Tablet by Helix Pharmaceuticals (Pvt) Ltd by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is LURISA 40mg Tablet by Helix Pharmaceuticals (Pvt) Ltd in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		

Manufacturer of API	M/s Solara Active Pharma Sciences Limited., R. S. No. 33 & 34, Mathur Road, Periyakalapet Puducherry -605 014, India		
API Lot No.	PLHP200002		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	NDP-221 T-01	NDP-221 T-02	NDP-221 T-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	03-2021	03-2021	03-2021
Date of Initiation	15-04-2021	16-04-2021	16-04-2021
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 286th meeting decided to approve registration of Sofovir-V 400mg/100mg Tablet.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. DDC/Solara/WHO-GMP/2021-22/06 in the name of M/s Solara Active Pharma Sciences Limited., R. S. No. 33 & 34, Mathur Road, Periyakalapet Puducherry -605 014, India Valid up to 03-12-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of ADC (I&E) granted by DRAP dated on 21/08/2020
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.#	Section#	Observation	Reply of firm
1.	**1.3.5**	Firm has provided GMP certificate based on the inspection and evaluation conducted on 11-02-2019. Which is valid until 10-02-2022. Valid GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be provided.	Firm has provided GMP certificate based on the inspection and evaluation conducted on 11-02-2019. Which is valid until 10-02-2022.
2.	**1.6.5**	**Provided GMP Certificates OF Drug Substance manufacturer are expired. Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin shall be provided.**	**Submitted**
3.	**3.2.S.4**	In Analytical method of Drug Substance assay is performed with following HPLC conditions: Wavelength 205nm Column temperature 50^{o}C Injection volume 20µl Autosampler temperature 8 ^{o}C Run time 30minutes Colum Intersil ODS-3V 150X4.6 mm, 5um Mobile Phase: Solution A (1.32 g of Di ammonium hydrogen phosphate in 1000 ml water and adjust pH 3.6±0.05 with orthophosphoric acid. Solution B (Acetonitrile and Methanol (600:400v/v) Solution A and B(50:50v/v) Whereas in analytical method of M/s Vision Pharmaceutical Pvt. Ltd. Document no. QC/STM/142 HPLC conditions for assay are as follows: Detector 230 nm Column 4.6-mmX 25cm ; 5-um packing L1 Flow rate 1ml/min Injection size 20 µl Temperature Ambient. Mobile phase Acetonitrile : Phosphate buffer pH 7.00 (25:15). Justification required for changing the method.	As the drug substance is non pharmacopeial we adopted the method as mentioned in SOP QC/STM/142. As Initially samples from different sources were taken and tested. We had tested the Raw material as per supplier method (solara Active Pharma Sciences) as mentioned. At the same time we also received sample from China source Jiangsu Yongan Pharmaceutical Co. Ltd and we also tested its material as well. Results of both the samples were same on the same. Now We are submitting Solara's method tested by Vision for your reference. Revised method submitted
4.	**3.2.S.4.**	Analytical Method validations studies for drug substances performed by Drug product manufacturer are missing.	Submitted
5.	**3.2.S.7.**	Data of real time stability of drug substances is provided for 12 months only. Whereas as per certificate of analysis firm is claiming shelf life of 04 years. Data for real time stability studies shall be submitted.	Submitted
6.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies & CDP against the innovator product.	As per DRAP Guideline in 293rd DRB meeting we can use Innovator/Reference/Comparator product for Pharmaceutical

			Equivalence. We use comparator product for pharmaceutical Equivalence as product is market leader and DRAP approved.
7.	**3.2.P.8.1**	• Stability studies data is provided for only 2 batches for accelerated stability studies and real time stability studies. Stability data of 03 batches shall be provided. • Firm has provided stability data for only 03 months for accelerated stability studies and real time stability studies.	Submitted
8.	**3.2.P.8.3**	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3	Submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit latest GMP inspection report/ GMP Certificate of finished drug product manufacturer before issuance of registration letter.**

522.	Name, address of Applicant / Marketing Authorization Holder	M/s Vision Pharmaceuticals (Pvt) Ltd Plot No 22-23, Industrial Triangle kahuta road Islamabad
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt) Ltd Plot No 22-23, Industrial Triangle kahuta road Islamabad
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.27310 dated 04/10/2021
	Details of fee submitted	PKR 30,000/-: dated 30/09/2021 (#7873822278)
	The proposed proprietary name / brand name	Lurasidone HCl 40mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Lurasidone HCl……40mg
	Pharmaceutical form of applied drug	Yellow color, round shaped film coated tablet
	Pharmacotherapeutic Group of (API)	Atypical Anti- Psychotics
	Reference to Finished product specifications	Innovator Specifications

	Proposed Pack size	2 ×10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	LATUDA (LURASIDONE HYDROCHLORIDE) Film coated Tablet by M/s Sunovion Pharma Inc, USFDA Approved.
	For generic drugs (me-too status)	Lurisa Tablet 40mg (Lurasidone HCl) tablet by Helix Pharma, Reg. No. 089358
	GMP status of the Finished product manufacturer	Firm has provided GMP certificate based on the inspection and evaluation conducted on 11-02-2019. Which is valid until 10-02-2022. Tablet (General) section approved.
	Name and address of API manufacturer.	M/s Solara Active Pharma Sciences Limited R. S. No. 33 & 34, Mathur Road, Periyakalapet Puducherry -605 014, India
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted detail of nomenclature, structure, general properties, solubility, manufacturers, description of manufacturing process and controls, tests for impurities & related substances, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substances.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (LDH-P 20001, LDH-P 20002, LDH-P 20003)
	Module-III (Drug Product):	The firm has submitted detail of description & composition of the drug product, manufacturer, description of manufacturing process and controls, impurities, specifications, analytical procedure and its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is LURISA 40mg

		Tablet by Helix Pharmaceuticals (Pvt) Ltd by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is LURISA 40mg Tablet by Helix Pharmaceuticals (Pvt) Ltd in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Solara Active Pharma Sciences Limited., R. S. No. 33 & 34, Mathur Road, Periyakalapet Puducherry -605 014, India		
API Lot No.	PLHP200002		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	NDP-220 T-01	NDP-220 T-02	NDP-220 T-03
Batch Size	1500 tab	1500 tab	1500 tab
Manufacturing Date	12-2020	01-2021	01-2021
Date of Initiation	19-01-2021	16-02-2021	15-02-2021
No. of Batches	03		

REQUEST OF EXEMPTION FROM ON SITE INSPECTION

The firm has requested for Exemption from On-site Investigation of their submitted stability data and provided the following documents in conjunction with the checklist approved by the Registration Board.

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has referred to previous inspection of stability data of the same dosage form on the basis of which Registration Board in 286th meeting decided to approve registration of Sofovir-V 400mg/100mg Tablet.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. DDC/Solara/WHO-GMP/2021-22/06 in the name of M/s Solara Active Pharma Sciences Limited., R. S. No. 33 & 34, Mathur Road, Periyakalapet Puducherry -605 014, India Valid up to 03-12-2024.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of ADC (I&E) granted by DRAP dated on 21/08/2020

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Sr.#	Section#	Observation	Reply of firm
1.	**1.3.5**	Firm has provided GMP certificate based on the inspection and evaluation conducted on 11-02-2019. Which is valid until 10-02-2022. Valid GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be provided.	Firm has provided GMP certificate based on the inspection and evaluation conducted on 11-02-2019. Which is valid until 10-02-2022.
2.	**1.6.5**	**Provided GMP Certificates OF Drug Substance manufacturer are expired. Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin shall be provided.**	**Submitted**
3.	**3.2.S.4**	In Analytical method of Drug Substance assay is performed with following HPLC conditions: Wavelength 205nm Column temperature 50^{o}C Injection volume 20µl Autosampler temperature 8 ^{o}C Run time 30minutes Colum Intersil ODS-3V 150X4.6 mm, 5um Mobile Phase: Solution A (1.32 g of Di ammonium hydrogen phosphate in 1000 ml water and adjust pH 3.6±0.05 with orthophosphoric acid. Solution B (Acetonitrile and Methanol (600:400v/v) Solution A and B(50:50v/v) Whereas in analytical method of M/s Vision Pharmaceutical Pvt. Ltd. Document no. QC/STM/142 HPLC conditions for assay are as follows: Detector 230 nm Column 4.6-mmX 25cm ; 5-um packing L1 Flow rate 1ml/min Injection size 20 µl Temperature Ambient. Mobile phase Acetonitrile : Phosphate buffer pH 7.00 (25:15).	As the drug substance is non pharmacopeial we adopted the method as mentioned in SOP QC/STM/142. As Initially samples from different sources were taken and tested. We had tested the Raw material as per supplier method (solara Active Pharma Sciences) as mentioned. At the same time we also received sample from China source Jiangsu Yongan Pharmaceutical Co. Ltd and we also tested its material as well. Results of both the samples were same on the same. Now We are submitting Solara's method tested by Vision for your reference. Revised method submitted

		Justification required for changing the method.	
4.	**3.2.S.4.**	Analytical Method validations studies for drug substances performed by Drug product manufacturer are missing.	Submitted
5.	**3.2.S.7.**	Data of real time stability of drug substances is provided for 12 months only. Whereas as per certificate of analysis firm is claiming shelf life of 04 years. Data for real time stability studies shall be submitted.	Submitted
6.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies & CDP against the innovator product.	As per DRAP Guideline in 293rd DRB meeting we can use Innovator/Reference/Comparator product for Pharmaceutical Equivalence. We use comparator product for pharmaceutical Equivalence as product is market leader and DRAP approved.
7.	**3.2.P.8.1**	• Stability studies data is provided for only 2 batches for accelerated stability studies and real time stability studies. Stability data of 03 batches shall be provided. • Firm has provided stability data for only 03 months for accelerated stability studies and real time stability studies.	Submitted
8.	**3.2.P.8.3**	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3	Submitted

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit latest GMP inspection report/ GMP Certificate of finished drug product manufacturer before issuance of registration letter.**

523.	Name, address of Applicant / Marketing Authorization Holder	M/s Medisure Laboratories (Pvt.) Ltd A-115, S.I.T.E., Super Highway, Karachi, Pakistan
	Name, address of Manufacturing site.	M/s Medisure Laboratories (Pvt.) Ltd A-115, S.I.T.E., Super Highway, Karachi, Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)

	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32413 dated 29/11/2021
	Details of fee submitted	PKR 30,000/-: dated 07/06/2021
	The proposed proprietary name / brand name	Laruda 80mg/Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each film coated tablet contains: Lurasidone Hydrochloride……85.904 mg (Equivalent to Lurasidone ……80mg)
	Pharmaceutical form of applied drug	light yellow colored, round, biconvex, film coated tablet bisecting line on one side and other side is plain
	Pharmacotherapeutic Group of (API)	Atypical Antipsychotic
	Reference to Finished product specifications	In-house Specifications
	Proposed Pack size	2 x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Latuda 80mg tablet by Sunovion Pharmaceuticals, Inc, USFDA Approved.
	For generic drugs (me-too status)	Lurisa 80 mg Tablet by Helix Pharma (Pvt) Ltd., Reg. No. 089359
	GMP status of the Finished product manufacturer	New license granted on 30/09/2019 Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	JIANGSU YONGAN PHARMACEUTICAL CO., LTD., No. 18, 237 Provincial Road, Economic Development Zone, Huaian, Jiangsu Province, China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	official monograph of lurasidone hydrochloride is not present in USP. the firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity d, g & related substances (impurity a & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug

		substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 12 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: 101101,101201,101202 for Real time Batches:101101,101201,101202 for Accelerated
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile Lurisa 80 mg Tablet by Helix Pharma (Pvt) Ltd.,	Pharmaceutical Equivalence have been established against the brand leader that is Lurisa 80 mg Tablet by Helix Pharma (Pvt) Ltd., (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Lurisa 80 mg Tablet by Helix Pharma (Pvt) Ltd., in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Jiangsu yongan pharmaceutical co., ltd., no. 18, 237 provincial road, economic development zone, huaian, jiangsu province, china		
API Lot No.	0200-201909001		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time:24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6,9,12 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	0.23 Kg	0.23 Kg	0.23 Kg
Manufacturing Date	09/2020	09-2020	09-2020
Date of Initiation	28-09-2020	28-10-2022	28-10-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Not submitted
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has provided Commercial invoice no. ZY19111101G/W, dated 11-11-2019
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section#	Observation	Reply of firm
1.	**1.3.5**	Firm has provided GMP certificate based on the inspection and evaluation conducted on 30-09-2019. Which is valid until 29-09-2021. Valid GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be provided.	
2.	**1.5.2.**	Firm has mentioned label claim Lurisadone Hydrochloride …85.904 mg (Eqivalent to Lurisadone ….80 mg). However, Innovator is using Lurisadone Hydrochloride…. 80 mg. Justification required.	
3.	**1.6.5**	**Provided GMP Certificates of Drug Substance manufacturer is not traceable. Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin shall be provided.**	
4.	**3.2.P.2**	As the qualitative composition of the formulation is not similar to innovator / reference product compatibility studies of the Drug Substance(s) with excipients shall be provided.	
5.	**3.2.S.4**	In Analytical method of Drug Substance is missing along with Method Validation. Justification required for changing the method.	

6.	**3.2.S.4.**	Analytical Method validations studies for drug substances performed by Drug product manufacturer are missing.	
7.	**3.2.S.7.**	Data of real time stability of drug substances is provided for 12 months only. Whereas as per certificate of analysis firm is claiming shelf life of 02 years. Data for real time stability studies shall be submitted.	
8.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies & CDP against the innovator product.	
9.	**3.2.P.8.1**	• In Stability Studies Batch size is 0.230 kg. Justification required. • In batch no. T-001, significant change of more than 5 % in assay has been observed in accelerated and real time stability data sheets.	•
10.	**3.2.P.8.3**	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3	

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

524.	Name, address of Applicant / Marketing Authorization Holder	M/s Daneen Pharma Private Limited 27-Sundar Industrial Estate, Sundar Raiwind Road, Lahore
	Name, address of Manufacturing site.	M/s Daneen Pharma Private Limited 27-Sundar Industrial Estate, Sundar Raiwind Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ **Is involved in none of the above (contract giver)**
	Status of application	☐ **New Drug Product (NDP)** ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ **Domestic and Export sales**
	Dy. No. and date of submission	Dy. No. 34242 dated 31/12/2021
	Details of fee submitted	PKR 30,000/-: dated 24/11/2021, Slip number 34264783007
	The proposed proprietary name / brand name	Zalpaz Injection 500mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Cefoperazone Sodium eq. to Cefoperazone ….250mg

		Sulbactam Sodium eq. to Sulbactam….250mg (JP specifications)
	Pharmaceutical form of applied drug	Intravenous
	Pharmacotherapeutic Group of (API)	Antibiotic
	Reference to Finished product specifications	Japanese Pharmacopoeia
	Proposed Pack size	1's
	Proposed unit price	As per PRC
	The status in reference regulatory authorities	Cefocef Injection by M/s Sawai Pharmaceutical Japan Approved.
	For generic drugs (me-too status)	Xorbact Injection by Curexa Health Private Limited, Reg no: 082734
	GMP status of the Finished product manufacturer	New GMP granted on 03/04/2019 Cephalosporin section approved.
	Name and address of API manufacturer.	Shandong Luoxin Pharmaceutical Group Hengxin Pharmaceutical Co., Ltd.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Cefoperazone+Sulbactam are non-pharmacopeial. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity & related substances, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (11C0311702001, 11C0311702002 & 11C0311702003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure, its validation studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Xorbact Injection

		(B#2080197) by M/s Highnoon Laboratories Pvt. Ltd by performing quality tests (Identification, Appearance, Reconstitution, pH) CDP N/A		
	Analytical method validation/verification of product	Method validation studies have been submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		Shandong Luoxin Pharmaceutical Group Hengxin Pharmaceutical Co., Ltd., West side of yanbin Road , Economic Development Zone , Feixian, Linyi, Shandong, China.		
API Lot No.		11C0312011001		
Description of Pack (Container closure system)		Clear glass Vial		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0,3 6 (Months) Real Time: 0,3, 6, (Months)		
Batch No.		001IT001	002IT001	003IT003
Batch Size		120 Vials	120 Vials	120 Vials
Manufacturing Date		10-03-2021	10-03-2021	07-04-2021
Date of Initiation		25-03-2021	25-03-2021	21-04-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	Not provided		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate valid till 30/08/2022		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of Purchase invoice dated 05/01/2021 is submitted		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted		

Remarks OF Evaluator:

Sr.#	Section#	Observation
1.	**1.3.5**	Firm has provided GMP Certificate which is valid until 07-03-2022 based on evaluation conducted on 08-03-2019.GMP inspection report/ GMP certificate of the manufacturing unit issued within the last three years shall be submitted.
2.	**1.6.5**	Provide valid GMP Certificate of drug substance manufacturer.
3.	**3.2.S.4**	• In Analytical Method drug substance manufacturer water limit is not more than 3 %. Whereas in Japanese Pharmacopoeia it is not more than 1.0 %. Justification required. Analytical procedure of drug substance manufacturer is in complete. • Analytical Method validation studies for drug substance are missing.
4.	**3.2.S.7**	In stability studies of Drug substance manufacturer data for 2-year real time stability studies has been provided. However as per COA DS manufacturer is claiming 3 years shelf life. 3 years real time stability data is required.
5.	**2.3.P.1**	Justification of overages in the formulation(s) described in 2.3.P.1
6.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies & CDP against the innovator product.
7.	**3.2.P.7**	• In Section 3.2.P.1. Type of Container Closure System is Type 1. Whereas in Section 3.2.P.8 T Is Mentioned USP Type III vials mentioned. Justification required. • Justification required for usage of USP Type- III glass for injectable.
8.	**3.2.P.8.**	• Justification required for not including sterility and bacterial Endotoxin testing in stability studies. • Justification required regarding batch size of 120 vials in stability studies. • Submit clear/readable copies of chromatograms, Raw data sheets.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

Case No.03 Registration applications of local manufacturing of human drugs submitted on CTD format (New Section)

The central licensing Board in its 282nd meeting held on 31-08-2021 has considered and approved the grant of Drug Manufacturing License by way of formulation with following five sections in the name of M/s Fleming Pharmaceutical, 23- Km Lahore- Sheikhupura Road, Lahore..

i. Oral Dry powder suspension (Penicillin)
ii. Capsule (Penicillin)
iii. Tablet (Penicillin)
iv. Dry Powder injectable(Penicillin)
v. Dry powder injectable (Carbapenem)

525.	Name, address of Applicant / Marketing Authorization Holder	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Name, address of Manufacturing site.	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale

		☐ Export sale ☒ **Domestic and Export sales**
	Dy. No. and date of submission	Dy. No. 23969 dated 24/08/2022
	Details of fee submitted	PKR 30,000/-: dated 12/08/2022(69080973)
	The proposed proprietary name / brand name	Flementin Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Amoxicillin (as Amoxicillin sodium) 1000 mg and Clavulanic acid (as Potassium Clavulanate) 200 mg.
	Pharmaceutical form of applied drug	Vial
	Pharmacotherapeutic Group of (API)	Penicillin antibacterial + beta-lactamase inhibitor
	Reference to Finished product specifications	BP Specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Augmentin Intravenous Injection by M/s GSK, MHRA Approved.
	For generic drugs (me-too status)	Calamox Injection by M/s Bosch Pharma, Reg. No. 021507
	GMP status of the Finished product manufacturer	New license granted on 14/09/2021 Dry Powder Injectable (Penicillin)
	Name and address of API manufacturer.	SinoPharm Weiqida Pharmaceutical Co. Ltd. Economic & Technological Development Zone, First Medical Zone, Datong Shanxi.China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm is submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 48 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months Batches: (47SA1705019, 59SA1707013, 63SA1709013)

	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader Stamentin Injection 1200 mg by Stallion Pharma (Batch M1003) by performing quality tests (Identification, Assay, Sterility etc.).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	SinoPharm Weiqida Pharmaceutical Co. Ltd. Economic & Technological Development Zone, First Medical Zone, Datong Shanxi.China		
API Lot No.	47SA2106040		
Description of Pack (Container closure system)	Flementin injection is filled in Glass vial further packed in unit carton along with patient leaflet insert		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003
Batch Size	1700 Vial	1700 Vial	1700 Vial
Manufacturing Date	02-2022	02-2022	02-2022
Date of Initiation	26-02-2022	26-02-2022	26-02-2022
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	New DML granted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SX20180229 issued by SFDA valid till 05/06/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of Commercial Invoice with Assistant Director DRAP signatures No.538/2022/DRAP dated 12-01-22 is submitted for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms,	Submitted

	Raw data sheets, COA, summary data sheets etc.	
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.no.	Section	Observationss
1.	**3.2.S.4**	• In analytical method conditions for HPLC testing are not in accordance with the conditions of Drug Substance manufacturer. • In analytical testing penicillanse are not used in sterility testing, in accordance with Pharmacopoeia and analytical method of drug substance manufacturer.
2.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies against the innovator product.
3.	**3.2.P.5.2**	In official pharmacopoeia (BP) reference standard are lithium clavulante and amoxicillin trihydrate. Whereas in analytical method of drug product manufacturer amoxicillin and clavulanic acid are used as working standard. justification required**.**
4.	**3.2.P.5.2**	In analytical method validation of drug product justification is required regarding limits of Mean recovery %age in accuracy, repeatability and intermediate precision etc. (i.e. limit of Mean recovery %age for 120 % concentration is 108-144.0%).
5.	**3.2.P.7**	• A detail of the container closure systems, description of the primary container closure systems, including materials of construction, unit count or fill size, container size or volume shall be provided. Please also provide USP type of glass vials. • In BMR it is mentioned that 20 cc glass vials have been used. However, innovator is using 25 or 50 ml vial. Furthermore, Co Amoxiclave 1000 mg/200 mg should be dissolved in 20 ml of solvent. This yields approximately 20.9 ml of solution for single-dose use. Justification required. • In BMR of Co-amoxiclave 600 mg Glass Vials Type III (10cc) are mentioned). Whereas in Section 3.2.P.1 it is Type-II Glass vials. Justification required.
6.	**3.2.P.8**	• Firm has provided stability data for only 03 months for accelerated stability studies and real time stability studies. • Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing. • Sterility testing is not included in stability data and Pharmaceutical equivalence studies. • Stability record of T-002 Batch of Co-amoxiclave 600 mg injection missing.

		• In stability data sheets resolution has not been calculated as per the official pharmacopeia i.e. BP. • Record of Digital data logger for temperature and humidity monitoring of stability chambers and audit trail reports on product testing for complete testing periods are missing.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

526.	Name, address of Applicant / Marketing Authorization Holder	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Name, address of Manufacturing site.	M/s Fleming Pharmaceutical. 23- Km Lahore- Sheikhupura Road, Lahore.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ **Domestic and Export sales**
	Dy. No. and date of submission	Dy. No. 23968 dated 24/08/2022
	Details of fee submitted	PKR 30,000/-: dated 16/08/2022(34449438664)
	The proposed proprietary name / brand name	Flementin Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Vial contains: Amoxicillin (as Amoxicillin sodium) 500 mg and Clavulanic acid (as Potassium Clavulanate) 100 mg.
	Pharmaceutical form of applied drug	Vial
	Pharmacotherapeutic Group of (API)	Penicillin antibacterial + beta-lactamase inhibitor
	Reference to Finished product specifications	BP Specification
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Augmentin Intravenous Injection by M/s GSK, MHRA Approved.
	For generic drugs (me-too status)	Calamox Injection by M/s Bosch Pharma, Reg. No. 021507
	GMP status of the Finished product manufacturer	New license granted on 14/09/2021 Dry Powder Injectable (Penicillin)
	Name and address of API manufacturer.	SinoPharm Weiqida Pharmaceutical Co. Ltd. Economic & Technological Development Zone, First Medical Zone, Datong Shanxi.China
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to

		nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm is submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 48 months Accelerated: 25°C ± 2°C / 60% ± 5%RH for 6 months Batches: (47SA1705019, 59SA1707013, 63SA1709013)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader Stamentin Injection 1200 mg by Stallion Pharma (Batch L00001) by performing quality tests (Identification, Assay, Sterility etc.).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	SinoPharm Weiqida Pharmaceutical Co. Ltd. Economic & Technological Development Zone, First Medical Zone, Datong Shanxi.China		
API Lot No.	47SA2106040		
Description of Pack (Container closure system)	Flementin injection is filled in Glass vial further packed in unit carton along with patient leaflet insert		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	T-001	T-002	T-003

Batch Size	1700 Vial	1700 Vial	1700 Vial
Manufacturing Date	02-2022	02-2022	02-2022
Date of Initiation	26-02-2022	26-02-2022	26-02-2022
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	New DML granted.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SX20180229 issued by SFDA valid till 05/06/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of Commercial Invoice with Assistant Director DRAP signatures No.538/2022/DRAP dated 12-01-22 is submitted for the purpose of test/analysis and stability studies is granted.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

S.no.	Section	Observations	
1.	**3.2.S.4**	• In analytical method conditions for HPLC testing are not in accordance with the conditions of Drug Substance manufacturer. • In analytical testing penicillanse are not used in sterility testing, in accordance with Pharmacopoeia and analytical method of drug substance manufacturer.	
2.	**3.2.P.2.2.1**	Justification shall be submitted for not performing Pharmaceutical equivalence studies against the innovator product.	
3.	**3.2.P.5.2**	In official pharmacopoeia (BP) reference standard are lithium clavulante and amoxicillin trihydrate. Whereas in analytical method of drug product manufacturer amoxicillin and clavulanic acid are used as working standard. justification required**.**	

4.	**3.2.P.5.2**	In analytical method validation of drug product justification is required regarding limits of Mean recovery %age in accuracy, repeatability and intermediate precision etc. (i.e. limit of Mean recovery %age for 120 % concentration is 108-144.0%).	
5.	**3.2.P.7**	• A detail of the container closure systems, description of the primary container closure systems, including materials of construction, unit count or fill size, container size or volume shall be provided. Please also provide USP type of glass vials. • In BMR it is mentioned that 20 cc glass vials have been used. However, innovator is using 25 or 50 ml vial. Furthermore, Co Amoxiclave 1000 mg/200 mg should be dissolved in 20 ml of solvent. This yields approximately 20.9 ml of solution for single-dose use. Justification required. • In BMR of Co-amoxiclave 600 mg Glass Vials Type III (10cc) are mentioned). Whereas in Section 3.2.P.1 it is Type-II Glass vials. Justification required.	•
6.	**3.2.P.8**	• Firm has provided stability data for only 03 months for accelerated stability studies and real time stability studies. • Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc. • Compliance Record of HPLC software 21CFR & audit trail reports on product testing. • Sterility testing is not included in stability data and Pharmaceutical equivalence studies. • Stability record of T-002 Batch of Co-amoxiclave 600 mg injection missing. • In stability data sheets resolution has not been calculated as per the official pharmacopeia i.e. BP. • Record of Digital data logger for temperature and humidity monitoring of stability chambers and audit trail reports on product testing for complete testing periods are missing.	•

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

Agenda of Evaluator (Mr. Ahsan Hafiz)

Case no. 4. Registration applications of local manufacturing of human drugs submitted on CTD format (Deferred cases)

527.	Name, address of Applicant / Marketing Authorization Holder	M/s Hansel Pharmaceuticals Private Limited, Plot No. 02, Pharma City, 30-km Multan Road, Lahore-Pakistan.
	Name, address of Manufacturing site.	M/s Hansel Pharmaceuticals Private Limited, Plot No. 02, Pharma City, 30-km Multan Road, Lahore-Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 24079 Dated 01-09-2021
	Details of fee submitted	PKR 20,000/- Dated 28-08-2020 PKR 10,000/- (Bank slip #6614935760)
	The proposed proprietary name / brand name	Femipla-Ject Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 1mL ampoule contains: Norethisterone Enanthate……..50mg Estradiol Valerate……..5mg
	Pharmaceutical form of applied drug	Oily solution for Injection (IM)
	Pharmacotherapeutic Group of (API)	Progestogens (Contraceptive) ATC Code: G03AC
	Reference to Finished product specifications	Hansel Specifications
	Proposed Pack size	1ml × 1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Estradiol valerate/Norethisterone enantate Solution for injection 5mg/50mg/mL (WHO prequalified product).
	For generic drugs (me-too status)	FEMI-JECT Injection by M/s Bayer pharma (Pvt.) Ltd. Lahore, (Reg # 022372).
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 15-05-2019. The firm has provided Liquid Injectable Hormone section.
	Name and address of API manufacturer.	**Norethisterone Enanthate:** M/s Zhejiang Xianju Junye Pharmaceutical Co., Ltd.,

		No.1 Lingxiu Road, Modern Industrial Centralization zone, Xianju, Taizhou, Zhejiang, China. **Estradiol Valerate:** M/s ASG. Biochem Pvt. Ltd., Ganganagar, 24 Parganas, West Bengal India.
	Module-II (Quality Overall Summary)	The firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubility's, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm has submitted details of nomenclature, structure, general properties, solubility, physical form, manufacturers, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substances (Norethisterone Enanthate+ Estradiol Valerate).
	Stability studies	**Norethisterone Enanthate:** Stability study conditions: Real time: 30°C±2°C/65% ± 5%RH for 24 months. Accelerated: 40°C±2°C/75%±5%RH for 6 months. Batches: (30761308001, 30761308002, 30761308003). **Estradiol Valerate**: Stability study conditions: Real time: 30°C±2°C/65% ± 5%RH for 48 months. Accelerated: 40°C±2°C/75%±5%RH for 6 months. Batches: (ESVZ01A002, ESVZ01A005, ESVZ01A006).
	Module-III (Drug Product):	The firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system

		and stability.	
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the comparator product Femi-Ject by Bayer Pharma by performing quality tests (Identification, Assay, pH, Particulate matter, Sterility). Dissolution profile in not applicable in Femipla-Ject Injection.	
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.	
STABILITY STUDY DATA			
Manufacturer of API	**Norethisterone Enanthate:** M/s Zhejiang Xianju Junye Pharmaceutical Co., Ltd., No.1 Lingxiu Road, Modern Industrial Centralization zone, Xianju, Taizhou, Zhejiang, China. **Estradiol Valerate:** M/s ASG. Biochem Pvt. Ltd., Ganganagar, 24 Parganas, West Bengal India.		
API Lot No.	Norethisterone Enanthate: 3076190701M Estradiol Valeartae: ESVZ01A016		
Description of Pack (Container closure system)	1 amber color ampoule of 1mL packed in unit carton along with disposable syringe, alcohol swab and a leaflet.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	FT-001	FT-002	FT-003
Batch Size	2000 Ampoules	2000 Ampoules	2000 Ampoules
Manufacturing Date	10-2019	10-2019	10-2019
Date of Initiation	08-10-2019	10-10-2019	12-10-2019
No. of Batches	03		
Administrative Portion			
1.	Reference of previous approval of applications with stability study data of the firm (if any)	It is the submission of first dossier on CTD format, thus no inspection conducted regarding stability studies of the applied product.	
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	**Norethisterone Enanthate:** The firm has submitted copy of GMP certificate for M/s Zhejiang Xianju Junye Pharmaceutical Co. issued by national medical products administration valid till 29-11-2024. **Estradiol valerate:** The firm has submitted copy of GMP certificate for M/s ASG Biochem Pvt. Ltd. issued by Director of Drugs Control, Govt. of West Bangal. The license is valid till 24-10-2024.	

3.	Documents for the procurement of API with approval from DRAP (in case of import).	**Norethisterone Enanthate**: The firm has submitted copy of invoice specifying import of Norethisterone enanthate 20gm (Batch # 3076190701M) attested by Assistant Director (I & E) Lahore dated 30-09-2019. **Estradiol Valerate:** The firm has submitted copy of invoice specifying import of estradiol valerate 20gm (Batch # 190401) attested by Assistant Director (I & E) Lahore dated 01-08-2019.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, raw data sheets, COA, summary data sheets etc.	The firm has submitted data of stability batches supported by attested respective documents like chromatograms, raw data sheets, COA, summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Not applicable.
6.	Record of digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).

Remarks of Evaluator:

Sr. No.	Observations	Response by the firm
1.	Provide copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug substance & Drug Product manufacturer.	The firm has provided copies of drug substance specifications and analytical procedures.
2.	Provide certificate of Analysis (CoA) of the drug substance (Estradiol valerate) from drug substance manufacturer.	The firm has submitted certificate of analysis of Estradiol valerate from drug substance manufacturer.
3.	Provide the details of the reference product including batch number, manufacturing date and expiry date.	The firm has submitted details of reference product: Name: FEMI-JECT Injection Batch number: MP06249 Mfg date: 09-2019 Expiry date: 09-2024
4.	Justify why you have not performed the tests of clarity of solution and bacterial endotoxin in the pharmaceutical equivalence study.	Not submitted
5.	Justify why tests of pH and ampoule sealing are included in specifications under analytical procedures (3.2.P.5.2). Moreover, provide the pharmacopoeial reference where the test of "ampoule sealing" is mentioned	Not submitted
6.	Justify the test of pH throughout stability studies for development batches of oily injection.	Not submitted

7.	Reference of previous approval of applications with stability study data of the firm (if any).	The firm has submitted previous approvals of products in this section.
8.	Submit compliance Record of HPLC software 21CFR. The submitted audit trail reports do not specify the software used in HPLC and further clarify the demo version of software.	The firm has not submitted audit trail record of HPLC software 21 CFR.

Decision of 321st meeting of registration board: Deferred for following:

- Evidence of required manufacturing facility / section from Licensing Division.
- Scientific justification for not performing the tests of clarity of solution and bacterial endotoxin in the pharmaceutical equivalence study.
- Scientific justification for the test and limits of pH and ampoule sealing test for oily injection.
- Scientific justification for performing the test of pH throughout stability studies for development batches of oily injection.

Sr. No.	Observations	Response by the firm
1.	Evidence of required manufacturing facility / section from Licensing Division.	Firm has provided approval of revised section namely Liquid Injectable (Hormone) (Reallocated from list floor to ground floor), vide letter no. F. 1-9/2001-Lic(Vol-II), dated 03-10-2019
2	Scientific justification for not performing the tests of clarity of solution and bacterial endotoxin in the pharmaceutical equivalence study.	Firm has provided Pharmaceutical equivalence study with test of clarity of solution and Bacterial endotoxin tests.
3	Scientific justification for the test and limits of pH and ampoule sealing test for oily injection.	pH & ampoule sealing are included in specifications under analytical procedure (3.2.P.5.2) Because product is non-pharmacopoeial, so in-house specifications are used for pH to control process of manufacturing. Whereas ampoules sealing test is used to verify sealing integrity of container closure to maintain sterility of product.
4	Scientific justification for performing the test of pH throughout stability studies for development batches of oily injection.	The product is non-pharmacopoeial so in-house specifications are used for pH throughout stability studies for development batches of oily injection to control process of manufacturing.

Decision: Registration Board decided to defer the case for further deliberation against the quality parameters and specifications of innovator's drg product.

528.	Name, address of Applicant / Marketing Authorization Holder	M/s Nagarsons Pharmaceuticals (Pvt) Ltd, Plot # 34, Street No. NS-2, National Industrial Zone, Rawat, Islamabad.
	Name, address of Manufacturing site.	M/s Vision Pharmaceuticals (Pvt.) Ltd, Plot # 22-23, Industrial triangle, Kahuta Road, Islamabad
	Status of the applicant	☐ Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)

	GMP status of the firm	**M/s Nagarsons Pharmaceuticals:** The firm is inspected on 23-05-2019 which concluded that overall GMP compliance could be graded as Good for visited sections as of today. The firm has provided 8 sections. **M/s Vision Pharmaceuticals:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	**M/s Vision Pharmaceuticals:** The firm has provided sterile Dry powder injection vials (General).
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8314: 15-03-2021
	Details of fee submitted	PKR 50,000/-: 07-01-2021
	The proposed proprietary name / brand name	Nagzole 40mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Omeprazole sodium eq. to Omeprazole (as lyophilized powder) …….40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Omeprazole 40mg powder for solution for infusion of M/s Sandoz Novartis (MHRA approved)
	For generic drugs (me-too status)	Risek Injection 40mg of M/s Getz Pharma Pakistan
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals (Pvt.) Ltd. Semi-basic Plant (DML # 000806). Plot No. 22-23, Industrial Triangle Kahuta Road, Islamabad.
	Module-II (Quality Overall Summary)	Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process

		validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module-III Drug Substance:	The firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Firm has submitted stability study data of 3 batches of drug substance at both accelerated as well as real time conditions. The accelerated stability data is conducted at 40°C ± 2°C / 75% ± 5% RH for 6 months. The real time stability data is conducted at 30°C ± 2 °C / 65% ± 5% RH for 36 months.
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols and report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence	The firm has performed pharmaceutical equivalence of the developed formulation Rapid 40mg Injection (B#2005707) and comparator product (B # 789P06) of M/s GETZ Pharma. Quality tests of both products including physical appearance, solubility, water content, pH and assay were compared.
	Analytical method validation/verification of product	Firm has submitted analytical method validation report of drug substance. Firm has submitted analytical method validation report of applied product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Vision Pharmaceuticals (Pvt.) Ltd. Semi-basic Plant (DML # 000806). Plot No. 22-23, Industrial Triangle Kahuta Road, Islamabad.
API Lot No.	1702901 1702902 1702903
Description of Pack (Container closure system)	Glass vial
Stability Storage Condition	Real Time: 30°C ± 2°C / 65% ± 5%RH

	Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Rapid 40mg I.V Injection			
Batch No.	1803707	1803708	1803709
Batch Size	10,000 vials	10,000 vials	10,000 vials
Manufacturing Date	03-2018	03-2018	03-2018
Date of Initiation	03-2018	03-2018	03-2018
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

#	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm (if any)	NA
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has procured material from their semi basic manufacturing facility.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Firm has submitted record of testing of all batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted audit trail on testing reports of product.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.

Sr. No.	Observations communicated	Response by the firm
1.	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	The firm has submitted analytical method verification report from M/s Vision Pharmaceuticals Pvt, Ltd. Islamabad.
2.	Certificate of analysis of both drug substance manufacturer and drug product manufacturer are required.	The firm has submitted COAs of 3 batches of omeprazole lyophilized powder. The firm stated that we have a combined QC of

		both Formulation (000517) and Semi-Basic (000806) facility having same equipment and analysts for both facilities.
3.	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed.	The firm has performed pharmaceutical equivalence of the developed formulation Rapid 40mg Injection (B#2005707) and Risek 40mg Injection (B # 789P06) manufactured by M/s GETZ Pharma. Quality tests of both products including physical appearance, solubility, water content, pH and assay were compared.
4.	Scientific justification is required for performing assay testing by UV method instead of HPLC method.	As the stability studies of the Bulk lyophilized material is performed by the Bulk manufacturer in the same QC lab with the same instrument (on HPLC) so just for verification purpose we performed the stability of the said product by UV. The firm has not submitted stability study data performed by HPLC alongwith raw data sheets, chromatograms and summary data sheets.
5.	Provide copy of Batch Manufacturing Record (BMR) for all the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3.	The firm has submitted copy of batch manufacturing record of 3 batches for which stability studies were carried out.
6.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Stability testing is performed by UV spectrometry therefore audit trail is not required.
7.	Documents for the procurement of drug substance with approval from DRAP is required.	We have procured omeprazole sodium lyophilized ready to fill powder our own Semi-basic facility.
8.	Summary of additional stability studies (if applicable) e.g. in-use studies for drug products which are to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life shall be provided.	The firm has not submitted the details of reconstitution diluents with which dilution was carried.
9.	Compatibility studies for the dry powder for injections and dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product.	Compatibility studies were not provided with required diluents.

Evaluation by PEC:

Sr. No.	Decision of 313th meeting of RB	Response by the firm
1.	Justification of adopting UV-visible spectrophotometric method for assay testing of applied formulation.	• As we have the facility for semi basic preparation & we are lyophilizing the omeprazole and conduct the testing on HPLC.

<table>
<tr><td></td><td></td><td>• In Omeprazole 40 mg Injection (commercial batch) we are filling the same lyophilized powder tested in our quality control laboratory.
• We performed the final month Stability testing on HPLC. Testing for 36th month is attached in Annexure I.</td></tr>
<tr><td>2.</td><td>Submission of results of in-use stability studies of the drug product to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life.</td><td>Testing after reconstitution shows satisfactory results
<table>
<tr><th>Reconstituted Diluent</th><th>Storage Condition</th><th>In-Use Shelf Life</th></tr>
<tr><td rowspan="2">NaCl 0.9% solution</td><td>2 – 8 ºC</td><td>24 Hours</td></tr>
<tr><td>25 ºC</td><td>12 Hours</td></tr>
</table>
Testing Reports with brief summary of results are attached in Annexure II.</td></tr>
<tr><td>3.</td><td>Submission of compatibility studies for the dry powder for injections to be performed as per the instructions provided in individual label of the drug product.</td><td>Omeprazole Dry Powder for Injection in reconstituted with 10ml of NaCl 0.9% solution and shows satisfactory results after 8 hours under storage condition 2 - 8 °C.</td></tr>
<tr><td>4.</td><td>Capacity assessment of manufacturing and testing facility of M/s Vision Pharmaceuticals Pvt. Ltd.</td><td>Capacity Assessment of manufacturing and testing facility of M/s Vision Pharma has been carried out.</td></tr>
</table>

Decision of 321st meeting of Registration Board: Registration Board noted the fact that firm had initially submitted stability studies data by UV spectrophotometric method for Assay test, while HPLC method was adopted for the 36th month time point of long term stability studies hence Registration Board deferred the case for submission of batch release data of recently manufactured commercial batches by M/s Vision pharmaceuticals wherein assay testing shall be performed using HPLC method**.**

Sr. No.	Decision of 321st meeting of RB	Response by the firm
1	Registration Board noted the fact that firm had initially submitted stability studies data by UV spectrophotometric method for Assay test, while HPLC method was adopted for the 36th month time point of long term stability studies hence Registration Board deferred the case for submission of batch release data of recently manufactured commercial batches by M/s Vision pharmaceuticals wherein assay testing shall be performed using HPLC method.	The Standard Analytical Procedure for Omeprazole 40mg Injection & Analytical Reports Along with supporting data of **3** latest commercial batches of Omeprazole sodium 40mg Injection have been submitted with HPLC testing.

Decision: Approved.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**
- **Firm will submit latest GMP inspection report/ GMP Certificate of finished drug product manufacturer before issuance of registration letter.**

Case No.5 Registration applications of local manufacturing of human drugs submitted on CTD format (New Section)

On the recommendations of panel of experts, the CLB in its 276th meeting held on 03rd September, 2020 has considered and approved the grant of Drug Manufacturing License in the name of M/s Alpenglow pharmaceuticals (Pvt) Ltd, Plot No. A7, Risalpur Export processing Zone, Risalpur.

i. Capsule (Cephalosporin)
ii. Dry Powder injection section (Cephalosporin) (1 molecule / 7 products)
iii. Dry powder suspension section (Cephalosporin) (1 molecule / 2 products)
iv. Tablet (Psychotropic)

529.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8636 Dated 04-04-2022
	Details of fee submitted	PKR 30,000/-: Dated 25-01-2022
	The proposed proprietary name / brand name	ALDROX 250mg/5ml Dry powder for Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml of reconstituted suspension contains: Cefadroxil as monohydrate…… 250mg
	Pharmaceutical form of applied drug	Dry powder for suspension
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, First-generation cephalosporins.
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by **UK MHRA**

	For generic drugs (me-too status)	Duricef 250mg /5mL Oral Suspension of Glaxo Smith Kline Pakistan Limited. (Reg # 010057)
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Pharmagen Limited., Address: Kot nabi Buksh wala, 34-Km, Ferozpur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefadroxil as Monohydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C±2°C/ 65% ± 5% RH for 36 months Accelerated: 40°C±2°C/75% ± 5% RH for 6 months Batches: (00221/001, 00221/002, 00221/003)
	Module-III (Drug Product):	The firm has submitted details of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the comparator product of Helicef 250mg/5ml dry suspension (Batch #) by pharma Pakistan Limited by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Loxadril 500mg capsule in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Pharmagen Limited., Address: Kot nabi Bukshwala, 34-Km, Ferozpur Road, Lahore.		
API Lot No.	00243 / 160 / 2021		
Description of Pack (Container closure system)	60 ml HDPE Amber coloured bottle		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	004	005	006
Batch Size	1000 bottles	1000 bottles	1000 bottles
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	14-06-2021	14-06-2021	14-06-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate of M/s Pharmagen limited, Lahore issued by Additional Director, Drug Regulatory Authority of Pakistan, Lahore. It is valid till 07-01-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Submitted
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted that our current HPLC system is not 21 CFR compliant, please accept out submitted dossier, we will try to upgrade our system as soon as possible.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.#	Section	Observation	Response of firm
1.	**3.2.S.4.1**	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical

		are required.	Ingredient by both Drug substance & Drug Product manufacturer have been submitted.
2.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer have been submitted.
3.	**3.2.S.4.4**	• The submitted COA of drug substance manufacturer is of Cefadroxil as monohydrate while identification shows Cefixime reference standard. Moreover, text editing in the COA is evident which is creating doubt. • The limits of water contents of drug substance are different from USP monograph. • The tests of optical rotation, crystallinity are not performed by drug substance manufacturer as recommended by Pharmacopoeia.	• Aas per firm Mistakenly the COA of Cefixime compacted was submitted. However, in provided COA limits/tests are not in accordance with USP monograph
4.	**3.2.S.4.5**	This section mentions that cefixime is a pharmacopoeial product. Clarification is required.	As per firm Due to a typographic mistake cefixime is written instead of cefadroxil.
5.	**3.2.S.5**	Provide COAs of reference standards used in the analysis of drug substance including source and lot number.	Firm has provided working standard COA of Batch no.: 002200/06/2021.
6.	**3.2.P.1**	• Submit master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cefadroxil monohydrate. • List all components of the dosage form, and their amount on a per unit basis (including overages*, if any), the function of the components, and a reference to their quality standards (e.g. compendial monographs or manufacturer's specifications).	• Firm has Submitted master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cefadroxil monohydrate.
7.	**3.2.P.2.2.1**	• Justify why pharmaceutical equivalence studies have not been performed against innovator product (Duricef). • Justify the addition of tests of optical rotation, weight variation, loss on drying, clarity and sterility in pharmaceutical equivalence studies since these tests are not recommended by pharmacopoeia. • The limit of pH mentioned is not as per recommendation of pharmacopoeia.	• Due to un availability of innovator pack. • Firm has stated that mistakenly these tests were included in this section. Firm has submitted revised specifications.
8.	**3.2.P.3**	A batch formula for proposed commercial batch size shall be provided that includes a	Submitted

		list of all components of the drug product to be used in the manufacturing process, their amounts on a per batch basis, and a reference to their quality standards.	
9.	**3.2.P.5.1**	• The submitted specification does not include test for dissolution, uniformity of dosage units, deliverable volume, water determination as recommended by USP. Moreover, justify the addition of tests of pH, loss on drying, weight variation, BET and sterility test in the specifications of Cefadroxil suspension.	• The firm has revised the specifications as per Pharmacopoeia. However, fee for such revision has not been submitted.
10.	**3.2.P.5.2**	Submit analytical procedures of Cefadroxil suspension stating actual concentrations of sample and standard instead of submitting USP monograph.	Submitted.
11.	**3.2.P.5.3**	• Provide standard and sample preparation methods used in analytical method verification studies. • Justify method verification studies of drug without performance of specificity test. Specify the details of the accuracy and specificity test including the details of concentration of 80%, 100% and 120% solutions.	• Submitted
12.	**3.2.P.6**	Provide COA of reference standard used in the analysis of drug product including source and lot number.	Firm has submitted Cefdroxil micronized working standard . lot no. 002200/06/2021.
13.	**3.2.P.8**	• The results of batch analysis and stability data reflect that tests of uniformity of dosage units, water contents, dissolution have not been performed throughout stability studies. Justify your stability study data without performance of tests recommended by pharmacopoeia. • The limit used for the test of pH in stability studies of cefadroxil suspension is not as per USP monograph. • Clarification regarding Batch size is required since you have mentioned as 1000 dry suspensions which is not correct. • Provide raw data sheets to justify the calculation of results for assay testing at each time point during the stability testing of each batch. • Submit copy of invoice for evidence of purchase of drug substance used in the development of analysis of each batch of drug product. • Provide copy of Batch Manufacturing Record (BMR) for the batches of drug product for which stability studies data is	• Not submitted. • Firm has provided commercial invoice specifying thre purchase of cefadroxil (micronized and compacted, 25 kg each), dated 29-04-2021 • BMR has been submitted.

		provided in Module 3 section 3.2.P.8.3. • The submitted copy of GMP certificate of drug substance manufacturer is not valid. Provide updated copy of GMP certificate. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted copy of GMP certificate of M/s Pharmagen limited, Lahore issued by Additional Director, Drug Regulatory Authority of Pakistan, Lahore. It is valid till 07-01-2022 No provided.

Decision: Deferred the case for following submissions:

- **COA from drug substance and drug product manufacturer in accordance with pharmacopoeia.**
- **Submit the valid copy of GMP Certificate of Drug substance manufacturer.**
- **Data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets involving the performance of all pharmacopoeial tests.**
- **Submission of fee of Rs. 7,500/- for pre-registration variation (specifications) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

530.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8635 Dated 04-04-2022
	Details of fee submitted	PKR 30,000/-: Dated 25-01-2022
	The proposed proprietary name / brand name	ALDROX 125mg/5ml Dry powder for Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml of reconstituted suspension contains: Cefadroxil as monohydrate…… 125mg
	Pharmaceutical form of applied drug	Dry powder for suspension
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, First-generation cephalosporins.
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	1’s

	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Approved by UK MHRA & ANSM (France)
	For generic drugs (me-too status)	Duricef 125mg /5mL Oral Suspension of Glaxo Smith Kline Pakistan Limited. (Reg # 008014)
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Pharmagen Limited., Address: Kot nabi Buksh wala, 34-Km, Ferozpur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefadroxil as Monohydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C±2°C/ 65% ± 5% RH for 36 months Accelerated: 40°C±2°C/75% ± 5% RH for 6 months Batches: (00221/001, 00221/002, 00221/003)
	Module-III (Drug Product):	The firm has submitted details of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the comparator product of Helicef 125mg/5ml dry suspension (Batch #) by pharma Pakistan Limited by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand

		in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Pharmagen Limited., Address: Kot nabi Bukshwala, 34-Km, Ferozpur Road, Lahore.		
API Lot No.		00243 / 160 / 2021		
Description of Pack (Container closure system)		60 ml HDPE Amber coloured bottle		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		004	005	006
Batch Size		10000 Capsules	10000 Capsules	10000 Capsules
Manufacturing Date		06-2021	06-2021	06-2021
Date of Initiation		14-06-2021	14-06-2021	14-06-2021
No. of Batches		03		
Administrative Portion				
7.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.		
8.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate of M/s Pharmagen limited, Lahore issued by Additional Director, Drug Regulatory Authority of Pakistan, Lahore. It is valid till 07-01-2022.		
9.	Documents for the procurement of API with approval from DRAP (in case of import).	Firm has provided Performa Invoice of procurement of 25 kg Cefadroxil (Micronized) and 25 kg Cefadroxil (compacted).		
10.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		
11.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted that our current HPLC system is not 21 CFR compliant, please accept out submitted dossier, we will try to upgrade our system as soon as possible.		
12.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted		

Remarks of Evaluator:

Sr.#	Section	Observation	Response of firm
1.	**3.2.S.4.1**	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer are required.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer have been submitted.
2.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer have been submitted.
3.	**3.2.S.4.4**	• The submitted COA of drug substance manufacturer is of Cefadroxil as monohydrate while identification shows Cefixime reference standard. Moreover, text editing in the COA is evident which is creating doubt. • The limits of water contents of drug substance are different from USP monograph. • The tests of optical rotation, crystallinity are not performed by drug substance manufacturer as recommended by Pharmacopoeia.	• As per firm Mistakenly the COA of Cefixime compacted was submitted. However, in provided COA limits/tests are not in accordance with USP monograph
4.	**3.2.S.4.5**	This section mentions that cefixime is a pharmacopoeial product. Clarification is required.	As per firm Due to a typographic mistake cefixime is written instead of cefadroxil.
5.	**3.2.S.5**	Provide COAs of reference standards used in the analysis of drug substance including source and lot number.	Firm has provided working standard COA of Batch no.: 002200/06/2021.
6.	**3.2.P.1**	• Submit master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cefadroxil monohydrate. • List all components of the dosage form, and their amount on a per unit basis (including overages*, if any), the function of the components, and a reference to their quality standards (e.g. compendial monographs or manufacturer's specifications).	• Firm has Submitted master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cefadroxil monohydrate.
7.	**3.2.P.2.2.1**	• Justify why pharmaceutical equivalence studies have not been performed against innovator product (Duricef). • Justify the addition of tests of optical rotation, weight variation, loss on drying, clarity and sterility in pharmaceutical	• Due to un availability of innovator pack.

		equivalence studies since these tests are not recommended by pharmacopoeia. • The limit of pH mentioned is not as per recommendation of pharmacopoeia.	• Firm has stated that mistakenly these tests were included in this section. Firm has submitted revised specifications.
8.	**3.2.P.3**	A batch formula for proposed commercial batch size shall be provided that includes a list of all components of the drug product to be used in the manufacturing process, their amounts on a per batch basis, and a reference to their quality standards.	Submitted
9.	**3.2.P.5.1**	• The submitted specification does not include test for dissolution, uniformity of dosage units, deliverable volume, water determination as recommended by USP. Moreover, justify the addition of tests of pH, loss on drying, weight variation, BET and sterility test in the specifications of Cefadroxil suspension.	• The firm has revised the specifications as per Pharmacopoeia. Howver, fee for such revision has not been submitted.
10.	**3.2.P.5.2**	Submit analytical procedures of Cefadroxil suspension stating actual concentrations of sample and standard instead of submitting USP monograph.	Submitted.
11.	**3.2.P.5.3**	• Provide standard and sample preparation methods used in analytical method verification studies. • Justify method verification studies of drug without performance of specificity test. Specify the details of the accuracy and specificity test including the details of concentration of 80%, 100% and 120% solutions.	• Submitted
12.	**3.2.P.6**	Provide COA of reference standard used in the analysis of drug product including source and lot number.	Firm has submitted Cefdroxil micronized working standard . lot no. 002200/06/2021.
13.	**3.2.P.8**	• The results of batch analysis and stability data reflect that tests of uniformity of dosage units, water contents, dissolution have not been performed throughout stability studies. Justify your stability study data without performance of tests recommended by pharmacopoeia. • The limit used for the test of pH in stability studies of cefadroxil suspension is not as per USP monograph. • Clarification regarding Batch size is required since you have mentioned as 1000 dry suspensions which is not correct. • Provide raw data sheets to justify the calculation of results for assay testing at	• Not submitted.

		each time point during the stability testing of each batch. • Submit copy of invoice for evidence of purchase of drug substance used in the development of analysis of each batch of drug product. • Provide copy of Batch Manufacturing Record (BMR) for the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3. • The submitted copy of GMP certificate of drug substance manufacturer is not valid. Provide updated copy of GMP certificate. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.	• Firm has provided commercial invoice specifying thre purchase of cefadroxil (micronized and compacted, 25 kg each), dated 29-04-2021 • BMR has been submitted. The firm has submitted copy of GMP certificate of M/s Pharmagen limited, Lahore issued by Additional Director, Drug Regulatory Authority of Pakistan, Lahore. It is valid till 07-01-2022 No provided.

Decision: Deferred the case for following submissions:

- **COA from drug substance and drug product manufacturer in accordance with pharmacopoeia.**
- **Submission of the valid copy of GMP Certificate of Drug substance manufacturer.**
- **Data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets involving the performance of all pharmacopoeial tests.**
- **Submission of fee of Rs. 7,500/- for pre-registration variation (specifications) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

531.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 8918 Dated 07-04-2022
	Details of fee submitted	PKR 30,000/-: Dated 25-01-2022
	The proposed proprietary name / brand name	ALDROX 500mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Cefadroxil as monohydrate…… 500mg

	Pharmaceutical form of applied drug	Hard Gelatin capsule
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, First-generation cephalosporins.
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	2 x 6's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Cefadroxil 500 mg Capsules. MHRA approved
	For generic drugs (me-too status)	Sokxil 500mg Capsules. Reg. NO. 54925
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Pharmagen Limited., Address: Kot nabi Buksh wala, 34-Km, Ferozpur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefadroxil as Monohydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C±2°C/ 65% ± 5% RH for 36 months Accelerated: 40°C±2°C/75% ± 5% RH for 6 months Batches: (00221/001, 00221/002, 00221/003)
	Module-III (Drug Product):	The firm has submitted details of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and	Pharmaceutical equivalence has been established

	comparative dissolution profile	against the comparator product of Loxadril 500mg capsule (Batch #) by Himont pharma Pakistan Limited by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Loxadril 500mg capsule in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Pharmagen Limited., Address: Kot nabi Bukshwala, 34-Km, Ferozpur Road, Lahore.		
API Lot No.		00243 / 160 / 2021		
Description of Pack (Container closure system)		Blister pack of 2x6's, Printed Unit Carton**,** Product Insert		
Stability Storage Condition		Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		004	005	006
Batch Size		10000 Capsules	10000 Capsules	10000 Capsules
Manufacturing Date		06-2021	06-2021	06-2021
Date of Initiation		14-06-2021	14-06-2021	14-06-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice (2021042801) specifying purchase of Cephradine compacted (100kg, Batch # 32052010034) attested by Assistant Director (I &E), Peshawar dated 18-05-2021.		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted		

5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks OF Evaluator:

Sr.#	Section	Observation	Response of firm
2	**3.2.S.4.1**	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer are required.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer have been submitted.
3	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer have been submitted.
4.	**3.2.S.4.4**	• The submitted COA of drug substance manufacturer is of Cefadroxil as monohydrate while identification shows Cefixime reference standard. Moreover, text editing in the COA is evident which is creating doubt. • The limits of water contents of drug substance are different from USP monograph. • The tests of optical rotation, crystallinity are not performed by drug substance manufacturer as recommended by Pharmacopoeia.	As per firm 'Mistakenly the COA of Cefixime compacted was submitted. However, in provided COA limits/tests are not in accordance with USP monograph'.
5	**3.2.S.4.5**	This section mentions that cefixime is a pharmacopoeial product. Clarification is required.	As per firm "Due to a typographic mistake cefixime is written instead of cefadroxil.
6	**3.2.S.5**	Provide COAs of reference standards used in the analysis of drug substance including source and lot number.	Firm has provided working standard COA of Batch no.: 002200/06/2021.
7	**3.2.P.1**	• Submit master formulation including theoretical fill weight per capsule alongwith details of equivalency factor for cefadroxil monhydrate. • List all components of the dosage form, and their amount on a per unit basis (including overages*, if any), the function of the components, and a	• Firm has Submitted master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cefadroxil monohydrate.

		reference to their quality standards (e.g. compendial monographs or manufacturer's specifications).	
8	**3.2.P.2.2.1**	• Justify why pharmaceutical equivalence and CDP studies have not been performed against innovator product. • Justify how same results are obtained for pharmaceutical equivalence and CDP studies for both Cefadroxil 250mg Capsule and Cefadroxil 500mg Capsule.	• Due to un availability of innovator pack. • Firm has stated that CDP esults of both products are different.
9	**3.2.P.2.2.2.4**	Justify why the tests of reconstitution time, clarity and color after reconstitution are included in this section. Moreover, flow chart of manufacturing also showed the process for dry powder for suspension.	Firm has stated that both reconstitution test and test for clarity of solution are for Ceftriaxone injection, while drafting these test appeared in these section. Firm has provided revised specifications
10	**3.2.P.3**	• A batch formula for proposed commercial batch size shall be provided that includes a list of all components of the drug product to be used in the manufacturing process, their amounts on a per batch basis, and a reference to their quality standards.	Submitted
11	**3.2.P.5.1**	• The submitted specification does not include test for dissolution, uniformity of dosage units and water determination as recommended by USP. Moreover, justify the addition of tests of pH, loss on drying, weight variation, BET and sterility test in the specifications of Cefadroxil capsule.	Firm has submitted revised specification. However, fee for such change has not been submitted.
12	**3.2.P.5.2**	Submit analytical procedures of Cefadroxil capsule stating actual concentrations of sample and standard instead of submitting USP monograph.	Submitted
13	**3.2.P.5.3**	• Provide standard and sample preparation methods used in analytical method verification studies. • Justify method verification studies of drug without performance of specificity test. Specify the details of the accuracy and specificity test including the details of concentration of 80%, 100% and 120% solutions.	Submitted
14	**3.2.P.6**	Provide COA of reference standard used in the analysis of drug product including source and lot number.	Form has provided COA of Cefadroxil (compacted), Batch no. 002201/07/2021.
15	**3.2.P.8**	• The results of batch analysis and stability data reflect that tests of uniformity of dosage units, water contents, dissolution have not been performed throughout stability studies.	Not submitted

		Justify your stability study data without performance of tests recommended by pharmacopoeia. • Justify the addition of test of pH in stability studies of cefadroxil capsule which is not present in USP monograph of applied product. • Provide raw data sheets to justify the calculation of results for assay testing at each time point during the stability testing of each batch. • Submit copy of invoice for evidence of purchase of drug substance used in the development of analysis of each batch of drug product. • Provide copy of Batch Manufacturing Record (BMR) for the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not submitted Data sheets are missing. Firm has provided Performa Invoice of procurement of 25 kg Cefadroxil (Micronized) and 25 kg Cefadroxil (compacted). Submitted. Not submitted

Decision: Deferred the case for following submissions:

- **COA from drug substance and drug product manufacturer in accordance with pharmacopoeia.**
- **Submission of the valid copy of GMP Certificate of Drug substance manufacturer.**
- **Data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets involving the performance of all pharmacopoeial tests.**
- **Submission of fee of Rs. 7,500/- for pre-registration variation (specifications) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

532.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales

	Dy. No. and date of submission	Dy. No. 8637 Dated 03-03-2022
	Details of fee submitted	PKR 30,000/-: Dated 25-01-2022
	The proposed proprietary name / brand name	ALDROX 250mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Cefadroxil as monohydrate…… 250mg
	Pharmaceutical form of applied drug	Hard Gelatin capsule
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, First-generation cephalosporins.
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	2 x 6's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	USFDA Discontinued.
	For generic drugs (me-too status)	Neutrocef (Neutro.)
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Pharmagen Limited., Address: Kot nabi Buksh wala, 34-Km, Ferozpur Road, Lahore.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cefadroxil as Monohydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C±2°C/ 65% ± 5% RH for 36 months Accelerated: 40°C±2°C/75% ± 5% RH for 6 months Batches: (00221/001, 00221/002, 00221/003)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers,

		description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.		
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the comparator product of Loxadril 500mg capsule (Batch #) by Himont pharma Pakistan Limited by performing quality tests. CDP has been performed against the same brand that is Loxadril 500mg capsule in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8).		
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Pharmagen Limited., Address: Kot nabi Bukshwala, 34-Km, Ferozpur Road, Lahore.		
API Lot No.		00243 / 160 / 2021		
Description of Pack (Container closure system)		Blister pack of 2x6's, Printed Unit Carton**,** Product Insert		
Stability Storage Condition		Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.		004	005	006
Batch Size		10000 Capsules	10000 Capsules	10000 Capsules
Manufacturing Date		06-2021	06-2021	06-2021
Date of Initiation		14-06-2021	14-06-2021	14-06-2021
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice (2021042801) specifying purchase of Cephradine compacted (100kg, Batch # 32052010034) attested by Assistant Director (I &E), Peshawar dated 18-05-2021.		

4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section	Observation	Response of firm
1	**1.5.9**	Evidence of approval of applied formulation (Aldrox 250mg Capsule) in reference regulatory authorities adopted by Registration Board in 275th meeting shall be submitted.	Firm has not provided evidence of RRA approval. However product was USFDA approved but discontinued.
2	**3.2.S.4.1**	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer are required.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer have been submitted.
3	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer have been submitted.
5	**3.2.S.4.4**	• The submitted COA of drug substance manufacturer is of Cefadroxil as monohydrate while identification shows Cefixime reference standard. Moreover, text editing in the COA is evident which is creating doubt. • The limits of water contents of drug substance are different from USP monograph. • The tests of optical rotation, crystallinity are not performed by drug substance manufacturer as recommended by Pharmacopoeia.	• Aas per firm 'Mistakenly the COA of Cefixime compacted was submitted. However, in provided COA limits/tests are not in accordance with USP monograph'.
6	**3.2.S.4.5**	This section mentions that cefixime is a pharmacopoeial product. Clarification is required.	As per firm "Due to a typographic mistake cefixime is written instead of cefadroxi"l.
7	**3.2.S.5**	Provide COAs of reference standards used in the analysis of drug substance	Firm has provided working standard COA of Batch no.:

		including source and lot number.	002200/06/2021.
8	**3.2.P.1**	• Submit master formulation including theoretical fill weight per capsule alongwith details of equivalency factor for cefadroxil monhydrate. • List all components of the dosage form, and their amount on a per unit basis (including overages*, if any), the function of the components, and a reference to their quality standards (e.g. compendial monographs or manufacturer's specifications).	• Firm has Submitted master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cefadroxil monohydrate.
9	**3.2.P.2.2.1**	• Justify why pharmaceutical equivalence and CDP studies have not been performed against innovator product. • Justify how same results are obtained for pharmaceutical equivalence and CDP studies for both Cefadroxil 250mg Capsule and Cefadroxil 500mg Capsule.	• Due to un availability of innovator pack. • Firm has stated that results of both CDP Studies are different.
10	**3.2.P.2.2.2.4**	Justify why the tests of reconstitution time, clarity and color after reconstitution are included in this section. Moreover, flow chart of manufacturing also showed the process for dry powder for suspension.	Firm has stated that both reconstitution test and test for clarity of solution are for Ceftriaxone injection, while drafting these test appeared in these section. Firm has provided revised specifications
11	**3.2.P.3**	• A batch formula for proposed commercial batch size shall be provided that includes a list of all components of the drug product to be used in the manufacturing process, their amounts on a per batch basis, and a reference to their quality standards.	Submitted
12	**3.2.P.5.1**	• The submitted specification does not include test for dissolution, uniformity of dosage units and water determination as recommended by USP. Moreover, justify the addition of tests of pH, loss on drying, weight variation, BET and sterility test in the specifications of Cefadroxil capsule.	Firm has submitted revised specification. However, fee for such change has not been submitted.
13	**3.2.P.5.2**	Submit analytical procedures of Cefadroxil capsule stating actual concentrations of sample and standard instead of submitting USP monograph.	Submitted
14	**3.2.P.5.3**	• Provide standard and sample preparation methods used in analytical method verification studies. • Justify method verification studies of drug without performance of specificity test. Specify the details of the accuracy and specificity test including the details	Submitted

		of concentration of 80%, 100% and 120% solutions.	
15	**3.2.P.6**	Provide COA of reference standard used in the analysis of drug product including source and lot number.	Form has provided COA of Cefadroxil (compacted), Batch no. 002201/07/2021.
16	**3.2.P.8**	• The results of batch analysis and stability data reflect that tests of uniformity of dosage units, water contents, dissolution have not been performed throughout stability studies. Justify your stability study data without performance of tests recommended by pharmacopoeia. • Justify the addition of test of pH in stability studies of cefadroxil capsule which is not present in USP monograph of applied product. • Provide raw data sheets to justify the calculation of results for assay testing at each time point during the stability testing of each batch. • Submit copy of invoice for evidence of purchase of drug substance used in the development of analysis of each batch of drug product. • Provide copy of Batch Manufacturing Record (BMR) for the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Not submitted Not submitted Data sheets are missing. Firm has provided Performa Invoice of procurement of 25 kg Cefadroxil (Micronized) and 25 kg Cefadroxil (compacted). Submitted. Not submitted

Decision: Deferred the case for following submissions:

- **Evidence of approval of applied formulation in reference regulatory authorities as decided by Registration Board in its 275th meeting.**
- **COA from drug substance and drug product manufacturer in accordance with pharmacopoeia.**
- **Data of stability batches supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets involving the performance of all pharmacopoeial tests.**
- **Submission of fee of Rs. 7,500/- for pre-registration variation (specifications) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

533.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan

	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 5859 Dated 03-03-2022
	Details of fee submitted	PKR 30,000/-: Dated 25-01-2022
	The proposed proprietary name / brand name	PENSEF 250mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Cephradine as monohydrate…… 250mg
	Pharmaceutical form of applied drug	Hard Gelatin capsule
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, First-generation cephalosporins.
	Reference to Finished product specifications	USP specifications
	Proposed Pack size	1x12's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	**Cefracare 250mg capsule** USFDA Approved.
	For generic drugs (me-too status)	Velosef 250 mg Capsule of M/s GSK
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Zhejiang Anglikang Pharmaceutical Co. Ltd., No. 1000 Shengzhou North Road, Shengzhou, Shaoxing, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cephradine as Monohydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G &

		related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 36 months Accelerated: 25°C ± 2°C / 60% ± 5% RH for 6 months Batches: (32051704109, 32051704110, 32051704111)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the brand leader that is Velosef 250 mg Capsule (Batch # 646D5G) by Glaxosmithkline Pakistan Limited by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Velosef 250 mg Capsule by Glaxosmithkline Pakistan Limited in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Zhejiang Anglikang Pharmaceutical Co. Ltd., No. 1000 Shengzhou North Road, Shengzhou, Shaoxing, China.		
API Lot No.	00203-08/110/2021		
Description of Pack (Container closure system)	Blister pack of 2x6's, Printed Unit Carton**,** Product Insert		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	004	005	006
Batch Size	10000 Capsules	10000 Capsules	10000 Capsules
Manufacturing Date	06-2021	06-2021	06-2021

Date of Initiation	14-06-2021	14-06-2021	14-06-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate of M/s Zhejiang Anglikang pharmaceutical Co. Ltd. China issued by China Food and Drug administration. It is valid till 30-08-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice (2021042801) specifying purchase of Cephradine compacted (100kg, Batch # 32052010034) attested by Assistant Director (I &E), Peshawar dated 18-05-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section	Observation	Response of firm
1.	3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance/ Active pharmaceutical ingredient by both drug substance & drug product manufacturer is required.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance/ Active pharmaceutical ingredient by both drug substance & drug product manufacturer have been submitted
2.	3.2.S.4.3	Analytical method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Analytical method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug product manufacturer have been submitted
3.	3.2.S.4.4	The Submitted COA of Drug substance and drug product manufacturer does not include contents of cephalexin as recommended by USP (NMT 5.0%) The submitted COA from drug product manufacturer is not readable. Provide readable copy of COA.	Firm has stated that in the testing of Raw material the peak of Cephalexin is also present in the chromatogram, so the results of cephalexin can be calculated from Chromatogram. COA of batch no. 32052010034 has been submitted.

4.	3.2.S.5	Provide COA of reference standards for both cephradine and cephalexin which is actually used in the analysis of drug substance including source and lot number.	Firm has provided in house working standard COA of Cephradine compacted of batch no. 32052010034
5.	3.2.S.7	The details of batches of stability study data of drug substance in module 3 are differnet from the bathes provided in module 2.	Firm has submitted following batches(32051704109, 32051704112, 32051704111)
6.	3.2.P.1	Submit master formulation including theoretical fill weight per bottle along with details of equivalency factor for cephradine. List all components of the dosage form , and their amount on a per unit basis (including overages, if any), the function of the components , and a reference to their quality standards (e.g. compendial monographs or manufacturer's specifications).	Submitted
7.	3.2.P.2.2.1	Justify how same results are obtained for Pharmaceutical equivalence and CDP studies for both Cephradine 250mg and 500mg Capsule.	CDP of both strengths are different. In dossier while compiling same CDP was attached for both strengths.
8.	3.2.P.2.2.4	Justify why the tests of reconstitution time, clarity and colour after reconstitution are included in this section. Moreover , flow chart of manufacturing also showed the process for dry powder for suspension.	Both reconstitution test and test for clarity of solution are for ceftriaxone injection, while drafting these test appeared in these section.
9.	3.2.P.3	A batch formula for proposed commercial batch size shall be provided that includes a list of all components of the drug product to be used in the manufacturing process, their amounts on a per batch basis, and a reference to their quality standards.	submitted
10.	3.2.P.5.1	The test for uniformity of dosage unit, deliverable volume and water determination are not added in specifications as recommended in USP monograph. Revise your specifications as per USP monograph along with submission of applicable fee. The assay limits mentioned in specifications are 90%-102% which are different from USP specifications (90%-125%)	Firm has submitted revised specifications. However requisite fee for change in specifications has not been submitted.
11.	3.2.P.5.2	Provide detailed method of analysis of the drug product in section 3.2.P.5.2 instead of providing copy of USP monograph.	Submitted

12.	3.2.P.5.3	Provide standard and sample preparation method used in analytical method verification studies. Justify method verification studies of drug without performance of specificity test.Specify the details of the accuracy and specificity test including the details of concentration of 80%, 1005 and 120% solutions. Test method for Empazin 25mg Tablet is provided in analytical method verification studies while applied formulation is cephradine Capsules. The peak area of standard solution concenteration in analytical method verification studies is approximately 6609294 while the peak area of the standard solution of same concenteration is stability studies is 585429. Clarify the difference in Peak areas.	Submitted The mistake occurred while compiling the empazin tablet dossier and pansef sapsule dossier. The actual area is near about 585429 approx. The are differences because of different in injection volume. The method was verified with actual injection volume.
13.	3.2.P.6	Provide COA of reference standard actually used in the analysis of drug product.	Firm has provided in house working standard COA of Cephradine compacted of batch no. 32052010034
14.	3.2.P.8	• The results of batch analysis and stability data reflect that tests of uniformity of dosage units, water contents, dissolution have not been performed throughout stability studies. Justify your stability study data without performance of tests recommended by Pharmacopoeia. • Justify the addition of test of pH in stability studies of Cefadroxil capsule which is not present in USP monograph applied product. • Provide raw data sheets to justify the calculation of results for assay testing at each time point during the the stability testing of each batch.	The dissolution test was performed at each interval of accelerated and real time stability study. USP dissolution parameter were adopted and all the results were found within the specified limit. Firm has not provided revised stability data sheets. pH test was performed as an internal test. The pH test was performed by same method as that of cephradine raw material. Raw data sheets submitted but chromatograms have not been submitted.

		• Submit copy of invoice for evidence of purchase of drug substance used in the development of analysis of each batch of drug product.	Firm has submitted invoice no. 2021042801, dated 28-01-2021, specifying import of 100 kg Cephradine compacted import, duly attested by Assistant Director, DRAP.
		• Provide copy of BMR for the batches of drug product for which stability studies data is provided in Module 3 section 3.2P.8.3	Submitted
		• Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing. .	As our pharma is new licensee, and we have not came into production. now we have HPLC (Shimadzu 10 AT) which is not 21 CFR Compliance. However we commit that we will soon perform the stability studies on a 21 CFR compliance HPLC system

Decision: Deferred the case for following submissions:

- **Data of stability batches supported by attested respective documents like chromatograms, summary data sheets involving the performance of all pharmacopoeial tests.**
- **Submission of the valid copy of GMP Certificate of Drug substance manufacturer.**
- **Submission of fee of Rs. 7,500/- for pre-registration variation (specifications) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

534.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7 , Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7 , Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 5860 Dated 03-03-2022
	Details of fee submitted	PKR 30,000/-: Dated 25-01-2022
	The proposed proprietary name / brand name	PENSEF 500mg Capsule

	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each capsule contains: Cephradine as monohydrate…….500mg
	Pharmaceutical form of applied drug	Hard Gelatin capsule
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, First-generation cephalosporins.
	Reference to Finished product specifications	USP
	Proposed Pack size	1x12's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	**Cefradine 500mg Capsules** (MHRA Approved).
	For generic drugs (me-too status)	Velosef 500 mg Capsule
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Zhejiang Anglikang Pharmaceutical Co. Ltd., No. 1000 Shengzhou North Road, Shengzhou, Shaoxing, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cephradine as Monohydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 5°C ± 3°C for 36 months Accelerated: 25°C ± 2°C / 60% ± 5% RH for 6 months Batches: (32051704109, 32051704110, 32051704111)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical

		procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the brand leader that is Velosef 500 mg Capsule by Glaxosmithkline Pakistan Limited by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form). CDP has been performed against the same brand that is Velosef 500 mg Capsule by Glaxosmithkline Pakistan Limited in Acid media (pH 1.0-1.2) & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Zhejiang Anglikang Pharmaceutical Co. Ltd., No. 1000 Shengzhou North Road, Shengzhou, Shaoxing, China.		
API Lot No.	00203-08/110/2021		
Description of Pack (Container closure system)	Blister pack of 2x6's, Printed Unit Carton**,** Product Insert		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	004	005	006
Batch Size	10000 Capsules	10000 Capsules	10000 Capsules
Manufacturing Date	06-2021	06-2021	06-2021
Date of Initiation	14-06-2021	14-06-2021	14-06-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate of M/s Zhejiang Anglikang pharmaceutical Co. Ltd. China issued by China Food and Drug administration. It is valid till 30-08-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice (2021042801) specifying purchase of Cephradine compacted (100kg, Batch # 32052010034)

		attested by Assistant Director (I &E), Peshawar dated 18-05-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section	Observation	Response of firm
1.	3.2.S.4.1	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance/ Active pharmaceutical ingredient by both drug substance & drug product manufacturer is required.	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance/ Active pharmaceutical ingredient by both drug substance & drug product manufacturer have been submitted
2.	3.2.S.4.3	Analytical method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Analytical method Verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug product manufacturer have been submitted
3.	3.2.S.4.4	The Submitted COA of Drug substance and drug product manufacturer does not include contents of cephalexin as recommended by USP (NMT 5.0%) The submitted COA from drug product manufacturer is not readable. Provide readable copy of COA.	Firm has stated that in the testing of Raw material the peak of Cephalexin is also present in the chromatogram, so the results of cephalexin can be calculated from Chromatogram. COA of batch no. 32052010034 has been submitted.
4	3.2.S.5	Provide COA of reference standards for both cephradine and cephalexin which is actually used in the analysis of drug substance including source and lot number.	Firm has provided in house working standard COA of Cephradine compacted of batch no. 32052010034
5.	3.2.S.7	The details of batches of stability study data of drug substance in module 3 are different from the bathes provided in module 2.	Firm has submitted following batches(32051704109, 32051704112, 32051704111)
6.	3.2.P.1	Submit master formulation including theoretical fill weight per bottle along	Submitted

		with details of equivalency factor for cephradine. List all components of the dosage form , and their amount on a per unit basis (including overages, if any), the function of the components , and a reference to their quality standards (e.g. compendial monographs or manufacturer's specifications).	
7.	3.2.P.2.2.1	• Justify why drug release studies /comparative Dissolution studies were not performed Against innovators product. • Justify how same results are obtained for Pharmaceutical equivalence and CDP studies for both Cephradine 250mg and 500mg Capsule	Du to unavailability of innovator. CDP of both strengths are different. In dossier while compiling same CDP was attached for both strengths.
8.	3.2.P.2.2.4	Justify why the tests of reconstitution time , clarity and colour after reconstitution are included in this section. Moreover , flow chart of manufacturing also showed the process for dry powder for suspension.	Both reconstitution test and test for clarity of solution are for ceftriaxone injection, while drafting these test appeared in these section.
9.	3.2.P.3	A batch formula for proposed commercial batch size shall be provided that includes a list of all components of the drug product to be used in the manufacturing process, their amounts on a per batch basis, and a reference to their quality standards.	submitted
10.	3.2.P.5.1	The test for uniformity of dosage unit, deliverable volume and water determination are not added in specifications as recommended in USP monograph. Revise your specifications as per USP monograph along with submission of applicable fee. The assay limits mentioned in specifications are 90%-102% which are different from USP specifications (90%-125%)	Firm has submitted revised specifications. However requisite fee for change in specifications has not been submitted.
11.	3.2.P.5.2	Provide detailed method of analysis of the drug product in section 3.2.P.5.2 instead of providing copy of USP monograph.	Submitted
12.	3.2.P.5.3	Provide standard and sample preparation method used in analytical method verification studies. Justify method verification studies of drug without performance of specificity test.Specify the details of the accuracy	Submitted

		and specificity test including the details of concentration of 80%, 1005 and 120% solutions. Test method for Empazin 25mg Tablet is provided in analytical method verification studies while applied formulation is cephradine Capsules. The peak area of standard solution concenteration in analytical method verification studies is approximately 6609294 while the peak area of the standard solution of same concenteration is stability studies is 585429. Clarify the difference in Peak areas.	The mistake occurred while compiling the empazin tablet dossier and pansef sapsule dossier. The actual area is near about 585429 approx. Thee are difference s because of different in injection volume. The method was verified with actual injection volume.
13.	3.2.P.6	Provide COA of reference standard actually used in the analysis of drug product.	Firm has provided in house working standard COA of Cephradine compacted of batch no. 32052010034
14.	3.2.P.8	• The results of batch analysis and stability data reflect that tests of uniformity of dosage units , water contents ,dissolution have not been performed throughout stability studies . Justify your stability study data without performance of tests recommended by Pharmacopoeia. • Justify the addition of test of pH in stability studies of Cefadroxil capsule which is not present in USP monograph applied product. • Provide raw data sheets to justify the calculation of results for assay testing at each time point during the the stability testing of each batch. • Submit copy of invoice for evidence of purchase of drug substance used in the development of analysis of each batch of drug product.	The dissolution test was performed at each interval of accelerated and real time stability study. USP dissolution parameter were adopted and all the results were found within the specified limit. Firm has not provided revised stabillty data sheets. pH test was performed as an internal test. The pH test was performed by same method as that of cephradine raw material. Raw data sheets submitted but chromatograms has not been submitted. Firm has submitted invoice no. 2021042801, dated 28-01-2021, specifying import of 100 kg Cephradine compacted import, duly attested by Assistant Director, DRAP.

		• Provide copy of BMR for the batches of drug product for which stability studies data is provided in Module 3 section 3.2P.8.3 • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing. .	Submitted As our pharma is new licensee, and we have not came into production. now we have HPLC (Shimadzu 10 AT) which is not 21 CFR Compliance. However we commit that we will soon perform the stability studies on a 21 CFR compliance HPLC system

Decision: Deferred the case for following submissions:

- **Data of stability batches supported by attested respective documents like chromatograms, summary data sheets involving the performance of all pharmacopoeial tests.**
- **Submission of the valid copy of GMP Certificate of Drug substance manufacturer.**
- **Submission of fee of Rs. 7,500/- for pre-registration variation (specifications) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

535.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No.5858 Dated 03-03-2022
	Details of fee submitted	PKR 30,000/-: Dated 25/01/2022
	The proposed proprietary name / brand name	PENSEF 250mg/5ml Dry powder for Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml contains: Cephradine as monohydrate……250mg
	Pharmaceutical form of applied drug	Dry powder for suspension
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, First-generation cephalosporins.
	Reference to Finished product specifications	USP
	Proposed Pack size	1x12's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	ANSPOR 250mg/5ML Powder for Suspension **USFDA Approved**.

	For generic drugs (me-too status)	Velosef 250MG/5ML Suspension
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Zhejiang Anglikang Pharmaceutical Co. Ltd., No. 1000 Shengzhou North Road, Shengzhou, Shaoxing, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Cephradine as Monohydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (32052010037, 32052010038, 32052010039)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	N/A.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.
STABILITY STUDY DATA		
Manufacturer of API	M/s Zhejiang Anglikang Pharmaceutical Co. Ltd., No. 1000 Shengzhou North Road, Shengzhou, Shaoxing, China.	

API Lot No.	32052010034		
Description of Pack (Container closure system)	60ml HDPE Bottle with embossed board unit carton UV coated.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	004	005	006
Batch Size	1000 Bottle	1000 Bottle	1000 Bottle
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	28-05-2021	28-05-2021	28-05-2021
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate of M/s Zhejiang Anglikang pharmaceutical Co. Ltd. China issued by China Food and Drug administration. It is valid till 30-08-2020.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Not provided
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section	Observation	Response of firm
1.	**3.2.S.4.1**	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer are required.	Firm has submitted USP specifications and Monograph
2.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision)	Firm has submitted Method Verification studies report encompassing system suitability,

		performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Accuracy and recovery, Repeatability, intermediate precision and specificity.
3.	**3.2.S.4.4**	• The submitted COAs from both drug substance and drug product manufacturer shows that the material used is of compacted nature. Justify the type of drug substance used in cephradine suspension since the same is used in Capsule dosage form. • Provide readable copy of COA performed by M/s Alpenglow Pharmaceuticals.	Firm has submitted that Mistakenly the COA of compacted was submitted. The material used in dry suspension is of micronized nature. Firm has submitted COA
4.	**3.2.S.5**	Provide COA of reference standard which is actually used in the analysis of drug substance alongwith source and lot no.	Firm has submitted COA of in-house working standard for Cephradine (micronized) no. 0023/110/2021,
5.	**3.2.P.1**	Submit master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cephradine monohydrate.	Master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cephradine monohydrate submitted.
6.	**3.2.P.2.2.1**	• Details of applicant and reference product used in pharmaceutical equivalence are required. • Submit data of compatibility studies of the drug product with recommended diluent in section 3.2.P.2.6. • Justify the performance of pharmaceutical equivalence studies with Velosef 250mg / 5ml IV Dry powder injection while applied formulation is dry powder for suspension. • Justify why drug release studies / comparative dissolution studies were not performed to justify your formulation development process.	• Firm has submitted Pharmaceutical equivalence studies against VELOSEF 250 mg mg/5ml powder for suspension • Firm has submitted that compatibility studies involving the reconstitution of Cephradine 250 mg/5ml dry suspension using purified water was performed. • The Pharmaceutical equivalence studies were performed with velosef dry powder for suspension. This is typographic mistake that velosef injection is mentioned. • As the cephradine suspension is formulated as per USP specifications, and USP does not define the test for dissolution of product nor FDA suggests, so the dissolution is not considered in specification of finished product. However, in the process of pharmaceutical development comparative dissolution was performed in three different medium under in-house set parameters. •
7.	**3.2.P.5.1**	• The test for uniformity of dosage unit, deliverable volume and water	• Firm has provided Revised specifications of finished product.

		determination are not added in specifications as recommended in USP monograph. Revise your specifications as per USP monograph along with submission of applicable fee. • The assay limits mentioned in specifications are 90% -102% which are different from USP specifications (90%-125%).	*However, fee for specification revision has not been provided.* • This is a typographic mistake. Actual limit is 90.0% -125.0%
8.	**3.2.P.5.2**	Provide detailed method of analysis of the drug product in section 3.2.P.5.2 instead of providing copy of USP monograph.	Submitted
9.	**3.2.P.5.3**	• Provide standard and sample preparation methods used in analytical method verification studies. • Justify method verification studies of drug without performance of specificity test. Specify the details of the accuracy test including the details of concentration of 80%, 100% and 120% solutions.	submitted
10.	**3.2.P.6**	Provide COA of reference standard actually used in the analysis of drug product.	Firm has provided COA of in house working standard of batch no. 0023/110/2021.
11.	**3.2.P.8**	• The results of batch analysis and stability data reflect that tests of uniformity of dosage units, water contents, dissolution have not been performed throughout stability studies. Justify your stability study data without performance of tests recommended by pharmacopoeia. • Justify the addition of test of pH in stability studies of cephradine capsule which is not present in USP monograph of applied product. • Provide raw data sheets to justify the calculation of results for assay testing at each time point during the stability testing of each batch. • Submit copy of commercial invoice for evidence of purchase of drug substance that have been used in the development of analysis of each batch of drug product. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted only raw data sheets at different testing time points. However, other information has not been provided.

Decision: Deferred the case for following submissions:

- **Data of stability batches supported by attested respective documents like chromatograms, summary data sheets involving the performance of all pharmacopoeial tests.**
- **Submit copy of commercial invoice for evidence of purchase of drug substance that have been used in the development of analysis of each batch of drug product.**
- **Submission of fee of Rs. 7,500/- for pre-registration variation (specifications) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

536.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7 , Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7 , Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 5857 Dated 03-03-2022
	Details of fee submitted	PKR 30,000/-: Dated 25-01-2022
	The proposed proprietary name / brand name	PENSEF 125mg/5mL Dry Powder for Suspension
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each 5ml after reconstitution contains: Cephradine as Monohydrate 125mg
	Pharmaceutical form of applied drug	Dry powder for suspension
	Pharmacotherapeutic Group of (API)	Anti-bacterials for systemic use, First-generation cephalosporins.
	Reference to Finished product specifications	USP
	Proposed Pack size	1x12's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Could not be confirmed.
	For generic drugs (me-too status)	Velosef 125MG/5ML Suspension
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Zhejiang Anglikang Pharmaceutical Co. Ltd., No. 1000 Shengzhou North Road, Shengzhou, Shaoxing, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.

	Module III (Drug Substance)	Official monograph of Cephradine as Monohydrate is present in USP. The firm as submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (32052010037, 32052010038, 32052010039)
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	N/A.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA

Manufacturer of API	M/s Zhejiang Anglikang Pharmaceutical Co. Ltd., No. 1000 Shengzhou North Road, Shengzhou, Shaoxing, China.		
API Lot No.	32052010034		
Description of Pack (Container closure system)	60ml HDPE Bottle with embossed board unit carton UV coated.		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	001	002	003
Batch Size	1000	1000	1000
Manufacturing Date	05-2021	05-2021	05-2021
Date of Initiation	28-05-2021	28-05-2021	28-05-2021
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	ZJ20150108 Date:08-03-2020
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of GMP certificate of M/s Zhejiang Anglikang pharmaceutical Co. Ltd. China issued by China Food and Drug administration. It is valid till 30-08-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section	Observation	Response of firm
1.	**1.5.9**	Evidence of approval of applied formulation (Pensef 125mg/5ml Dry powder for suspension) in reference regulatory authorities adopted by Registration Board in 275th meeting shall be submitted.	Firm has not provided evidence. However, product was USFDA approved but discontinued.
2.	**3.2.S.4.1**	Copies of the Drug substance specifications and analytical procedures used for routine testing of the drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer are required.	Firm has submitted USP specifications and Monograph
3.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Firm has submitted Method Verification studies report encompassing system suitability, Accuracy and recovery, Repaetabilty, intermediate precision and specificity.
4.	**3.2.S.4.4**	• The submitted COAs from both drug substance and drug product manufacturer shows that the material used is of compacted nature. Justify the type of drug substance used in cephradine suspension since the same is used in Capsule dosage form. • Provide readable copy of COA performed by M/s Alpenglow Pharmaceuticals.	Firm has submitted that Mistakenly the COA of compacted was submitted. The material used in dry suspension is of micronized nature. Firm has submitted COA

5.	**3.2.S.5**	Provide COA of reference standard which is actually used in the analysis of drug substance alongwith source and lot no.	Firm has submitted COA of in-house working standard for Cephradine (micronized) no. 0023/110/2021,
6.	**3.2.P.1**	Submit master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cephradine monohydrate.	Master formulation including theoretical fill weight per bottle alongwith details of equivalency factor for cephradine monohydrate submitted.
7.	**3.2.P.2.2.1**	• Details of applicant and reference product used in pharmaceutical equivalence are required. • Submit data of compatibility studies of the drug product with recommended diluent in section 3.2.P.2.6. • Justify the performance of pharmaceutical equivalence studies with Velosef 250mg / 5ml IV Dry powder injection while applied formulation is dry powder for suspension. • Justify why drug release studies / comparative dissolution studies were not performed to justify your formulation development process.	• Firm has submitted Pharmaceutical equivalence studies against VELOSEF 250 mg mg/5ml powder for suspension • Firm has submitted that compatibility studies involving the reconstitution of Cephradine 250 mg/5ml dry suspension using purified water was performed. • The Pharmaceutical equivalence studies were performed with velosef dry powder for suspension. This is typographic mistake that velosef injection is mentioned. As the cephradine suspension formulated as per USP specificatio and neither USP does not defined t test for dissolution of product r FDA suggests, so the dissolution not considered in specification finished product. However in t process of pharmaceuti development comparative dissoluti was performed in three differe medium under in-house parameters. •
8.	**3.2.P.5.1**	• The test for uniformity of dosage unit, deliverable volume and water determination are not added in specifications as recommended in USP monograph. Revise your specifications as per USP monograph along with submission of applicable fee. • The assay limits mentioned in specifications are 90% -102% which are different from USP specifications (90%-125%).	• Firm has provided Revised specifications of finished product. *However, fee for specification revision has not been provided.* • This is a typographic mistake. Actual limit is 90.0% -125.0%

9.	**3.2.P.5.2**	Provide detailed method of analysis of the drug product in section 3.2.P.5.2 instead of providing copy of USP monograph.	Submitted
10.	**3.2.P.5.3**	• Provide standard and sample preparation methods used in analytical method verification studies. • Justify method verification studies of drug without performance of specificity test. Specify the details of the accuracy test including the details of concentration of 80%, 100% and 120% solutions.	• submitted
11.	**3.2.P.6**	Provide COA of reference standard actually used in the analysis of drug product.	Firm has provided COA of in house working standard of batch no. 0023/110/2021.
12.	**3.2.P.8**	• The results of batch analysis and stability data reflect that tests of uniformity of dosage units, water contents, dissolution have not been performed throughout stability studies. Justify your stability study data without performance of tests recommended by pharmacopoeia. • Justify the addition of test of pH in stability studies of cephradine capsule which is not present in USP monograph of applied product. • Provide raw data sheets to justify the calculation of results for assay testing at each time point during the stability testing of each batch. • Submit copy of commercial invoice for evidence of purchase of drug substance that have been used in the development of analysis of each batch of drug product. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted only raw data sheets at different testing time points. However, other information has not been provided.

Decision: Deferred the case for following submissions:

- **Evidence of approval of applied formulation in reference regulatory authorities as decided by Registration Board in its 275th meeting.**
- **Submission of valid GMP Certificate of Drug Substance manufacturer.**
- **Data of stability batches supported by attested respective documents like chromatograms, summary data sheets involving the performance of all pharmacopoeial tests.**
- **Submit copy of commercial invoice for evidence of purchase of drug substance that have been used in the development of analysis of each batch of drug product.**
- **Submission of fee of Rs. 7,500/- for pre-registration variation (specifications) as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**

537.	Name, address of Applicant / Marketing Authorization Holder	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District Nowshera (KP) Pakistan
	Name, address of Manufacturing site.	M/s Alpenglow Pharmaceuticals Plot # A/7, Export Processing Zone Risalpur, District

		Nowshera (KP) Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. Dated 24/02/2022
	Details of fee submitted	PKR 30,000/-: Dated 20/10/2021
	The proposed proprietary name / brand name	CIAXON 2 gm IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Ceftriaxone as Sodium……2 gm
	Pharmaceutical form of applied drug	Dry Powder for Injection
	Pharmacotherapeutic Group of (API)	Antibacterials for systemic use, Third-generation cephalosporins.
	Reference to Finished product specifications	USP
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Rocephin 2 gm IV Injection (USFDA Approved).
	For generic drugs (me-too status)	Oxidil 2 gm IV injection
	GMP status of the Finished product manufacturer	New license granted on 22-09-2020.
	Name and address of API manufacturer.	M/s Sinopharm Weiqida Pharmaceutical Co., Ltd. Address: First Medical Zone, Economic & Technological Development Zone, Datong, Shanxi, China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Ceftriaxone Sodium is present in USP. The firm has submitted details of nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 72 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (011302001, 011302002, 011302003)
	Module-III (Drug Product):	The firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the brand leader that is Aventrix 250mg Injection by Sanofi Aventis Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of dosage form).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificty.

STABILITY STUDY DATA

Manufacturer of API	M/S Sinopharm Weiqida Pharmaceutical Co., Ltd.		
API Lot No.	Q0121039028		
Description of Pack (Container closure system)	Transparent PVC tray Sealed with printed A.foil filled with Dry Sterile Powder ceftriaxone in clear glass vial One Ampoule of water for injection and aluminum Foil with embossed board unit carton UV coated. (1's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No.	013	014	015
Batch Size	750 Vials	750 Vials	750 Vials
Manufacturing Date	06-2021	06-2021	06-2021

Date of Initiation	09-06-2021	09-06-2021	09-06-2021
No. of Batches	03		

DOCUMENTS /DATA PROVIDED BY THE APPLICANT

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate No. SX20180229 issued by CFDA valid till 05/06/2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	• Copy of letter No.0090/2021/DRAP-CPS/1330 CD(I&E) dated 16/04/2021 is submitted wherein the permission to import different APIs ceftriaxone as sodium for the purpose of test/analysis and stability studies is granted. • AHPAO505150 dated 04/05/2021
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Submitted
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Submitted

Remarks of Evaluator:

Sr.#	Section	Observation
1.	**3.2.S.4.1**	Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required.
2.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.
3.	**3.2.S.4.4**	The tests for crystallinity and particulate matter are not performed by drug product manufacturer. The assay limit specified by drug substance manufacturer (>84.0%) is different from that specified by drug product manufacturer (NLT 79%). Justification is required.
4.	**3.2.S.5**	Provide COA of reference standard which is actually used in the analysis of drug substance.
5.	**3.2.P.1**	Submit master formulation including theoretical fill weight per vial.
6.	**3.2.P.2.2.1**	• Pharmaceutical equivalence of the applied drug shall be established with the innovator/reference product and results of all the quality tests of the developed formulation and the innovator / reference product shall be submitted.

		• Compatibility studies for the dry powder for injections and dry powder for suspension shall be performed as per the instructions provided in individual label of the drug product.
7.	**3.2.P.3.5**	Justify your process validation protocols without any process for optimization of sterilization process and sealing of vials etc.
8.	**3.2.P.5.1**	Specifications of the drug product does not include tests as recommended by USP including test for constituted solution, crystallinity and complete assay test.
9.	**3.2.P.5.2**	Provide detailed testing method for the applied drug product instead of submitting copy of USP monograph.
10.	**3.2.P.5.3**	Provide standard and sample preparation method used in analytical method verification studies. Specify the details of the accuracy and specificity test including the details of concertation of 80%, 100% and 120% solutions. Test method for Empazin 25mg Tablet is provided in analytical method verification studies.
11.	**3.2.P.5.3**	• Justification of method of specificity test in analytical method verification studies shall be submitted. Clarification is required. • Analytical method verification reports of each parameter like specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer shall be submitted. • The peak area of standard solution concentration in analytical method verification studies is approximately 6472293 while the peak area of the standard solution of same concentration in stability studies is 436282 approximately. Clarify the difference in peak areas.
12.	**3.2.P.6**	Provide COA of reference standard actually used in the analysis of drug product.
13.	**3.2.P.8**	• In-use studies for drug products which are to be reconstituted before use, along with proposed in-use storage statement and in-use shelf-life shall be provided. • Provide raw data sheets to justify the calculation of results for assay testing at each time point during the stability testing of each batch. • The tests for water contents, constituted solution etc are not performed during stability studies since these tests are required to make assessment of the stability profile. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing. • Reference of previous approval of applications with stability study data of the firm (if any).

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

Case No. 6. Registration applications of local manufacturing of human drugs submitted on CTD format

538.	Name, address of Applicant / Marketing Authorization Holder	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Name, address of Manufacturing site.	M/s Getz Pharma (Pvt.) Limited 29-30/27, Korangi Industrial Area, Karachi.
	Status of the applicant	☒ Manufacturer

		☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 30257: Dated 05-11-2021
	Details of fee submitted	PKR 50,000/-: Dated 01-12-2021
	The proposed proprietary name / brand name	GABICA CR Tablets 330mg
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each extended release tablet contains: Pregabalin……330mg
	Pharmaceutical form of applied drug	Red colored, oblong shaped, biconvex film-coated tablet, bisect line on one side and plain on other side.
	Pharmacotherapeutic Group of (API)	Anti-epileptics ATC code: N03AX16
	Reference to Finished product specifications	Not mentioned
	Proposed Pack size	14's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Lyrica CR 330mg of M/s Upjohn (USFDA Approved)
	For generic drugs (me-too status)	Not Applicable
	GMP status of the Finished product manufacturer	Last GMP Inspection dated 03-12-2021 concludes that M/s Getz Pharma Pvt. Ltd. is considered to be operating at an acceptable level of compliance of GMP requirements. Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Aurisco pharmaceutical Limited., Badu Industrial park Zone, Tiantai, Zhejiang Province, 317200, P.R. China.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Pregabalin is present in USP pharmacopeia. The firm has submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers,

		description of manufacturing process and controls, tests for impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 18 months Accelerated: 40°C ± 2°C/75% ± 5%RH for 6 months Batches: (P10-130808, P10-130901, P10-130902)
	Module-III (Drug Product):	The firm has submitted details of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the reference product Lyrica CR Tablet 330mg (Batch # AW6452) by M/s Pfizer Inc, NY by performing quality tests (Appearance, average weight, assay, dissolution). CDP has been performed against the same product in acidic media (pH 1.2), acetate buffer (pH 4.5) & phosphate buffer (pH 6.8). The f_2 values are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have been submitted including system suitability, linearity, range, accuracy, precision, specificity and stability of drug product.

STABILITY STUDY DATA	
Manufacturer of API	M/s Aurisco pharmaceutical Limited., Badu Industrial park Zone, Tiantai, Zhejiang Province, 317200, P.R. China.
API Lot No.	PREA-190901 PREA-190902 PREA-190906
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton
Stability Storage Condition	Real time: 30°C ± 2°C / 75% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 06 months Accelerated: 06 months

<table>
<tr><td colspan="2">Frequency</td><td colspan="3">Accelerated: 0, 3, 6 (Months)
Real Time: 0, 3, 6 (Months)</td></tr>
<tr><td colspan="2">Batch No.</td><td>520DS01</td><td>520DS02</td><td>520DS03</td></tr>
<tr><td colspan="2">Batch Size</td><td>2500 Tablets</td><td>2500 Tablets</td><td>2500 Tablets</td></tr>
<tr><td colspan="2">Manufacturing Date</td><td>19-11-2019</td><td>11-12-2019</td><td>11-12-2019</td></tr>
<tr><td colspan="2">Date of Initiation</td><td>30-12-2019</td><td>30-12-2019</td><td>30-12-2019</td></tr>
<tr><td colspan="2">No. of Batches</td><td colspan="3">03</td></tr>
<tr><td colspan="5">Administrative Portion</td></tr>
<tr><td>1.</td><td>Reference of previous approval of applications with stability study data of the firm (if any)</td><td colspan="3">Firm has referred to onsite inspection report of their product MIRAB 25mg & 50mg Tablet which was conducted on 12th December, 2017 and was presented in 289th meeting of Registration Board held on 14th -16th May 2019. The case was approved and the inspection report confirms following points:
• The HPLC software is 21CFR Compliant as per record available with the firm.
• Audit trail on the testing reports is available.
• Adequate monitoring and control are available for stability chamber. Chambers are controlled and monitored through software having alarm system for alerts as well.
• Related manufacturing area, equipment, personnel and utilities are GMP compliant.</td></tr>
<tr><td>2.</td><td>Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.</td><td colspan="3">The firm has submitted copy of GMP certificate no. DE_HH_01_GMP_2018_0033 issued by Freie und Hansestadt Hamburg, Deutschland valid till 23-03-2021.</td></tr>
<tr><td>3.</td><td>Documents for the procurement of API with approval from DRAP (in case of import).</td><td colspan="3">Copy of commercial invoice attested by AD I&E DRAP, Karachi, has been submitted.
<table><tr><th>Batch No.</th><th>Invoice No.</th><th>Quantity Imported</th><th>Date of approval by DRAP</th></tr><tr><td>PREA-190901
PREA-190902
PREA-190906</td><td>JC201907011-1</td><td>400Kg</td><td>27-09-2019</td></tr></table></td></tr>
<tr><td>4.</td><td>Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td><td colspan="3">Firm has submitted data of stability batches along with batch manufacturing record, analytical record and attested documents like chromatograms, Raw data sheets, COA, summary data sheets etc.</td></tr>
<tr><td>5.</td><td>Compliance Record of HPLC software 21CFR & audit trail reports on product testing</td><td colspan="3">Firm has submitted compliance certificate of HPLC software and audit trail reports on product testing.</td></tr>
</table>

6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Firm has submitted Record of Digital data logger for temperature & humidity monitoring of stability chambers (real time and accelerated).

Remarks of Evaluator:

Sr. #	Section	Observation	Reply
1.		Differential fee of PKR 25,000/- shall be submitted since the application was received in R&I section of DRAP after 7th May 2021.	Submitted .
2.	**1.3.4**	Submit copy of GMP inspection report conducted within three years or GMP certificate.	Submitted certificate no. 06/2022-drap(k), Based on evaluation 13-01-2022 and valid until 12-01-2024.
3.	**1.5.6**	Mention the reference specifications of finished drug product since the applied drug product is not present in available Pharmacopoeia.	Innovator specifications
4.	**3.2.S.4.1 & 3.2.S.4.2**	Provide copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug substance & Drug Product manufacturer.	Firm has provided analytical method of drug substance by both Drug substance & Drug Product manufacturer. However, analytical method is not in accordance with official pharmacopoeia i.e. USP and BP. Furthermore, Drug product manufacturer method is not in accordance with drug substance manufacturer. Firm has not performed enantiomeric purity, water and sulphated ash etc in accordance with pharmacopoeia.
5.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Firm has provided raw material method verification report including specificity, linearity, Repeatability, range parameters. Firm has not perform accuracy parameter and provided following reason: with reference to ICH Guidelines "VALIDATION OF ANALYTICAL PROCEDURES: TEXT AND METHODOLOGY Q2 (R1)" it is mentioned in section 4.1.1 Drug Substance *"accuracy may be inferred once precision, linearity and specificity have been established".* This is bring to your kind attention that since we have performed method verification studies as per ICH Q2 (R1) therefore, requirement of accuracy is not applicable.
6.	**3.2.P.8**	Submit valid GMP certificate of drug substance manufacturer, since the	Submitted valid manufacturing license till 06-09-2025.

		submitted GMP certificate was valid till 23-03-2021.	

Decision: Approved with innovator's specifications. Firm shall submit performance of drug substance analysis along with analytical method verifcation studies as per BP monograph, before issuance of registration letter.

- **Manufacturer will place first three production batches on long term stability studies throughout proposed shelf life and on accelerated studies for six months as per the commitment submitted in the registration application.**
- **Manufacturer will perform process validation of first three batches as per the commitment submitted in the registration application.**

539.	Name, address of Applicant / Marketing Authorization Holder	M/s Medisure Laboratories Pakistan (Pvt) Ltd, Plot A-115, S.I.T.E., Super Highway, Karachi Pakistan.
	Name, address of Manufacturing site.	M/s Medisure Laboratories Pakistan (Pvt) Ltd, Plot A-115, S.I.T.E., Super Highway, Karachi Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 32414 Dated 29-11-2021
	Details of fee submitted	PKR 20,000/-: Dated 26-04-2021 PKR 10,000/- as differential fee: Dated 17-06-2021
	The proposed proprietary name / brand name	Desvel 50mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each extended release film coated tablet contains: 72mg of Desvenlafaxine succinate equivalent to Desvenlafaxine……50mg
	Pharmaceutical form of applied drug	White colored, round, biconvex, extended release and film coated tablet bisecting line on one side and other side is plain.
	Pharmacotherapeutic Group of (API)	Selective serotonin and norepinephrine reuptake inhibitors (SNRIs).
	Reference to Finished product specifications	In-house specification
	Proposed Pack size	1 x 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Pristiq Tablet 50mg by M/s Pfizer Pharmaceuticals U.S.A., Inc., (USFDA Approved).

	For generic drugs (me-too status)	Lafaxine 50mg Tablet by M/s Genix Pharma, Reg. No. 070458
	GMP status of the Finished product manufacturer	New License granted on 07/10/2020 Tablet (General & General Antibiotic) section approved
	Name and address of API manufacturer.	M/s Aurore Pharmaceuticals Pvt. Ltd., Plot # 68, 69, 2nd floor Jubilee Heights, Madhapur, Hyderabad, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Desvenlafaxine is present in USP. The firm has submitted details of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: T-001, T-002, T-003
	Module-III (Drug Product):	The firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the comparator product Lafaxine 50mg Tablet by M/s Genix Pharma by performing quality tests (Identification, Assay, Dissolution, and Uniformity of dosage form). CDP has been performed against the said product

		in Acid media (pH 1.0-1.2), acetate buffer (pH 4.5) & phosphate buffer (pH 6.8). The values for f_1 and f_2 are in the acceptable range.		
	Analytical method validation/verification of product	Method verification studies have been submitted including linearity, range, accuracy, precision, and specificity.		
STABILITY STUDY DATA				
Manufacturer of API		M/s Aurore Pharmaceuticals Pvt. Ltd., Plot # 68, 69, 2nd floor Jubilee Heights, Madhapur, Hyderabad, India.		
API Lot No.		DVSF190003		
Description of Pack (Container closure system)		Alu-Alu blister packed in unit carton (1×10's)		
Stability Storage Condition		Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period		Real time: 6 months Accelerated: 6 months		
Frequency		Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)		
Batch No. Accelerated		T-001	T-002	T-003
Batch Size		0.3Kg	0.3Kg	0.3Kg
Manufacturing Date		06-2020	07-2020	07-2020
Date of Initiation		07-07-2020	06-07-2020	06-07-2020
No. of Batches		03		
Administrative Portion				
1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.		
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of license (No: 99/RR /AP/B/C) for M/s Aurore Pharmaceutical (Pvt) Ltd, Telangana State, India. The license is valid till 29-10-2023.		
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice specifying the import of Desvenlafaxine 1kg (batch # DVSP190003) attested by Assistant Director (I & E) dated 24-04-2020.		
4.	Data of stability batches will be supported by attested respective documents like chromatograms, raw data sheets, COA, summary data sheets etc.	Data of stability batches supported by attested respective documents like chromatograms, raw data sheets, COA, summary data sheets have been submitted.		
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	The firm has submitted audit trail reports on product testing.		
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted.		

Remarks of Evaluator:

Sr.#	Section	Observation
1	**1.5.2**	The applied label claim shows 76mg of Desvenlafaxine succinate eq to 50mg of Desvenlafaxine while master formulation shows 72mg of Desvenlafaxine succinate eq. to 50mg of Desvenlafaxine. The applied label claim of Desvel 100mg Tablet shows 152mg of Desvenlafaxine succinate eq to 100mg of Desvenlafaxine while master formulation shows 144mg of Desvenlafaxine succinate eq. to 100mg of Desvenlafaxine.
2	**1.5.3**	The proposed brand name does not cover extended release pattern of applied formulation.
3.	**3.2.S.4.1 & 3.2.S.4.2**	Provide copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug substance & Drug Product manufacturer.
4.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.
5.	**3.2.S.7.3**	The storage conditions under which stability study data of drug substance conducted is not as per Zone-IVA conditions.
6.	**3.2.P.2.2.1**	• Provide results of pharmaceutical equivalence data by performing all the quality tests of developed formulation and the innovator / reference / comparator product. • Justify why pharmaceutical equivalence and CDP studies were not performed against innovator product. • Justify why comparative dissolution profile was not conducted in three BCS media across the physiological pH range.
7.	**3.2.P.5.1**	Justify the sampling time points for dissolution test which are not as per recommendations of FDA.
8.	**3.2.P.6**	Submit copy of COA of primary / secondary reference standard including source and lot number which is actually used in the testing of stability batches.
9.	**3.2.P.8**	• Specify the batch size of stability batches in terms of number of units produced. • Justify the significant change in assay value of real time and accelerated stability study data of batch no. T003. • Reference of previous approval of applications with stability study data of the firm (if any).

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

540.	Name, address of Applicant / Marketing Authorization Holder	M/s Medisure Laboratories Pakistan (Pvt) Ltd, Plot A-115, S.I.T.E., Super Highway, Karachi Pakistan.
	Name, address of Manufacturing site.	M/s Medisure Laboratories Pakistan (Pvt) Ltd, Plot A-115, S.I.T.E., Super Highway, Karachi Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)

	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 25415 Dated 13-09-2021
	Details of fee submitted	PKR 20,000/-: Dated 26-04-2021 PKR 10,000/- as Differential fee: Dated 17-06-2021
	The proposed proprietary name / brand name	Desvel 100mg Tablet
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each extended release film coated tablet contains: 144 mg of Desvenlafaxine succinate equivalent to Desvenlafaxine……100mg
	Pharmaceutical form of applied drug	Yellow colored, round, biconvex, extended release and film coated tablet, both sides are plain.
	Pharmacotherapeutic Group of (API)	Selective serotonin and nor-epinephrine reuptake inhibitors (SNRIs).
	Reference to Finished product specifications	In house Specifications
	Proposed Pack size	1 x 10's
	Proposed unit price	As per SRO (not allotted yet)
	The status in reference regulatory authorities	Pristiq Tablet 100mg by M/s Pfizer Pharmaceuticals U.S.A., Inc., (USFDA Approved).
	For generic drugs (me-too status)	Lafaxine 100mg Tablet by M/s Genix Pharma, (Reg. No. 070473)
	GMP status of the Finished product manufacturer	The firm is granted GMP certificate based on inspection conducted on 30-09-2019. Tablet (General & General Antibiotic) section approved.
	Name and address of API manufacturer.	M/s Aurore Pharmaceuticals Pvt. Ltd., Plot # 68, 69, 2nd floor Jubilee Heights, Madhapur, Hyderabad, India.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Desvenlafaxine is present in USP. The firm as submitted detail of nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 24 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: T-001, T-002, T-003.
	Module-III (Drug Product):	The firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical equivalence has been established against the comparator product Lafaxine 100mg Tablet (Batch # 011T064) by M/s Genix Pharma by performing quality tests like Identification, Assay, Dissolution, and Uniformity of dosage form. CDP has been performed against the same product in Acid media (pH 1.0-1.2), acetate buffer & Phosphate Buffer (pH 6.8). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, and specificity.

STABILITY STUDY DATA	
Manufacturer of API	M/s Aurore Pharmaceuticals Pvt. Ltd., Plot # 68, 69, 2nd floor Jubilee Heights, Madhapur, Hyderabad, India.
API Lot No.	DVSF190003
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (1×10's)
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH
Time Period	Real time: 6 months Accelerated: 6 months
Frequency	Accelerated: 0, 2, 4, 6 (Months) Real Time: 0, 3, 6 (Months)

Batch No. Accelerated	T-001	T-002	T-003
Batch Size	43 Blister	43 Blister	43 Blister
Manufacturing Date	06-2020	06-2020	06-2020
Date of Initiation	18-06-2020	07-07-2020	07-07-2020
No. of Batches	03		

Administrative Portion

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of license (No: 99/RR /AP/B/C) for M/s Aurore Pharmaceutical (Pvt) Ltd, Telangana State, India. The license is valid till 29-10-2023.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice specifying the import of Desvenlafaxine 1kg (batch # DVSP190003) attested by Assistant Director (I & E) dated 24-04-2020.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, raw data sheets, COA, summary data sheets etc.	Data of stability batches supported by attested respective documents like chromatograms, raw data sheets, COA, summary data sheets have been submitted.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has submitted audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated) has been submitted.

Remarks of Evaluator:

Sr.#	Section	Observation
1	**1.5.2**	The applied label claim shows 76mg of Desvenlafaxine succinate eq to 50mg of Desvenlafaxine while master formulation shows 72mg of Desvenlafaxine succinate eq. to 50mg of Desvenlafaxine. The applied label claim of Desvel 100mg Tablet shows 152mg of Desvenlafaxine succinate eq to 100mg of Desvenlafaxine while master formulation shows 144mg of Desvenlafaxine succinate eq. to 100mg of Desvenlafaxine.
2	**1.5.3**	The proposed brand name does not cover extended release pattern of applied formulation.
3.	**3.2.S.4.1 & 3.2.S.4.2**	Provide copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance by both Drug substance & Drug Product manufacturer.
4.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.
5.	**3.2.S.7.3**	The storage conditions under which stability study data of drug substance conducted is not as per Zone-IVA conditions.
6.	**3.2.P.2.2.1**	• Provide results of pharmaceutical equivalence data by performing all the quality tests of developed formulation and the innovator / reference / comparator product.

		• Justify why pharmaceutical equivalence and CDP studies were not performed against innovator product. • Justify why comparative dissolution profile was not conducted in three BCS media across the physiological pH range.
7.	**3.2.P.5.1**	Justify the sampling time points for dissolution test which are not as per recommendations of FDA.
8.	**3.2.P.6**	Submit copy of COA of primary / secondary reference standard including source and lot number which is actually used in the testing of stability batches.
9.	**3.2.P.8**	• Specify the batch size of stability batches in terms of number of units produced. • Justify the significant change in assay value of real time and accelerated stability study data of batch no. T003. • Reference of previous approval of applications with stability study data of the firm (if any).

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

541.	Name, address of Applicant / Marketing Authorization Holder	M/s Polyfine Chempharma, 51 – Industrial Estate Hayatabad Peshawar – Pakistan
	Name, address of Manufacturing site.	M/s Polyfine Chempharma, 51 – Industrial Estate Hayatabad Peshawar – Pakistan
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☐ Domestic sale ☐ Export sale ☒ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 23342 Dated 26-08-2021
	Details of fee submitted	PKR 20,000/-: Dated 13-10-2020
	The proposed proprietary name / brand name	POLDEX 30mg Capsule
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Dexlansoprazole (as dual delayed release pellets) …… 30mg
	Pharmaceutical form of applied drug	Blue Size '2' capsule
	Pharmacotherapeutic Group of (API)	Proton pump inhibitors
	Reference to Finished product specifications	Manufacturer's Specification
	Proposed Pack size	3 x 10's
	Proposed unit price	As per SRO

	The status in reference regulatory authorities	Dexilant Capsule 30mg by M/S Takeda Pharma USA, USFDA Approved.
	For generic drugs (me-too status)	Razodex Capsule 30mg by M/S Getz Pharma Regn No. 086976
	GMP status of the Finished product manufacturer	The firm is considered to be operating at satisfactory level of cGMP compliance, copy already submitted with the application.
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals, Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad-Pakistan.
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm submitted detail of nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, tests for impurity Sulphone, impurity Sulphide & total impurity, specifications, analytical procedures and its verification, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 36 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 6 months Batches: (DLP125T, DLP124T, DLP123T)
	Module-III (Drug Product):	The firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	Pharmaceutical Equivalence have been established against the reference product from the market that is Razodex 30mg Capsule by M/S Getz Pharma by performing quality tests (Identification, Assay, Dissolution, Uniformity of

		dosage form). CDP has been performed against the same brand that is Razodex 30mg Capsule by M/S Getz Pharma in Acid media & Phosphate Buffer (pH 5.5 & 7.0). The values for f1 and f2 are in the acceptable range.
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	Vision Pharmaceuticals, Plot No. 22-23, Industrial Triangle, Kahuta Road, Islamabad- Pakistan.		
API Lot No.	DLP125T, DLP124T, DLP123T		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (3×10's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6, 9, 12, 18, 24 (Months)		
Batch No.	TD-01	TD-02	TD-03
Batch Size	1200 Capsules	1200 Capsules	1200 Capsules
Manufacturing Date	02-2020	02-2020	02-2020
Date of Initiation	11-03-2020	11-03-2020	11-03-2020
No. of Batches	03		

Administrative Portion		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N.A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	Copy of GMP certificate is available
3.	Documents for the procurement of API with approval from DRAP (in case of import).	Copy of Invoice is available
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Submitted
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	HPLC software 21CFR Compliance
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	Record of digital data logger for temperature and humidity monitoring of stability chambers are available

Remarks of Evaluator:

Sr.#	Section	Observation
1.		Submit differential fee for the registration of applied product, since the notification for revision of fee vide SRO No. F.7-11/2012-B&A/DRA was published on 7th May 2021 while this application was received in R&I section of DRAP after 7th May 2021.
2.	**1.3.5**	Submit copy of inspection report conducted within period of three years.
3.	**3.2.S.4.1 & 3.2.S.4.2**	Submit data in section 3.2.S.4.1 and 3.2.S.4.2 as per the guidance document approved by Registration Board which specifies that "Copies of the Drug substance specifications and analytical procedures used for routine testing of the Drug substance /Active Pharmaceutical Ingredient by both Drug substance & Drug Product manufacturer is required."
4.	**3.2.S.4.3**	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.
5.	**3.2.S.4.4**	Provide results of analysis of relevant batch(es) of Drug Substance performed by Drug Product manufacturer used during product development and stability studies.
6.	**3.2.P.1**	Justify the quantity of ready to fill pellets used in master formulation keeping in view label claim and potency of pellets.
7.	**3.2.P.2.2.1**	• Why pharmaceutical equivalence and CDP studies were not performed against innovator product (Dexilant). • Justify why the pharmaceutical equivalence study does not include complete testing of the drug product and the comparator product including the tests recommended by innovator product.
8.	**3.2.P.4**	Clarify the type of capsule shell used in dexlansoprazole pellets since innovator product has specified hypromellose capsule shells.
9.	**3.2.P.5.1**	• Justify how you have adopted specifications and analytical procedures of drug substance manufacturer. • The tests of content uniformity and loss on drying were not included in the submitted specifications as recommended by literature of innovator product.
10.	**3.2.P.5.2**	Submit analytical procedures of all the tests recommended by innovator drug product.
11.	**3.2.P.5.4**	The copies of complete analysis of at least two batches shall be provided as per guidance document.
12.	**3.2.P.8**	• The results of batch analysis and stability data reflect that tests of content uniformity and loss on drying have not been performed throughout stability studies. Justify your stability study data without performance of these tests. • Justify the selection of time points for stability studies in the light of relevant guidelines. • Submit copy of invoice for evidence of purchase of pellets used in the development of analysis of each batch of drug product. • Provide copy of Batch Manufacturing Record (BMR) for the batches of drug product for which stability studies data is provided in Module 3 section 3.2.P.8.3. • Submit copy of GMP certificate of drug substance manufacturer. • Submit compliance Record of HPLC software 21CFR & audit trail reports on product testing. • Record of Digital data logger for temperature and humidity monitoring of

		stability chambers (real time and accelerated).

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

542.	Name, address of Applicant / Marketing Authorization Holder	M/s Radiant Pharma (Pvt.) Ltd., 43-E Sundar Industrial Estate, Sundar Raiwind Road, Lahore Pakistan.
	Name, address of Manufacturing site.	M/s Radiant Pharma (Pvt.) Ltd., 43-E Sundar Industrial Estate, Sundar Raiwind Road, Lahore Pakistan.
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	GMP status of the firm	The firm is granted GMP certificate based on inspection conducted on 31-07-2018.
	Dy. No. and date of submission	Dy. No. 22633 dated 04-11-2019
	Details of fee submitted	PKR 20,000/-: dated 04-11-2019
	The proposed proprietary name / brand name	Dexlanso 30mg Capsules
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Dual delayed release pellets of Dexlansoprazole equivalent to Dexlansoprazole …. 30mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator Specifications
	Proposed Pack size	2x7's and 3x10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	DEXILANT 30mg capsule by M/s Takeda Pharma (USFDA Approved).
	For generic drugs (me-too status)	Delanzo DR Capsules 30mg of M/s Sami Pharma (Reg. No. 089145)
	GMP status of the Finished product manufacturer	New license granted on 11/07/2019 Dry Powder For General Injection section approved
	Name and address of API manufacturer.	Vision Pharmaceuticals, Plot No.22-23, Industrial Triangle, Kahuta Road, Islamabad, Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties,

		solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	The firm as submitted details of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, tests for impurity D, G & related substances (impurity A & unspecified), specifications, analytical procedures and its verification, batch analysis and justification of specification, working standard, container closure system and stability studies of drug substance.
	Stability studies	Stability study conditions: Real time: 30˚C ± 2˚C / 65% ± 5%RH for 06 months Accelerated: 40˚C ± 2˚C / 75% ± 5% RH for 36 months
	Module-III (Drug Product):	The firm has submitted detail of manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedure (including dissolution testing at acidic and buffer medium) and its verification studies, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug product.
	Pharmaceutical equivalence and comparative dissolution profile	The firm has submitted data of pharmaceutical equivalence and CDP of trial formulation with reference product Dexilant 60mg Capsule (B # 508308) of M/s Takeda Pharma.
	Analytical method validation/verification of product	Analytical method validation of drug product has been submitted.

STABILITY STUDY DATA			
Manufacturer of API	Vision Pharmaceuticals, Plot No.22-23, Industrial Triangle, Kahuta Road, Islamabad, Pakistan		
API Lot No.	DLP376		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30˚C ± 2˚C / 65% ± 5%RH Accelerated: 40˚C ± 2˚C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Dexlanso 30mg Capsules			
Batch No.	CTX-007	CTX-008	CTX-009

Batch Size	560 Capsules	560 Capsules	560 Capsules
Manufacturing Date	09-2019	10-2019	10-2019
Date of Initiation	02-10-2019	04-10-2019	07-10-2019
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT

1.	Reference of previous approval of applications with stability study data of the firm (if any)	The firm has not submitted any document.
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate for M/s Vision Pharmaceuticals, Islamabad issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the purchase of Dexlansoprazole pellets 22.5% (4 Kg) from M/s Vision Pharmaceuticals dated 12-12-2018.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches alongwith respective documents like chromatograms, Raw data sheets, COA and summary data sheets have been submitted.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	Audit trail on reports on testing of product not submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	The firm has submitted record of data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).

Remarks of Evaluator:

Sr. No.	Observations communicated	Response by the firm
1.	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well as non-compendial drug substance(s) shall be submitted.	Analytical method verification studies performed by drug product manufacturer has been submitted.
2.	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed.	The firm has submitted data of pharmaceutical equivalence and CDP of trial formulation with reference product Dexilant 30mg Capsule (B # 507726) of M/s Takeda Pharma.
3.	Updated GMP status of the applicant shall be submitted.	The firm is granted GMP certificate based on inspection conducted on 31-07-2018.
4.	Provide results of analysis of relevant batch(es) of Drug Substance used during product development and stability	The firm has submitted copies of COAs from drug substance and drug product manufacturer.

	studies, along with Certificate of Analysis (COA) of the same batch from Drug Substance manufacturer.	
5.	CoA of primary / secondary reference standard including source and lot number shall be provided.	The firm has submitted COA of working standard from M/s Vision Pharmaceuticals, Islamabad.
6.	Documents for the procurement of pellets including purchase invoice from local source shall be submitted.	The firm has submitted copy of invoice for the purchase of Dexlansoprazole pellets 22.5% (4Kg) from M/s Vision Pharmaceuticals dated 12-12-2018.

On site verification inspection is still awaited.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

543.	Name, address of Applicant / Marketing Authorization Holder	M/s Radiant Pharma (Pvt.) Ltd., 43-E Sunder Industrial Estate, Sunder Raiwind Road, Lahore Pakistan
	Name, address of Manufacturing site.	M/s Radiant Pharma (Pvt.) Ltd., 43-E Sunder Industrial Estate, Sunder Raiwind Road, Lahore
	Status of the applicant	☒ Manufacturer ☐ Importer ☐ Is involved in none of the above (contract giver)
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	GMP status of the firm	The firm is granted GMP certificate based on inspection conducted on 31-07-2018.
	Dy. No. and date of submission	Dy. No. 22633 dated 04-11-2019
	Details of fee submitted	PKR 20,000/-: dated 04-11-2019
	The proposed proprietary name / brand name	Dexlanso 60mg Capsules
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each Capsule Contains: Dual delayed release pellets of Dexlansoprazole equivalent to Dexlansoprazole ……. 60mg
	Pharmaceutical form of applied drug	Capsule
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator's Specifications
	Proposed Pack size	2 × 7's and 3 × 10's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	DEXILANT 60mg capsule by M/s Takeda Pharma (USFDA Approved).

	For generic drugs (me-too status)	Delanzo DR Capsules 60mg of M/s Sami Pharma (Reg. No. 089146)
	Name and address of API manufacturer.	M/s Vision Pharmaceuticals, Plot No.22-23, Industrial Triangle, Kahuta Road, Islamabad, Pakistan
	Module-II (Quality Overall Summary)	Firm has submitted QOS as per WHO QOS-PD template. Summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance and drug product is submitted.
	Module III (Drug Substance)	Official monograph of Dexlansoprazole Dual Delayed Released Pellets is present in Innovator's Specs. The firm as submitted detail of nomenclature, structure, general properties, solubility, physical form, manufacturers, description of manufacturing process and controls, specifications, analytical procedures and its verification, batch analysis and justification of specification, working standard, container closure system and stability studies of drug substance
	Stability studies	Stability study conditions: Real time: 30°C ± 2°C / 65% ± 5%RH for 06 months Accelerated: 40°C ± 2°C / 75% ± 5%RH for 36 months
	Module-III (Drug Product):	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical equivalence and comparative dissolution profile	The firm has submitted data of pharmaceutical equivalence and CDP of trial formulation with reference product Dexilant 60mg Capsule (B # 508308) of M/s Takeda Pharma.
	Analytical method validation/verification of product	Analytical method validation of drug product has been submitted.
STABILITY STUDY DATA		

Manufacturer of API	M/s Vision Pharmaceuticals Pvt. Ltd., Plot No.22-23, Industrial Triangle, Kahuta Road, Islamabad, Pakistan		
API Lot No.	DLP376		
Description of Pack (Container closure system)	Alu-Alu blister packed in unit carton (2×7's)		
Stability Storage Condition	Real time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 6 months Accelerated: 6 months		
Frequency	Accelerated: 0, 3, 6 (Months) Real Time: 0, 3, 6 (Months)		
Dexlanso 60mg Capsules			
Batch No.	CTX-001	CTX-002	CTX-003
Batch Size	1400 Capsules	1400 Capsules	1400 Capsules
Manufacturing Date	08-2019	08-2019	08-2019
Date of Initiation	29-08-2019	30-08-2019	03-09-2019
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
1.	Reference of previous approval of applications with stability study data of the firm (if any)	N/A
2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate for M/s Vision Pharmaceuticals, Islamabad issued by Additional Director DRAP, Islamabad. It is valid till 10-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of invoice for the purchase of Dexlansoprazole pellets 22.5% (4 Kg) from M/s Vision Pharmaceuticals dated 12-12-2018.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	Data of stability batches alongwith respective documents like chromatograms, Raw data sheets, COA and summary data sheets have been submitted.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing	Audit trail on reports on testing of product not submitted.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated)	The firm has submitted record of data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).

Remarks of Evaluator

Sr. No.	Observations communicated	Response by the firm
1.	Analytical method verification studies including specificity, accuracy and repeatability (method precision) performed by the Drug Product manufacturer for both compendial as well	Analytical method verification studies performed by drug product manufacturer has been submitted.

	as non-compendial drug substance(s) shall be submitted.	
2.	Pharmaceutical equivalence of the applied drug shall be established with the innovator / reference / comparator product and results of all the quality tests of the developed formulation and the innovator / reference / comparator product shall be submitted and discussed.	The firm has submitted data of pharmaceutical equivalence and CDP of trial formulation with reference product Dexilant 60mg Capsule (B # 508308) of M/s Takeda Pharma.
3.	Updated GMP status of the applicant shall be submitted.	The firm is granted GMP certificate based on inspection conducted on 31-07-2018.
4.	Provide results of analysis of relevant batch(es) of Drug Substance used during product development and stability studies, along with Certificate of Analysis (COA) of the same batch from Drug Substance manufacturer.	The firm has submitted copies of COAs from drug substance and drug product manufacturer.
5.	CoA of primary / secondary reference standard including source and lot number shall be provided.	The firm has submitted COA of working standard from M/s Vision Pharmaceuticals, Islamabad.
6.	Documents for the procurement of pellets including purchase invoice from local source shall be submitted.	The firm has submitted copy of invoice for the purchase of Dexlansoprazole pellets 22.5% (4 Kg) from M/s Vision Pharmaceuticals dated 12-12-2018.

On-site inspection report is still awaited.

Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.

544.	Name, address of Applicant / Marketing Authorization Holder	M/s Gray's Pharmaceuticals Plot # 2, St. N-3, National Industrial Zone, Rawat.
	Name, address of Manufacturing site.	M/s Bio-Labs (Pvt) Ltd, Plot No. 145industrial Triangle Kahuta road Islamabad.
	Status of the applicant	☐Manufacturer ☐ Importer ☒ Is involved in none of the above (contract giver)
	GMP status of the firm	**M/s Gray's Pharma:** **M/s Bio-Labs (Pvt) Ltd:** The firm is granted GMP certificate based on inspection conducted on 23-04-2019.
	Evidence of approval of manufacturing facility	**M/s Bio-Labs (Pvt) Ltd:** The manufacturer has provided Lyophilized vial (General) section.
	Status of application	☐ New Drug Product (NDP) ☒ Generic Drug Product (GDP)
	Intended use of pharmaceutical product	☒ Domestic sale ☐ Export sale ☐ Domestic and Export sales
	Dy. No. and date of submission	Dy. No. 13163; Dated: 06-05-2021

	Details of fee submitted	PKR 50,000/-: Dated: 25-02-2021
	The proposed proprietary name / brand name	Panazole 40mg IV Injection
	Strength / concentration of drug of Active Pharmaceutical ingredient (API) per unit	Each vial contains: Pantoprazole sodium eq. to Pantoprazole (lyophilized powder)..…….40mg
	Pharmaceutical form of applied drug	Lyophilized Powder for injection
	Pharmacotherapeutic Group of (API)	Proton Pump Inhibitor
	Reference to Finished product specifications	Innovator's specifications
	Proposed Pack size	1's
	Proposed unit price	As per SRO
	The status in reference regulatory authorities	Protonix IV 40mg Injection of M/s Wyeth Pharms (USFDA Approved)
	For generic drugs (me-too status)	Toprazole 40mg Injection by M/s Morgan Technologies Services (Reg # 045728).
	Name and address of API manufacturer.	M/s Rajasthan Antibiotics Ltd. A-619 & 630 RIICO Industrial Area, Bhiwadi – India.
	Module-II (Quality Overall Summary)	Firm has summarized information related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, Characterization, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance. The firm has summarized information of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Module-III Drug Substance:	The firm has submitted detailed drug substance data related to nomenclature, structure, general properties, solubilities, physical form, manufacturers, description of manufacturing process and controls, impurities, specifications, analytical procedures and its validation, batch analysis and justification of specification, reference standard, container closure system and stability studies of drug substance.
	Stability Studies of Drug Substance (Conditions & duration of Stability studies)	Stability study conditions: Real time: 30°C±2°C / 65% ± 5%RH for 36 months Accelerated: 40°C±2°C/ 75% ± 5%RH for 6 months

		Batches: (PSS-032/10, PSS-033/10, PSS-034/10)
	Module-III Drug Product:	Firm has submitted data of drug product including its description, composition, pharmaceutical development, manufacture, manufacturing process and process control, process validation protocols and report, control of excipients, control of drug product, specifications, analytical procedures, validation of analytical procedures, batch analysis, justification of specifications, reference standard or materials, container closure system and stability.
	Pharmaceutical Equivalence	The firm has submitted pharmaceutical equivalence data against the comparator product Zopent 40mg Injection (Batch No:) by NabiQasim Industries by performing quality tests (Physical appearance, water content, pH, BET, Assay).
	Analytical method validation/verification of product	Method verification studies have submitted including linearity, range, accuracy, precision, specificity.

STABILITY STUDY DATA			
Manufacturer of API	M/s Rajasthan Antibiotics Ltd. A-619 & 630 RIICO Industrial Area, Bhiwadi Dist. Alwar (Rajasthan) – India.		
API Lot No.	17-12902, APSS18001,		
Description of Pack (Container closure system)	Glass vial		
Stability Storage Condition	Real Time: 30°C ± 2°C / 65% ± 5%RH Accelerated: 40°C ± 2°C / 75% ± 5%RH		
Time Period	Real time: 24 months Accelerated: 06 months		
Frequency	Real Time: 0, 3, 6, 9, 12, 18, 24 (Months) Accelerated: 0, 3, 6 (Months)		
Pan Cap 40mg IV Injection			
Batch No.	L-181	L-105	L-134
Batch Size	7000 vials	7100 vials	8000 vials
Manufacturing Date	09-2018	04-2017	12-2017
Date of Initiation	15-11-2018	03-06-2017	26-02-2018
No. of Batches	03		

DOCUMENTS / DATA PROVIDED BY THE APPLICANT		
#	Documents To Be Provided	Status
1.	Reference of previous approval of applications with stability study data of the firm (if any).	The firm has not submitted any document.

2.	Approval of API/ DML/GMP certificate of API manufacturer issued by concerned regulatory authority of country of origin.	The firm has submitted copy of GMP certificate (No. DC/A-I/WHO-GMP/2020/1961) issued by Government of Rajasthan dated 09-12-2020. The certificate is valid till 26-02-2022.
3.	Documents for the procurement of API with approval from DRAP (in case of import).	The firm has submitted copy of commercial invoice for the purchase of Pantoprazole sodium sterile (Batch no. UIPSS20037) attested by AD (I & E) dated 24-02-2021.
4.	Data of stability batches will be supported by attested respective documents like chromatograms, Raw data sheets, COA, summary data sheets etc.	The firm has submitted data of stability batches along with chromatograms, raw data sheets, COA and summary data sheets.
5.	Compliance Record of HPLC software 21CFR & audit trail reports on product testing.	The firm has not submitted audit trail reports on product testing.
6.	Record of Digital data logger for temperature and humidity monitoring of stability chambers (real time and accelerated).	The Firm has submitted record of data logger for temperature and humidity monitoring of real time and accelerated stability chambers.
The firm has submitted new data which need to be evaluated		
Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.		

Item No. XV: Agenda of Evaluator-X (Mst. Najia Saleem)

Case no. 01 Registration applications for local manufacturing of (veterinary) drugs (Priority Registration applications of Export Facilitation)

a. New Cases

Assistant Director PR-I/EFD vide letter NO.1-6/2019-PR-I (EFD) dated 06-10-2022 has informed that DRAP Authority in its 133rd meeting held on 13th April 2022, decided to grant registration on priority basis to the pharmaceutical i.e one molecule for each 100,000 USD worth of export of medicines (to a maximum of 15 such molecules) during a fiscal year. In compliance to the aforementioned decision, **M/s Selmore Pharmaceuticals Pvt Ltd., 36-Km, Multan Road Lahore** has achieved the benchmark of **350,158.20 USD** during the fiscal Year **2020-2021.** Following applications submitted by the firm for priority consideration/ evaluation in lieu of export facilitation are submitted before the Board for its consideration please:		
545.	Name and address of manufacturer / Applicant	M/s Selmore Pharmaceuticals Pvt Ltd., 36-Km, Multan Road Lahore.
	Brand Name +Dosage Form + Strength	Amprosel 50 powder
	Composition	Each 100 gram Contains: Amprolium Hydrochloride…50gm
	Diary No. Date of R& I & fee	Dy.No 4498 dated 25-04-2019 Rs.20,000/- dated 24-04-2019
	Pharmacological Group	Antiprotozoal
	Type of Form	Form-5
	Finished product Specification	USP specifications

	Pack size & Demanded Price	100gm, 500gm, and 1Kg; Decontrolled
	Me-too status	Unipro-50% Powder of M/s Univet Pharmaceuticals, Rawalpindi. (Reg. No. 033255)
	GMP status	Panel inspection dated 14-03-2022 for grant of additional Sections recommends grant of following additional sections Liquid injectable Cephalosporin (Vet) Dry Powder Injectable Cephalosporin (Vet) Liquid injectable Vial-I General (Vet) Liquid injectable vial-II General (Vet) External Liquid Preparation (Vet) External Powder Preparation (Vet)
	Remarks of the Evaluator [X]	• Oral powder (Veterinary) section confirmed vide letter No.F.1-13/2000-Lic (Vol-II) dated 23-01-2019 • Firm has revised finished product specification from inhouse to "USP specifications" along with the fee of Rs. 7,500/- via deposit slip no 541652473.
	Decision: Approved.	
546.	Name and address of manufacturer / Applicant	M/s Selmore Pharmaceuticals Pvt Ltd., 36-Km, Multan Road Lahore.
	Brand Name +Dosage Form + Strength	Bromodoxel Powder
	Composition	Each 1000gm Contains: Doxycycline Hyclate …400gm Tylosin Tartrate…200gm Colistin Sulfate…500MIU Bromhexine HCl…10gm
	Diary No. Date of R& I & fee	Dy.No 4499 dated 25-04-2019 Rs.20,000/- dated 24-04-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form-5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 500gm, and 1Kg; Decontrolled
	Me-too status	Fit Respi Water Soluble Powder of M/s D-Maarson Pharmaceuticals, Rawat, Islamabad. (Reg. No. 078268)
	GMP status	Panel inspection dated 14-03-2022 for grant of additional Sections recommends grant of following additional sections Liquid injectable Cephalosporin (Vet) Dry Powder Injectable Cephalosporin (Vet) Liquid injectable Vial-I General (Vet) Liquid injectable vial-II General (Vet) External Liquid Preparation (Vet) External Powder Preparation (Vet)
	Remarks of the Evaluator [X]	• Oral powder (Veterinary) section confirmed vide letter No.F.1-13/2000-Lic (Vol-II) dated 23-01-2019

		• Firm has revised finished product specification from inhouse to "as per innovator's specifications" along with the fee of Rs. 7,500/- via deposit slip no 812114242. • Moreover, the firm has submitted the following conversion of Colistin sulphate from MIU to Kg. 19000 MIU of Colistin Sulphate is equivalent to 1Kg.
	Decision: Approved with innovator's specifications.	
547.	Name and address of manufacturer / Applicant	M/s Selmore Pharmaceuticals Pvt Ltd., 36-Km, Multan Road Lahore.
	Brand Name +Dosage Form + Strength	Actimec DS Injection 10ml
	Composition	Each ml contains: Ivermectin…3.15%
	Diary No. Date of R& I & fee	Dy.No 26570 dated 09-10-2020 Rs.20,000/- dated 08-10-2020
	Pharmacological Group	Anthelmintic
	Type of Form	Form-5
	Finished product Specification	BP Vet. specifications
	Pack size & Demanded Price	10ml glass vial; Decontrolled
	Me-too status	Mecti Injection 10ml of M/s International Pharma Labs. Lahore. (Reg. No. 094430)
	GMP status	Panel inspection dated 14-03-2022 for grant of additional Sections recommends grant of following additional sections Liquid injectable Cephalosporin (Vet) Dry Powder Injectable Cephalosporin (Vet) Liquid injectable Vial-I General (Vet) Liquid injectable vial-II General (Vet) External Liquid Preparation (Vet) External Powder Preparation (Vet)
	Remarks of the Evaluator [X]	Approval of Liquid injectable vial-I General (Vet) and Liquid injectable vial-II General (Vet) sections confirmed vide Letter No.F.1-13/2000-Lic (Vol-II) dated 04-07-2022
	Decision: Approved.	
548.	Name and address of manufacturer / Applicant	M/s Selmore Pharmaceuticals Pvt Ltd., 36-Km, Multan Road Lahore.
	Brand Name +Dosage Form + Strength	Actimec DS Injection 50ml
	Composition	Each ml contains: Ivermectin…3.15%
	Diary No. Date of R& I & fee	Dy.No 26571 dated 09-10-2020 Rs.20,000/- dated 08-10-2020
	Pharmacological Group	Anthelmintic
	Type of Form	Form-5
	Finished product Specification	BP Vet. specifications
	Pack size & Demanded Price	50ml glass vial; Decontrolled
	Me-too status	Mecti DS Injection 50ml of M/s International Pharma Labs. Lahore. (Reg. No. 094428)

	GMP status	Panel inspection dated 14-03-2022 for grant of additional Sections recommends grant of following additional sections Liquid injectable Cephalosporin (Vet) Dry Powder Injectable Cephalosporin (Vet) Liquid injectable Vial-I General (Vet) Liquid injectable vial-II General (Vet) External Liquid Preparation (Vet) External Powder Preparation (Vet)
	Remarks of the Evaluator [X]	Approval of Liquid injectable vial-I General (Vet) and Liquid injectable vial-II General (Vet) sections confirmed vide Letter No.F.1-13/2000-Lic (Vol-II) dated 04-07-2022
	Decision: Approved.	
549.	Name and address of manufacturer / Applicant	M/s Selmore Pharmaceuticals Pvt Ltd., 36-Km, Multan Road Lahore.
	Brand Name +Dosage Form + Strength	Actimec DS Injection 100ml
	Composition	Each ml contains: Ivermectin…3.15%
	Diary No. Date of R& I & fee	Dy.No 26572 dated 09-10-2020 Rs.20,000/- dated 08-10-2020
	Pharmacological Group	Anthelmintic
	Type of Form	Form-5
	Finished product Specification	BP Vet. specifications
	Pack size & Demanded Price	100ml glass vial; Decontrolled
	Me-too status	Elvomec Star Injection 3.15% of M/s Elko Organization (Pvt) Ltd., Karachi. (Reg. No. 063728)
	GMP status	Panel inspection dated 14-03-2022 for grant of additional Sections recommends grant of following additional sections Liquid injectable Cephalosporin (Vet) Dry Powder Injectable Cephalosporin (Vet) Liquid injectable Vial-I General (Vet) Liquid injectable vial-II General (Vet) External Liquid Preparation (Vet) External Powder Preparation (Vet)
	Remarks of the Evaluator [X]	Approval of Liquid injectable vial-I General (Vet) and Liquid injectable vial-II General (Vet) sections confirmed vide Letter No.F.1-13/2000-Lic (Vol-II) dated 04-07-2022
	Decision: Approved.	

Case No. 02 Registration applications of import cases

a. New Cases (Veterinary)

550.	Name and address of Applicant	M/s Vet Links International, Z-77, B.M.C.H. Society, Amir Khusro Road, Block 7/8, Behind Faysal Bank, Off Shaheed-e-Millat Road, Karachi, Pakistan
	Detail of Drug Sale License	Not provided

	Name and address of manufacturer	M/s Vilsan Veteriner Ilaclari Ticaret Sanayi A.S. Bahkhisar Mahallesi Koy Ici Kume Evleri No: 765A Akyurt/Ankara-Turkey
	Name and address of marketing authorization holder	M/s Vilsan Veteriner Ilaclari Ticaret Sanayi A.S. Istanbul Anadolu Yakasi Organize Sanayi Bolgesi Aydinli Mah. 2. Sanayi Cad. No.:16 34953 Tuzla- Istanbul
	Name of exporting country	Turkey
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 1525 Dated 22-03-2019
	Fee including differential fee	Rs : 1,00,000 Dated 22-03-2019
	Brand Name +Dosage Form + Strength	Mastivil Intramammary Suspension for Lactating Period
	Composition	Each 5G Tube Contains: Procaine Penicillin G…100,000 IU Streptomycin Sulphate…100mg Neomycin Sulphate…100mg Prednisolone…10mg
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibacterial/ Corticosteroid
	Shelf life	2 years
	Demanded Price	0.85 USD
	Pack size	5g x 24
	International availability	N/A
	Me-too status	Multiject IM Injection by Nawan Trading Corp. (Reg. No. 018871)
	Detail of certificates attached	Photocopy of CoPP certificate (No. 16/024) dated 12-06-2006 issued by The Ministry of Food Agriculture and Livestock, General Directorate of Food and Control Eskisehir Yolu 9, Km Lodumlu Ankara, Turkey. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site. Scanned copy of Authorization Letter GMP certificate: No. GMP/TR/V/YI/S075/2017 issued by The Ministry of Food Agriculture and Livestock of Turkey
	Remarks of the Evaluator [X]	**Shortcomings:** • The provided photocopies of CoPP and FSC are not legalized and scanned copies of GMP certificate of manufacturer and letter of Authorization (LOA) are provided; and. Moreover, validity of CoPP, GMP certificate of manufacturer and LOA could not be confirmed. Submit valid original duly attested/ legalized CoPP, GMP certificate of manufacturer and LOA. • Provide valid copy of DSL • 06 months accelerated and real time stability study data upto claimed shelf life of 03 batches according to the conditions of zone IV-A. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board.

		• In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986. • Provide conversion of Procaine Penicillin G from IU to mg.
	Decision: Deferred for following: • **Valid original duly attested/ legalized CoPP, GMP certificate of manufacturer and LOA.** • **Valid copy of DSL** • **06 months accelerated and real time stability study data upto claimed shelf life of 03 batches according to the conditions of zone IV-A.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.** • **Conversion of Procaine Penicillin G from IU to mg.** • **Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting.**	
551.	Name and address of Applicant	M/s Vet Links International, Z-77, B.M.C.H. Society, Amir Khusro Road, Block 7/8, Behind Faysal Bank, Off Shaheed-e-Millat Road, Karachi, Pakistan
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Vilsan Veteriner Ilaclari Ticaret Sanayi A.S. Bahkhisar Mahallesi Koy Ici Kume Evleri No: 765A Akyurt/Ankara-Turkey
	Name and address of marketing authorization holder	M/s Vilsan Veteriner Ilaclari Ticaret Sanayi A.S. Istanbul Anadolu Yakasi Organize Sanayi Bolgesi Aydinli Mah. 2. Sanayi Cad. No.:16 34953 Tuzla- Istanbul
	Name of exporting country	Turkey
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 1526 Dated 22-03-2019
	Fee including differential fee	Rs : 1,00,000 Dated 22-03-2019
	Brand Name +Dosage Form + Strength	Vilacol Oral Powder for Oral Solution
	Composition	Each 1ml Contains: Amoxicillin Trihydrate…640mg Colistin Sulphate…130.6mg
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibacterial
	Shelf life	2 years (Not supported by stability data)
	Demanded Price	4,37 USD; 17,77 USD; 34,44 USD
	Pack size	100gm, 500gm, 1Kg

	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	Originally legalized CoPP certificate (No. 017/0027) dated 23-11-2006 issued by The Ministry of Food Agriculture and Livestock, General Directorate of Food and Control Eskisehir Yolu 9, Km Lodumlu Ankara, Turkey. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site. Scanned copy of Authorization Letter
	Remarks of the Evaluator [X]	**Shortcomings:** • Scanned copy of legalized letter of Authorization (LOA) is provided while provided originally legalized copy of CoPP. Moreover, validity of CoPP and LOA could not be confirmed. Submit valid original duly attested/ legalized CoPP, and LOA. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide valid copy of DSL • 06 months accelerated and real time stability study data upto claimed shelf life of 03 batches according to the conditions of zone IV-A. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Original valid duly attested/ legalized CoPP, and LOA.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Valid copy of DSL** • **06 months accelerated and real time stability study data upto claimed shelf life of 03 batches according to the conditions of zone IV-A.** • **Finished product specification in the light of decision taken in 267th meeting of Registration Board.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
552.	Name and address of Applicant	M/s Vet Links International, Z-77, B.M.C.H. Society, Amir Khusro Road, Block 7/8, Behind Faysal Bank, Off Shaheed-e-Millat Road, Karachi, Pakistan
	Detail of Drug Sale License	**Not provided**
	Name and address of manufacturer	M/s Vilsan Veteriner Ilaclari Ticaret Sanayi A.S. Bahkhisar Mahallesi Koy Ici Kume Evleri No: 765A Akyurt/Ankara-Turkey
	Name and address of marketing authorization holder	M/s Vilsan Veteriner Ilaclari Ticaret Sanayi A.S. Istanbul Anadolu Yakasi Organize Sanayi Bolgesi Aydinli Mah. 2. Sanayi Cad. No.:16 34953 Tuzla- Istanbul
	Name of exporting country	Turkey
	Type of Form	Form-5A

	Diary No. & Date of R& I	Dy.No 1527 Dated 22-03-2019
	Fee including differential fee	Rs : 1,00,000 Dated 22-03-2019
	Brand Name +Dosage Form + Strength	Vilamoks LA Suspension for Injection
	Composition	Each 1ml contains: Amoxicillin Trihydrate Eq. To Amoxicillin Base…150mg
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibacterial
	Shelf life	2 years
	Demanded Price	189 USD, 357 USD, 720 USD
	Pack size	50ml, 100ml, 250ml
	International availability	N/A
	Me-too status	Xlmox Injection of M/s Mediexcel Pharmaceuticals, Islamabad.(Reg. No.103885)
	Detail of certificates attached	Originally legalized CoPP certificate (No. 13/074) dated 15-06-2006 issued by The Ministry of Food Agriculture and Livestock, General Directorate of Food and Control Eskisehir Yolu 9, Km Lodumlu Ankara, Turkey. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site. Scanned copy of Authorization Letter
	Remarks of the Evaluator [X]	• Scanned copy of legalized letter of Authorization (LOA) is provided while provided originally legalized copy of CoPP. Moreover, validity of CoPP and LOA could not be confirmed. Submit valid original duly attested/ legalized CoPP, and LOA. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • 06 months accelerated and real time stability study data upto claimed shelf life of 03 batches according to the conditions of zone IV-A. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986. • Separate registration is granted to separate pack size/fill volume of injectable dosage form. However, multiple pack sizes of injectable dosage form are demanded in a single application. So clarification is required for which pack size/ fill volume you want to apply this dossier.
	Decision: Deferred for following: • **Original valid duly attested/ legalized CoPP, and LOA.** • **Valid copy of DSL** • **06 months accelerated and real time stability study data upto claimed shelf life of 03 batches according to the conditions of zone IV-A.** • **Finished product specification in the light of decision taken in 267th meeting of Registration Board.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	

	• **Demanded pack size.**	
553.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name and address of marketing authorization holder	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 2271 Dated 01-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 01-04-2019
	Brand Name +Dosage Form + Strength	Flor 30 Solution for Injection
	Composition	Each ml Contains: Florfenicol…300mg
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	24 months
	Demanded Price	N/A
	Pack size	50ml
	International availability	N/A
	Me-too status	Florfenicen Injectable Solution of M/s Mustafa Brothers, Faisalabad. (Reg. No.103910)
	Detail of certificates attached	**CERTIFICATE OF PHARMACEUTICAL PRODUCT** **Certified by:** Bureau of Animal Husbandry & Veterinary of Shandong Province, China **Product License NO:** Vet. Drug No. (2014)150252540 **Issued on:** 06/11/2018 **Free sale:** Free sale of the product in exporting country: Yes confirms from COPP GMP certificate No.: 151100B0/17202 Validity: 10-07-2019 **Authorization Letter** 11-12-2017 Validity: 3 years
	Remarks of the Evaluator [X]	**Shortcomings:** • The submitted photocopy of letter of Authorization (LOA) and GMP certificate are **expired now, but valid upon submission,** Provide legalized valid original LOA and GMP certificate. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board.

		• Submit Rs.7500/- for revision of finished product specifications. • Provide accelerated and real time stability studies data of three batches at zone IV-A conditions as per requirement of 278th meeting of Registration Board. The firm has submitted vide letter no. UME-10/2022.DOC-021 dated 07-10-2022 that all the deficiencies were duly notified to the supplier and will be addressed at the earliest possible time. Kindly give us a **time extension** to furnish the requisite information/documents from the principal as the legalized and notarized documents may take time from the principal.
	Decision: Deferred for following: • **Legalized valid original LOA and GMP certificate.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Fee Rs.7500/- for revision of finished product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions.**	
554.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name and address of marketing authorization holder	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 227169 Dated 01-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 01-04-2019
	Brand Name +Dosage Form + Strength	Flumeglu Solution for Injection
	Composition	Each ml contains: Flunixin Meglumine…50mg
	Finished Product Specification	USP
	Pharmacological Group	Non-steroidal anti-inflammatory drug
	Shelf life	24 months
	Demanded Price	N/A
	Pack size	50ml
	International availability	N/A
	Me-too status	Logon Injection of M/s S.J & G Fazul Ellahie (Pvt.) Ltd, Karachi. (Reg. No.097927)
	Detail of certificates attached	**CERTIFICATE OF PHARMACEUTICAL PRODUCT** **Certified by:** Bureau of Animal Husbandry & Veterinary of Shandong Province, China

		NO: Vet. Drug No. (2014)150252102 **Issued on:** 06/11/2018 **Free sale:** Free sale of the product in exporting country: Yes confirms from COPP GMP certificate No.: 151100B0/17202 Validity: 10-07-2019 **Authorization Letter** 11-12-2017 Validity: 3 years
	Remarks of the Evaluator [X]	**Shortcomings:** • The submitted original letter of Authorization (LOA) and copy of GMP certificate are **expired now, but valid upon submission,** Provide legalized valid original LOA and GMP certificate. • Provide accelerated and real time stability studies data of three batches at zone IV-A conditions as per requirement of 278th meeting of Registration Board. • Revise label claim on form 5A in line with reference product and composition in CoPP. Submit full fee of registration for revision of label claim. The firm has submitted vide letter no. UME-10/2022.DOC-021 dated 07-10-2022 that all the deficiencies were duly notified to the supplier and will be addressed at the earliest possible time. Kindly give us a **time extension** to furnish the requisite information/documents from the principal as the legalized and notarized documents may take time from the principal.
	Decision: Deferred for following: • **Legalized valid original LOA and GMP certificate.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Revision of label claim on form 5A in line with reference product and composition in CoPP.** • **Fee Rs. 100,000/- for correction/ pre-approval change of formulation as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions.**	
555.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name and address of marketing authorization holder	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 2268 Dated 01-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 01-04-2019

	Brand Name +Dosage Form + Strength	Enroplan 10 Solution for Injection
	Composition	Each ml contains: Enrofloxacin…100mg
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	24 months
	Demanded Price	N/A
	Pack size	100ml
	International availability	N/A
	Me-too status	Floxa-10 Injection of M/s Evergreen Pharmaceuticals, Lahore. (Reg. No.102192)
	Detail of certificates attached	**CERTIFICATE OF PHARMACEUTICAL PRODUCT** **Certified by:** Bureau of Animal Husbandry & Veterinary of Shandong Province, China **NO:** Vet. Drug No. (2014)150252523 **Issued on:** 06/11/2018 **Free sale:** Free sale of the product in exporting country: Yes confirms from COPP GMP certificate No.: 151100B0/17202 Validity: 10-07-2019 **Authorization Letter** 11-12-2017 Validity: 3 years
	Remarks of the Evaluator [X]	**Shortcomings:** • The submitted photocopy of letter of Authorization (LOA) and GMP certificate **are expired now, but valid upon submission,** Provide legalized valid original LOA and GMP certificate. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Submit Rs.7500/- for revision of finished product specifications. • Provide accelerated and real time stability studies data of three batches at zone IV-A conditions as per requirement of 278th meeting of Registration Board. The firm has submitted vide letter no. UME-10/2022.DOC-021 dated 07-10-2022 that all the deficiencies were duly notified to the supplier and will be addressed at the earliest possible time. Kindly give us a **time extension** to furnish the requisite information/documents from the principal as the legalized and notarized documents may take time from the principal.
	Decision: Deferred for following: • **Legalized valid original LOA and GMP certificate.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Fee Rs.7500/- for revision of finished product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.**	

	• **06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions.**	
556.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name and address of marketing authorization holder	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 2267 Dated 01-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 01-04-2019
	Brand Name +Dosage Form + Strength	Ceftihyde RTU Injection
	Composition	Each ml contains: Ceftiofur HCl eq. to Ceftiofur…50mg
	Finished Product Specification	As per innovator's specifications
	Pharmacological Group	Antibiotic
	Shelf life	24 months
	Demanded Price	N/A
	Pack size	50ml
	International availability	N/A
	Me-too status	Cefur-RTU Injection of M/s Nawan Laboratories (Pvt) Ltd., Karachi. (Reg. No.049605)
	Detail of certificates attached	**CERTIFICATE OF PHARMACEUTICAL PRODUCT** **Certified by:** Bureau of Animal Husbandry & Veterinary of Shandong Province, China **NO:** Vet. Drug No. (2014)150252292 **Issued on:** 06/11/2018 **Free sale:** Free sale of the product in exporting country: Yes confirms from COPP GMP certificate No.: 151100B0/17202 Validity: 10-07-2019 **Authorization Letter** 11-12-2017 Validity: 3 years
	Remarks of the Evaluator [X]	**Shortcomings:** • The submitted photocopy of letter of Authorization (LOA) and GMP certificate are expired now, but valid upon submission, Provide legalized valid original LOA and GMP certificate. • Provide accelerated and real time stability studies data of three batches at zone IV-A conditions as per requirement of 278th meeting of Registration Board.

		The firm has submitted vide letter no. UME-10/2022.DOC-021 dated 07-10-2022 that all the deficiencies were duly notified to the supplier and will be addressed at the earliest possible time. Kindly give us a **time extension** to furnish the requisite information/documents from the principal as the legalized and notarized documents may take time from the principal.
	Decision: Deferred for following: • **Legalized valid original LOA and GMP certificate.** • **06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions.**	
557.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name and address of marketing authorization holder	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 2270 Dated 01-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 01-04-2019
	Brand Name +Dosage Form + Strength	Oxyplan 20 Solution for Injection
	Composition	Each ml contains: Oxytetracycline…200mg
	Finished Product Specification	**Chinese pharmacopoeial specifications**
	Pharmacological Group	Antibiotic
	Shelf life	24 months
	Demanded Price	N/A
	Pack size	100ml
	International availability	N/A
	Me-too status	Oxy-LA Injection of M/s Selmore Pharmaceuticals (Pvt.) Ltd., Lahore. (Reg. No.035014) (confirm salt form)
	Detail of certificates attached	**CERTIFICATE OF PHARMACEUTICAL PRODUCT** **Certified by:** Bureau of Animal Husbandry & Veterinary of Shandong Province, China **Product License NO:** Vet. Drug No. (2014)150252787 **Issued on:** 06/11/2018 **Free sale:** Free sale of the product in exporting country: Yes confirms from COPP GMP certificate No.: 151100B0/17202 Validity: **10-07-2019** **Authorization Letter**

		11-12-2017 Validity: 3 years
	Remarks of the Evaluator [X]	**Shortcomings:** • The submitted photocopy of letter of Authorization (LOA) and GMP certificate are expired now, but valid upon submission, Provide legalized valid original LOA and GMP certificate. • Clarification regarding salt form of API applied in this dossier is required; and revise label claim and master formula in line with reference product, accordingly. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Submit full fee of registration for revision of finished product specifications, label claim and master formula. • Provide accelerated and real time stability studies data of three batches at zone IV-A conditions as per requirement of 278th meeting of Registration Board. The firm has submitted vide letter no. UME-10/2022.DOC-021 dated 07-10-2022 that all the deficiencies were duly notified to the supplier and will be addressed at the earliest possible time. Kindly give us a **time extension** to furnish the requisite information/documents from the principal as the legalized and notarized documents may take time from the principal.
	Decision: Deferred for following: • **Legalized valid original LOA and GMP certificate.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Clarification regarding salt form of API and revise label claim and master formula in line with reference product, accordingly** • **Fee Rs. 100,000/- for correction/ pre-approval change of formulation and finished product specification as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions.**	
558.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Arab Veterinary Industrial Co. ”AVICO” P.O.Box 150906, Amman 11115-Jordan
	Name and address of marketing authorization holder	M/s Arab Veterinary Industrial Co. ”AVICO” P.O.Box 150906, Amman 11115-Jordan
	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 2272 Dated 01-04-2019

	Fee including differential fee	Rs : 1,00,000 Dated 01-04-2019
	Brand Name +Dosage Form + Strength	Avimox L.A Suspension for Injection
	Composition	Each ml contains: Amoxicillin as trihydrate…150mg
	Finished Product Specification	USP
	Pharmacological Group	Antibiotic
	Shelf life	03 Years
	Demanded Price	N/A
	Pack size	100ml
	International availability	N/A
	Me-too status	Moxillin Injection of M/s Grand Pharma (Pvt) Ltd., Rawat, Islamabad.(Reg. No. 103810) **100ml**
	Detail of certificates attached	Original Legalized GMP certificate **No:** 6856 **Certified by:** Ministry of Agriculture/The Veterinary Department- Pharmacy & Drugs Control Division/ In The Hashemite Kingdom of Jordan. **Issued on:** 23-06-2022 Validity: 3 years **Original Legalized free sale certificate:** Certificate No: 002233 Certified by: Ministry Of Agriculture/The Veterinary Department- Pharmacy & Drugs Control Division/ In The Hashmite Kingdom of Jordan certifies that Avimox L.A Injection manufactured by Avico is registered & freely sold in Jordan with the same name & Composition. **Issued on**: 10-03-2019 Original Legalized Power of attorney for **Avimox injection** by Arab Veterinary Industrial Co. "AVICO" P.O Box 150906 Amman 11115- Jordan to U.M. Enterprises, 18 C 3rd Floor Dolmen Estate Block-7, Shaheed e Millat Road, Karachi.
	Remarks of the Evaluator [X]	• Provided 06 month accelerated and 36months real time stability studies data of three batches at zone IV-A conditions. • Firm has revised finished product specification to "USP specifications" along with the fee of Rs. 7,500/- via deposit slip no 8521843822
	Decision: Deferred for following: • **Confirmation of dedicated manufacturing facility.** • **Original Legalized Power of attorney for Avimox LA injection**	
559.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Arab Veterinary Industrial Co. "AVICO" P.O.Box 150906, Amman 11115-Jordan
	Name and address of marketing authorization holder	M/s Arab Veterinary Industrial Co. "AVICO" P.O.Box 150906, Amman 11115-Jordan

	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4031 Dated 19-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 01-04-2019
	Brand Name +Dosage Form + Strength	Coliprim Injection
	Composition	Each 1ml Contains: Trimethoprim…40mg Sulphadiazine Sodium…200mg
	Finished Product Specification	Manufacturer's specifications
	Pharmacological Group	Antibiotic
	Shelf life	02 Years
	Demanded Price	N/A
	Pack size	50ml, 100ml and 250ml
	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	**Photocopy of Legalized GMP certificate: reference to file submitted in December 2019.** **Certificate No:** 000304 **Certified by:** Ministry of Agriculture/The Veterinary Department- Pharmacy & Drugs Control Division/ In The Hashemite Kingdom of Jordan. **Issued on:** 11/01/2017 Legalized Original free sale certificate: Certificate No: 002232 Certified by: Ministry Of Agriculture/The Veterinary Department- Pharmacy & Drugs Control Division/ In The Hashmite Kingdom of Jordan certifies that Coliprim Injection manufactured by Avico is registered & freely sold in Jordan with the same name & Composition and **pack size of 100ml.** **Issued on**: 10-03-2019 **Letter of Authorization (Photocopy)** Arab Veterinary Industrial Co. "AVICO" P.O Box 150906 Amman 11115- Jordan & U.M. Enterprises, 18 C 3rd Floor Dolmen Estate Block-7, Shaheed e Millat Road, Karachi. Issued on: **12th of June, 2012**
	Remarks of the Evaluator [X]	• The submitted photocopy of letter of Authorization (LOA) and GMP certificate are expired now, but valid upon submission, Provide legalized valid original LOA and GMP certificate. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non

		pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Submit Rs.7500/- for revision of finished product specifications. • Separate registration is granted to separate pack size/fill volume of injectable dosage form. However, multiple pack sizes of injectable dosage form are demanded in a single application. So clarification is required for which pack size/ fill volume you want to apply this dossier. • Provide 06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions as per requirement of 278th meeting of Registration Board.
	Decision: Deferred for following: • **Legalized valid original LOA and GMP certificate.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Submit Rs.7500/- for revision of finished product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Demanded pack size.** • **06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions**	
560.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	Huang Gang Animal Medicine Factory of China Animal Husbandry Industry Co. Ltd. No. 395, Lukou Industrial, Huangzhou Industrial Area, huang Gang City, Hubei Province, China.
	Name and address of marketing authorization holder	Huang Gang Animal Medicine Factory of China Animal Husbandry Industry Co. Ltd. No. 395, Lukou Industrial, Huangzhou Industrial Area, huang Gang City, Hubei Province, China.
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4411 Dated 24-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 24-04-2019
	Brand Name +Dosage Form + Strength	Tylvalosin Tartrate 20% Premix
	Composition	Each Gram Contains: Tylvalosin Tartrate…200mg
	Finished Product Specification	**The national standards for Veterinary drugs**
	Pharmacological Group	Macrolide antibiotic
	Shelf life	02 Years
	Demanded Price	N/A

	Pack size	100gm, 500gm, 1Kg, 5Kg and 20Kg
	International availability	N/A
	Me-too status	Could not be confirmed
	Detail of certificates attached	**Photocopy of Legalized GMP certificate: reference to file submitted in December 2019.** **Certificate No:** 000304 **Certified by:** Ministry of Agriculture/The Veterinary Department- Pharmacy & Drugs Control Division/ In The Hashemite Kingdom of Jordan. **Issued on:** 11/01/2017 **Original Legalized free sale certificate:** Certificate No: 191100B0/013124 Certified by: China Council for the promotion of International Trade China Chamber of International Commerce **Issued on**: 10-03-2019 **Letter of Authorization (Photocopy)** Arab Veterinary Industrial Co. "AVICO" P.O Box 150906 Amman 11115- Jordan & U.M. Enterprises, 18 C 3rd Floor Dolmen Estate Block-7, Shaheed e Millat Road, Karachi. Issued on: **12th of June, 2012**
	Remarks of the Evaluator [X]	• The submitted photocopy of letter of Authorization (LOA) and GMP certificate are expired now, but valid upon submission, Provide legalized valid original LOA and GMP certificate. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Submit Rs.7500/- for revision of finished product specifications. • Provide 06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions as per requirement of 278th meeting of Registration Board.
	Decision: Deferred for following: • **Legalized valid original LOA and GMP certificate.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Submit Rs.7500/- for revision of finished product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **06 months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A conditions**	
561.	Name and address of Applicant	M/s Pelican Pharma Pvt Ltd., Wazirabad Road, Morr Masjid Sambrial, District Sialkot, 51070, Pakistan
	Detail of Drug Sale License	Not provided

	Name and address of manufacturer	M/s Pharmadix Corp S.A.C. Av. Santa Lucia N 218 Urb. Ind. La Aurora, Ate, Lima-Peru
	Name and address of marketing authorization holder	Agrovet Market S.A Av. Canada 3798, San Luis- Peru
	Name of exporting country	Peru
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4027 Dated 18-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 18-04-2019
	Brand Name +Dosage Form + Strength	Neo-Terraciclina Water Soluble Powder
	Composition	Each 100G Contains: Neomycin Sulphate…20G Oxytetracycline HCl…20G
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years (Not supported by stability data)
	Demanded Price	N/A
	Pack size	1Kg
	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	**Free sale Certificate:** (**Photocopy)** Issued by: General Directorate of Livestock and agricultural inputs and Agri-food safety Deputy office of Livestock inputs. Certificate No.: 2018-0759 Date of issuance: 11-10-2018 **Validity 6 months** **GMP certificate:** (**Photocopy)** Certificate No. 2024-2016-MINAGRI-SENASA-DIAIA-SIP Date of issuance: 06-06-2016 **Sole Distributor Certificate: (Photocopy)** 07-02-2018 Validity: 3 years
	Remarks of the Evaluator [X]	• Copies of attested FSC and GMP certificate of manufacturer are provided along with commitment to provide original documents at the time of evaluation. Moreover, copy of sole distributor certificate is submitted. However, sole distributor certificate and GMP certificates are expired now but valid upon submission and **FSC is expired even upon submission**. Submit original, valid duly attested/ legalized FSC, GMP certificate of manufacturer and LOA/ sole agency certificate. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide valid copy of DSL • Provide accelerated and real time stability studies of three batches of applied product according to zone IV-A conditions upto claimed shelf life.

		• Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • "Pack size" is not mentioned in form-5A. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Original, valid duly attested/ legalized FSC, GMP certificate of manufacturer and LOA/ sole agency certificate.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Valid copy of DSL** • **06 months accelerated and real time stability studies data of three batches upto claimed shelf life of applied product according to zone IV-A conditions.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
562.	Name and address of Applicant	M/s Pelican Pharma Pvt Ltd., Wazirabad Road, Morr Masjid Sambrial, District Sialkot, 51070, Pakistan
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Pharmadix Corp S.A.C. Av. Santa Lucia N 218 Urb. Ind. La Aurora, Ate, Lima-Peru
	Name and address of marketing authorization holder	Agrovet Market S.A Av. Canada 3798, San Luis- Peru
	Name of exporting country	Peru
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4028 Dated 18-04-2019
	Fee including differential fee	Rs : 50,000 Dated 18-04-2019
	Brand Name +Dosage Form + Strength	Diflovet OS Oral Solution
	Composition	Each 100ml Contains: Difloxacin as HCl…10gm
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years (Not supported by stability data)
	Demanded Price	N/A
	Pack size	Not demanded
	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	**Free sale Certificate:** (**Photocopy)** Issued by: General Directorate of Livestock and agricultural inputs and Agri-food safety Deputy office of Livestock inputs. Certificate No.: 2018-0718 Date of issuance: **04-10-2018** **Validity 6 months**

		GMP certificate: (**Photocopy)** Certificate No. 2024-2016-MINAGRI-SENASA-DIAIA-SIP Date of issuance: 06-06-2016 **Sole Distributor Certificate: (Photocopy)** 07-02-2018 Validity: 3 years
	Remarks of the Evaluator [X]	• Copies of attested FSC and GMP certificate of manufacturer are provided along with commitment to provide original documents at the time of evaluation. Moreover, copy of sole distributor certificate is submitted. However, sole distributor certificate and GMP certificates are expired now but valid upon submission and **FSC is expired even upon submission**. Submit original, valid duly attested/ legalized FSC, GMP certificate of manufacturer and LOA/ sole agency certificate. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide valid copy of DSL • Provide accelerated and real time stability studies of three batches of applied product according to zone IV-A conditions upto claimed shelf life. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • "Pack size" is not mentioned in form-5A. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Original, valid duly attested/ legalized FSC, GMP certificate of manufacturer and LOA/ sole agency certificate.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Valid copy of DSL** • **06 months accelerated and real time stability studies data of three batches upto claimed shelf life of applied product according to zone IV-A conditions.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
563.	Name and address of Applicant	M/s Pelican Pharma Pvt Ltd., Wazirabad Road, Morr Masjid Sambrial, District Sialkot, 51070, Pakistan
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Pharmadix Corp S.A.C. Av. Santa Lucia N 218 Urb. Ind. La Aurora, Ate, Lima-Peru
	Name and address of marketing authorization holder	Agrovet Market S.A Av. Canada 3798, San Luis- Peru
	Name of exporting country	Peru

	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4030 Dated 18-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 18-04-2019
	Brand Name +Dosage Form + Strength	Amoxycol Water Soluble Powder
	Composition	Each 1gram Contains: Amoxicillin Base…200mg Colistin Sulphate As Colistin…40mg
	Finished Product Specification	Chinese Veterinary Pharmacopoeia
	Pharmacological Group	Antibiotic
	Shelf life	2 years (Not supported by stability data)
	Demanded Price	N/A
	Pack size	1 kg
	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	**Free sale Certificate:** (**Photocopy)** Issued by: General Directorate of Livestock and agricultural inputs and Agri-food safety Deputy office of Livestock inputs. Certificate No.: 2018-0925 Date of issuance: **17-12-2018** **Validity 6 months** **GMP certificate:** (**Photocopy)** Certificate No. 2024-2016-MINAGRI-SENASA-DIAIA-SIP Date of issuance: 06-06-2016 **Sole Distributor Certificate: (Photocopy)** 07-02-2018 Validity: 3 years
	Remarks of the Evaluator [X]	• Copies of attested FSC and GMP certificate of manufacturer are provided along with commitment to provide original documents at the time of evaluation. Moreover, copy of sole distributor certificate is submitted. However, FSC, sole distributor certificate and GMP certificates are expired now but valid upon submission. Submit original, valid duly attested/ legalized FSC, GMP certificate of manufacturer and LOA/ sole agency certificate. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide valid copy of DSL • Provide accelerated and real time stability studies of three batches of applied product according to zone IV-A conditions upto claimed shelf life. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • "Pack size" is not mentioned in form-5A. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii)

		Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Original, valid duly attested/ legalized FSC, GMP certificate of manufacturer and LOA/ sole agency certificate.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Valid copy of DSL** • **06 months accelerated and real time stability studies data of three batches upto claimed shelf life of applied product according to zone IV-A conditions.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
564.	Name and address of Applicant	M/s Pelican Pharma Pvt Ltd., Wazirabad Road, Morr Masjid Sambrial, District Sialkot, 51070, Pakistan
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Pharmadix Corp S.A.C. Av. Santa Lucia N 218 Urb. Ind. La Aurora, Ate, Lima-Peru
	Name and address of marketing authorization holder	Agrovet Market S.A Av. Canada 3798, San Luis- Peru
	Name of exporting country	Peru
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4029 Dated 18-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 18-04-2019
	Brand Name +Dosage Form + Strength	Tylamox Water Soluble Powder
	Composition	Each 100g Contains: Tylosin as Tartrate…50g Amoxicillin as Trihydrate…10g
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years (Not supported by stability data)
	Demanded Price	N/A
	Pack size	Not demanded
	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	**Free sale Certificate:** (**Photocopy)** Issued by: General Directorate of Livestock and agricultural inputs and Agri-food safety Deputy office of Livestock inputs. Certificate No.: 2018-0717 Date of issuance: **04-10-2018** **Validity 6 months** **GMP certificate:** (**Photocopy)** Certificate No. 2024-2016-MINAGRI-SENASA-DIAIA-SIP Date of issuance: 06-06-2016 **Sole Distributor Certificate: (Photocopy)** 07-02-2018

		Validity: 3 years
	Remarks of the Evaluator [X]	• Copies of attested FSC and GMP certificate of manufacturer are provided along with commitment to provide original documents at the time of evaluation. Moreover, copy of sole distributor certificate is submitted. However, sole distributor certificate and GMP certificates are expired now but valid upon submission and **FSC is expired even upon submission**. Submit original, valid duly attested/ legalized FSC, GMP certificate of manufacturer and LOA/ sole agency certificate. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide valid copy of DSL • Provide accelerated and real time stability studies of three batches of applied product according to zone IV-A conditions upto claimed shelf life. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • "Pack size" is not mentioned in form-5A. • Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Original, valid duly attested/ legalized FSC, GMP certificate of manufacturer and LOA/ sole agency certificate.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Valid copy of DSL** • **06 months accelerated and real time stability studies data of three batches upto claimed shelf life of applied product according to zone IV-A conditions.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
565.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Name: M/s U.M. Enterprises, Address: Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan Date of issuance: 01-09-2021. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name and address of marketing authorization holder	M/s Qilu Animal Health Products Co. Ltd. No. 243, Gongye North Road, Jinan, Shandong, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4705 Dated 29-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 29-04-2019

	Brand Name +Dosage Form + Strength	Alphamox LA Suspension for Injection
	Composition	Each 1ml Contains: Amoxicillin As Amoxicillin Trihydrate…150mg
	Finished Product Specification	As per innovator's specifications
	Pharmacological Group	Antibiotic
	Shelf life	24 months
	Demanded Price	N/A
	Pack size	100ml glass vial
	International availability	N/A
	Me-too status	Xlmox Injection of M/s Mediexcel Pharmaceuticals, Islamabad. (Reg. No. 103885)
	Detail of certificates attached	**ORIGINAL LEGALIZED CoPP** **Certified by:** Bureau of Animal Husbandry & Veterinary of Shandong Province, China **Certificate NO:** Vet. Drug No. (2016)150256176 **Issued on:** 06/11/2018 **Free sale:** Free sale of the product in exporting country: Yes, confirms from COPP **GMP:** Yes confirm from COPP **Authorization Letter (copy, original attached in Flumeglu dossier)** Date of issuance: 11-12-2017 Validity: 3 years
	Remarks of the Evaluator [X]	• Provided 6 months accelerated and 24 months' real time stability studies data of three batches at zone IV-A conditions • The submitted copy of letter of Authorization (LOA) is expired now, but valid upon submission. The firm has committed to submit legalized valid original LOA when they will receive it from their Principal.
	Decision: Deferred for following: • **Confirmation of dedicated manufacturing facility** • **legalized valid original LOA**	
566.	Name and address of Applicant	M/s Saadat International, 117 Habitat Flat, Shadman II, Jail Road, Lahore, Pakistan
	Detail of Drug Sale License	Valid copy required
	Name and address of manufacturer	Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria (QC and Batch Release) 48 Vasil Petleshkov Str Peshtera 4550, Bulgaria (Manufacture)
	Name and address of marketing authorization holder	M/s Huvepharma NV. Uitbreidingstraat 80, 2600 Antwerpen, Belgium
	Name of exporting country	Bulgaria
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4476 Dated 24-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 24-04-2019
	Brand Name +Dosage Form + Strength	Gallifen 200mg/ml Suspension for Oral Solution

	Composition	Each ml Contains: Fenbendazole…200mg
	Finished Product Specification	Not mentioned
	Pharmacological Group	Anthelmintic
	Shelf life	30 months
	Demanded Price	Decontrolled
	Pack size	1Liter, 2.5Liter and 5 Liter
	International availability	Gallifen 200 mg/ml suspension for use in drinking water (Federal Agency for Medicines and Health Products, **Belgium approved**)
	Me-too status	Not provided
	Detail of certificates attached	• Original legalized Certificate of Pharmaceutical Product Certificate No: BG 34/2018 Issued on: 10/07/2018, Certified by: Bulgarian Food Safety Agency Ministry of Agriculture, Food and Forestry 15 Pencho Slaveikov Blvd. Sofia 1606, Bulgaria • Free sale of the product in exporting country: Yes, confirm from COPP • GMP status: conform to GMP as recommended by the WHO Periodicity of routine inspections: 2 years • Certificate of agreement dated between M/s HuvePharma EOOD, 3a Nikolay Haytov street 1113 Sofia, Bulgaria and M/s Saadat International, 117 Habitat Flat, Shadman II, Jail Road, Lahore, Pakistan. **(Original legalized attached in Pharmasin WSG dossier)**
	Remarks of the Evaluator [X]	**Shortcomings:** • Provide valid copy of DSL since the already submitted copy is expired. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Provide real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions. Only 24-months real time stability studies data has been submitted while the claimed shelf life is 30 months. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Decision: Deferred for following: • **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.**	
567.	Name and address of Applicant	M/s Saadat International, 117 Habitat Flat, Shadman II, Jail Road, Lahore, Pakistan
	Detail of Drug Sale License	Valid copy required

	Name and address of manufacturer	Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria (QC and Batch Release) 48 Vasil Petleshkov Str Peshtera 4550, Bulgaria (Manufacture)
	Name and address of marketing authorization holder	M/s Huvepharma NV. Uitbreidingstraat 80, 2600 Antwerpen, Belgium
	Name of exporting country	Bulgaria
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 7570 Dated 29-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 29-05-2019
	Brand Name +Dosage Form + Strength	Pharmasin 100% w/w Water Soluble Granules
	Composition	Each 1.1 gram granules contain: Tylosin Tartrate 110gm Eq. To Tylosin Activity…100gm
	Finished Product Specification	Not mentioned
	Pharmacological Group	Macrolide antibiotics
	Shelf life	36 months
	Demanded Price	Decontrolled
	Pack size	HDPE bottle 125gm, PE/Al/PET bag 125gm
	International availability	Pharmasin 100% w/w Water Soluble Granules (Federal Agency for Medicines and Health Products, **Belgium approved)**
	Me-too status	Not provided
	Detail of certificates attached	• Original legalized Certificate of Pharmaceutical Product Certificate No: BG 9/2019 Issued on: 29/01/2019, Certified by: Bulgarian Food Safety Agency Ministry of Agriculture, Food and Forestry 15 Pencho Slaveikov Blvd. Sofia 1606, Bulgaria • Free sale of the product in exporting country: Yes, confirm from COPP • GMP status: conform to GMP as recommended by the WHO Periodicity of routine inspections: 2 years • Original legalized Certificate of agreement dated between M/s HuvePharma EOOD, 3a Nikolay Haytov street 1113 Sofia, Bulgaria and M/s Saadat International, 117 Habitat Flat, Shadman II, Jail Road, Lahore, Pakistan.
	Remarks of the Evaluator [X]	**Shortcomings:** • Provide valid copy of DSL since the already submitted copy is expired. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Provide real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions; since the already submitted 36-months real time stability studies data is not as per zone IV-A/ IV-B conditions.

		• Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • "Demanded Pack size" is not mentioned in form-5A.
	Decision: Deferred for following: • **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Demanded Pack size**	
568.	Name and address of Applicant	M/s Saadat International, 117 Habitat Flat, Shadman II, Jail Road, Lahore, Pakistan
	Detail of Drug Sale License	Valid copy required
	Name and address of manufacturer	Biovet Joint Stock Company 39, Petar Rakov St. 4500 Peshtera, Bulgaria (QC and Batch Release) 48 Vasil Petleshkov Str Peshtera 4550, Bulgaria (Manufacture)
	Name and address of marketing authorization holder	M/s Huvepharma NV. Uitbreidingstraat 80, 2600 Antwerpen, Belgium
	Name of exporting country	Bulgaria
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 7569 Dated 29-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 29-05-2019
	Brand Name +Dosage Form + Strength	Pharmasin 200mg/ml Solution for Injection
	Composition	Each 50ml Contains: Tylosin…10gm
	Finished Product Specification	Not mentioned
	Pharmacological Group	Macrolide antibiotics
	Shelf life	24 months
	Demanded Price	Decontrolled
	Pack size	100ml
	International availability	Pharmasin 200mg/ml Solution for Injection (Federal Agency for Medicines and Health Products, **Belgium approved**)
	Me-too status	Not provided
	Detail of certificates attached	• Original legalized Certificate of Pharmaceutical Product Certificate No: BG 8/2019 Issued on: 29/01/2019, Certified by: Bulgarian Food Safety Agency Ministry of Agriculture, Food and Forestry 15 Pencho Slaveikov Blvd. Sofia 1606, Bulgaria • Free sale of the product in exporting country: Yes, confirm from COPP • GMP status: conform to GMP as recommended by the WHO Periodicity of routine inspections: 2 years

		• Certificate of agreement dated between M/s HuvePharma EOOD, 3a Nikolay Haytov street 1113 Sofia, Bulgaria and M/s Saadat International, 117 Habitat Flat, Shadman II, Jail Road, Lahore, Pakistan. **(Original legalized Certificate of agreement attached in Pharmasin WSG dossier)**
	Remarks of the Evaluator [X]	**Shortcomings:** • Provide valid copy of DSL since the already submitted copy is expired. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Provide real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions; since the already submitted 36-months real time stability studies data is not as per zone IV-A/ IV-B conditions. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • "Demanded Pack size" is not mentioned in form-5A.
	Decision: Deferred for following: • **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Demanded Pack size**	
569.	Name and address of Applicant	M/s Maacs Pharmaceuticals. 194-N, Phase 8, DHA, Lahore, Cantt.
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Biofaktor Sp. Z o.o. 96-100, UI. Czysta 4, Poland
	Name and address of marketing authorization holder	M/s Biofaktor Sp. Z o.o. 96-100, UI. Czysta 4, Poland
	Name of exporting country	Poland
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4412 Dated 24-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 24-04-2019
	Brand Name +Dosage Form + Strength	Fortamox 500mg Powder for Oral Solution
	Composition	Each Gram Contains: Amoxicillin Trihydrate…500mg
	Finished Product Specification	Inhouse
	Pharmacological Group	Beta lactam antibiotic
	Shelf life	2 years
	Demanded Price	Rs. 19500/ 1000gm
	Pack size	1000gm, 100gm and 50gm

	International availability	Not provided
	Me-too status	The submitted reference to generic products could not be verified since both contains 500mg of Amoxicillin base per gram while the applied product contains Amoxicillin trihydrate 500mg/gram.
	Detail of certificates attached	Photocopy of Certificate of Pharmaceutical Product Certificate **(not embassy attested)** No. 846/18 Issued on 14/11/2018, Certified by chief Pharmaceutical Inspector, 12 Senatorska Street, 00-082 Warsaw, Poland. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through routine inspection with 3 year periodicity. • Letter of authorization not provided.
	Remarks of the Evaluator [X]	**Shortcomings:** • Provide valid copy of DSL. • Provide original legalized valid CoPP and Letter of authorization between product license holder and distributor. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Provide real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions; since the already submitted 24-months real time stability studies data is not as per zone IV-A/ IV-B conditions. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Valid copy of DSL.** • **Original legalized valid CoPP and Letter of authorization between product license holder and distributor.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
570.	Name and address of Applicant	M/s Maacs Pharmaceuticals, 194-N, Phase 8, DHA, Lahore, Cantt.
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Biofaktor Sp. Z o.o. 96-100, UI. Czysta 4, Poland
	Name and address of marketing authorization holder	M/s Biofaktor Sp. Z o.o. 96-100, UI. Czysta 4, Poland
	Name of exporting country	Poland

	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4413 Dated 24-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 24-04-2019
	Brand Name +Dosage Form + Strength	Enrofloxan 100mg/ml Oral Solution
	Composition	Each ml contains: Enrofloxacin…100mg
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Demanded Price	Rs. 2200/ 1000ml
	Pack size	1000ml, and 100ml
	International availability	Not provided
	Me-too status	Kariflox 10% Oral Solution of M/s Unicare Enterprises, Faisalabad. (Reg. No. 081715)
	Detail of certificates attached	Photocopy **(not embassy attested)** of Certificate of Pharmaceutical Product Certificate No. 845/18 Issued on 14/11/2018, Certified by chief Pharmaceutical Inspector, 12 Senatorska Street, 00-082 Warsaw, Poland. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through routine inspection with 3 year periodicity. • Letter of authorization not provided.
	Remarks of the Evaluator [X]	**Shortcomings:** • Provide valid copy of DSL. • Provide original legalized valid CoPP and Letter of authorization between product license holder and distributor. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Provide real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions; since the already submitted 24-months real time stability studies data is not as per zone IV-A/ IV-B conditions. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Valid copy of DSL.** • **Original legalized valid CoPP and Letter of authorization between product license holder and distributor.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
571.	Name and address of Applicant	M/s Maacs Pharmaceuticals, 194-N, Phase 8, DHA, Lahore, Cantt.

	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Biofaktor Sp. Z o.o. 96-100, UI. Czysta 4, Poland
	Name and address of marketing authorization holder	M/s Biofaktor Sp. Z o.o. 96-100, UI. Czysta 4, Poland
	Name of exporting country	Poland
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4414 Dated 24-04-2019
	Fee including differential fee	Rs : 1,00,000 Dated 24-04-2019
	Brand Name +Dosage Form + Strength	Doxyfort 500mg Powder for oral Solution
	Composition	Each gram contains: Doxycycline Hyclate…500mg
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Demanded Price	Rs. 15000/ 1000gm
	Pack size	1000gm, 500gm, and 100gm
	International availability	Not provided
	Me-too status	Doxyveto- 50 S Soluble Powder of M/s VMD Pakistan Rawalpindi. (Reg. No. 023470)
	Detail of certificates attached	Photocopy of **(not embassy attested)** Certificate of Pharmaceutical Product Certificate No. 847/18 Issued on 14/11/2018, Certified by chief Pharmaceutical Inspector, 12 Senatorska Street, 00-082 Warsaw, Poland. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through routine inspection with 3 year periodicity. • Letter of authorization not provided.
	Remarks of the Evaluator [X]	**Shortcomings:** • Provide valid copy of DSL. • Provide original legalized valid CoPP and Letter of authorization between product license holder and distributor. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Provide real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions; since the already submitted 24-months real time stability studies data is not as per zone IV-A/ IV-B conditions. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Valid copy of DSL.** • **Original legalized valid CoPP and Letter of authorization between product license holder and distributor.**	

	• **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
572.	Name and address of Applicant	M/s Orient Traders International, CM-10, Block A, Kazimabad, Model Colony, Karachi, Pakistan
	Detail of Drug Sale License	Name: M/s Orient Traders International Address: CM-10, Block A, Kazimabad, Model Colony, Karachi Validity: 26th January 2024 Status: Drug License By Way of Wholesale (Form No.07).
	Name and address of manufacturer	M/s Laboratoires Biove, 3 Rue de, Lorraine, 62510 Arques, France (bulk manufacturing, manufacturing of the finished product, packaging, labelling & QC)
	Name and address of marketing authorization holder	M/s V.M.D. N. V. Hoge Mauw 900 2370 Arendonk-Belgium
	Name of exporting country	Belgium
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 5195 Dated 03-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 03-05-2019
	Brand Name +Dosage Form + Strength	Citrodox-700 Soluble Powder
	Composition	Each gram contains: Doxycycline Hyclate…500mg
	Finished Product Specification	Ph. Eur
	Pharmacological Group	Tetracycline antibiotic
	Shelf life	2 years
	Demanded Price	N/A
	Pack size	100gm, and 1Kg
	International availability	Doxyveto 500 mg/g powder for use in drinking water/milk replacer for cattle, pig, chicken **(MHRA approved)**
	Me-too status	Doxyfas 50% Water Soluble Powder of M/s Intervac (Pvt) Ltd., Sheikhupura. (Reg. No. 103933)
	Detail of certificates attached	▪ Original legalized Certificate of Pharmaceutical Product Certificate No. 000005 Issued on 26/08/2022, Certified by *Federal Agency for medicines and health products – famhp, Eurostation II, Victor Hortaplein 40/40, 1060 Brussels, Belgium*. The CoPP confirms free sale status of the product in exporting country as well as GMP status of the manufacturing site through routine inspection with 2 year periodicity. ▪ Scanned copy of letter of authorization (LOA) dated 14-09-2021, validity 3 years, is given. (**Referred to Tulinovet 100mg/ml dated 04-06-2021 for original LOA.)**
	Remarks of the Evaluator [X]	➢ 06 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions. • The firm has revised the following pack sizes from 100mg, 500mg, 1Kg, 10Kg and 25Kg to **100gm and 1Kg** only.

	Decision: Approved as per Policy for inspection of manufacturer abroad. The firm shall submit valid notarized Letter of Authorization before issuance of registration letter.	
573.	Name and address of Applicant	M/s Eli Lilly Pakistan Pvt Ltd., 5-A, 5th Office Floor, Al-Tijarah Centre, 32-1-A, Block 6, PECHS, Main Shahra-E-Faisal Karachi, Pakistan
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Andres Pintaluba, S.A. C/Prudenci Bertrana, 5 y 10, Pol. Ind. Agro-Reus, Tarragona, 43206, Spian
	Name and address of marketing authorization holder	Elanco spain SLU, Avenida de la Industria 30, 28108, Alcobendas, Madrid
	Name of exporting country	Spain
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No. 6272 Dated 15-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 15-05-2019
	Brand Name +Dosage Form + Strength	Denagard 10% Premix
	Composition	Each Kg contains: Tiamulin as Tiamulin Hydrogen Fumarate…100g
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	3 years
	Demanded Price	Decontrolled
	Pack size	25Kg bags
	International availability	DENAGARD 100 mg/g MEDICINAL PREMIX for pigs, poultry and rabbits **(CIMA vet, Spain approved)**
	Me-too status	Not provided
	Detail of certificates attached	▪ Scanned copy of Free Sale Certificate dated 14-11-2018 issued by Spanish agency of Medicines and Medical Devices, confirms free sale status of the product in exporting country ▪ Originally legalized copy of GMP certificate No. ES/057HV/18 issued by Spanish agency of Medicines and Medical Devices, based on inspection conducted 01-02-2018. ▪ Submitted LoA from Elanco Animal Health, 2500 Innovation Way, Greenfield, Indiana, USA instead of product License Holder.
	Remarks of the Evaluator [X]	**Shortcomings:** • Provide valid copy of DSL. • Provide legalized original valid GMP certificate as more than three years have elapsed since the date of last inspection of the manufacturing site and legalized original valid FSC as scanned copy of FSC is provided. • Provide original legalized valid Letter of authorization/sole agency agreement between product license holder and distributor since already submitted LoA is from Elanco Animal Health, 2500 Innovation Way, Greenfield, Indiana, USA instead of product License Holder. • Tiamulin as Tiamulin Hydrogen Fumarate…100g/Kg is mentioned in label claim on form-5A while Tiamulin

		Hydrogen Fumarate…100mg/gram is mentioned on FSC and master formula. Revise label claim/ master formula in line with reference product and submit full fee of registration for revision of label claim/ master formula. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Provide 06 month accelerated and 36-month real time stability studies data of three batches at zone IV-A/ IV-B conditions; since the already submitted 36-months real time stability studies data is not as per zone IV-A/ IV-B conditions. • Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986.
	Decision: Deferred for following: • **Valid copy of DSL.** • **Legalized original valid FSC and GMP certificate** • **Original legalized valid Letter of authorization/sole agency agreement between product license holder and distributor since already submitted LoA is from Elanco Animal Health, 2500 Innovation Way, Greenfield, Indiana, USA instead of product License Holder.** • **Revision of label claim/ master formula in line with reference product and full fee of registration for revision of label claim/ master formula as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **06 month accelerated and 36-month real time stability studies data of three batches at zone IV-A/ IV-B conditions.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.**	
574.	Name and address of Applicant	M/s Hi-Tech Pharmaceuticals. 1-C Shadman Chowk, Jail Road, Lahore, Pakistan
	Detail of Drug Sale License	Name: M/s Hi-Tech Pharmaceuticals Address: 1-C Shadman Chowk, Jail Road, Lahore. Validity: 11 October 2020. Status: License to sell drugs as a Distributor (Form No.11).
	Name and address of manufacturer	M/s Nita-Farm LLC. 1, Osipova V.I. Street, Saratov, Russia
	Name and address of marketing authorization holder	M/s Nita-Farm LLC. 1, Osipova V.I. Street, Saratov, Russia
	Name of exporting country	Russia
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6654 Dated 21-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 21-05-2019
	Brand Name +Dosage Form + Strength	Azitronit Injection

	Composition	Each 100ml vial contains: Azithromycin…10gm Lidocaine HCl…1gm
	Finished Product Specification	
	Pharmacological Group	Antibacterial
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	100ml
	International availability	Not provided
	Me-too status	Not provided
	Detail of certificates attached	▪ Photocopy of Legalized GMP certificate No: 120905 Certified by: RTS LLC POCC PTC. 0001.OC. AA Office 29, 57 Profsoyznaya str., 117420, Moscow Russia. Validity: 26-12-2020 ▪ Original legalized FSC No. **Рэц 01/689/2018** Issued on 13/03/2018, Certified by *Russian Export Center joint- stock company, the Russian Federation* confirms free sale status of the product in exporting country. ▪ Photocopy of distribution agreement between product license holder and distributor dated 2017 is provided.
	Remarks of the Evaluator [X]	• Provide valid copy of DSL. • The submitted GMP certificate is photocopy which is expired now but valid upon submission. Provide legalized original valid GMP certificate. • The submitted agreement between product license holder and distributor is photocopy, Provide legalized original valid agreement. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Provide 06-months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions; since only real time data is submitted which is not as per zone IV-A/ IV-B conditions. • Demanded Pack size is not mentioned in form-5A.
	Decision: Deferred for following: • **Valid copy of DSL.** • **Legalized original valid GMP certificate.** • **Legalized original valid agreement between product license holder and distributor.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.**	

	• **06-months accelerated and real time stability studies data upto claimed shelf life of three batches at zone IV-A/ IV-B conditions.** • **Demanded Pack size.**	
575.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Arab Veterinary Industrial Co. "AVICO" P.O.Box 150906, Amman 11115-Jordan
	Name and address of marketing authorization holder	M/s Arab Veterinary Industrial Co. "AVICO" P.O.Box 150906, Amman 11115-Jordan
	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 5259 Dated 06-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 06-05-2019
	Brand Name +Dosage Form + Strength	Avistrep Suspension for Injection
	Composition	Each 1ml Contains: Penicillin G Procaine…200mg Dihydrostreptomycin Sulphate…250mg
	Finished Product Specification	Manufacturer's specifications
	Pharmacological Group	Antibiotic
	Shelf life	02 Years
	Demanded Price	N/A
	Pack size	50ml and 100ml glass vials
	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	Photocopy of Legalized GMP certificate: (Original legalized GMP certificate attached in file Trimectin Cattle Suspension (Dy. No. 26140 dated 05-12-2019) **Certificate No:** 008342 **Certified by:** Director of Veterinary & Animal Health, Ministry of Agriculture, The Hashemite Kingdom of Jordan. **Issued on:** 25/09/2019 **Validity**: 3 years **Original Legalized free sale certificate:** Certificate No: 003670 Certified by: Ministry Of Agriculture/The Veterinary Department- Pharmacy & Drugs Control Division/ In The Hashmite Kingdom of Jordan certifies that Avistrep Injection Suspension manufactured by Avico is registered & freely sold in Jordan with the same name, Composition and pack (50ml and 100ml). **Issued on**: 21-04-2019 **Letter of Authorization (Photocopy)** Arab Veterinary Industrial Co. "AVICO" P.O Box 150906 Amman 11115- Jordan & U.M. Enterprises, 18 C 3rd Floor Dolmen Estate Block-7, Shaheed e Millat Road, Karachi. Issued on: **12th of June, 2012**

	Remarks of the Evaluator [X]	• The submitted photocopy of letter of Authorization (LOA) is issued **10 years ago,** Provide legalized valid original LOA. • Scope of submitted GMP certificate does not cover penicillin injectable., provide legalized original valid relevant GMP certificate. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Submit Rs.7500/- for revision of finished product specifications. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Separate registration is granted to separate pack size/fill volume of injectable dosage form. However, multiple pack sizes of injectable dosage form are demanded in a single application. So clarification is required for which pack size/ fill volume you want to apply this dossier. ➢ The firm has submitted label for 50ml pack size in accordance with The Drugs (Labeling and Packing) Rules, 1986. ➢ 6 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions.(for both 50ml and 100ml)
	Decision: Registration Board deferred the case for submission of reply to the above cited shortcomings within six months.	
576.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Arab Veterinary Industrial Co. ”AVICO” P.O.Box 150906, Amman 11115-Jordan
	Name and address of marketing authorization holder	M/s Arab Veterinary Industrial Co. ”AVICO” P.O.Box 150906, Amman 11115-Jordan
	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 8473 Dated 14-06-2019
	Fee including differential fee	Rs : 1,00,000 Dated 14-06-2019
	Brand Name +Dosage Form + Strength	Allergamine Injection
	Composition	Each 1ml Contains: Diphenhydramine HCl…20mg
	Finished Product Specification	Manufacturer’s specifications
	Pharmacological Group	Antihistamine
	Shelf life	02 Years
	Demanded Price	N/A
	Pack size	20ml amber glass vials

	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	Photocopy of Legalized GMP certificate: (Original legalized GMP certificate attached in file Trimectin Cattle Suspension (Dy. No. 26140 dated 05-12-2019) **Certificate No:** 008342 **Certified by:** Director of Veterinary & Animal Health, Ministry of Agriculture, The Hashemite Kingdom of Jordan. **Issued on:** 25/09/2019 **Validity**: 3 years **Original Legalized free sale certificate:** Certificate No: 004317 Certified by: Ministry Of Agriculture/The Veterinary Department- Pharmacy & Drugs Control Division/ In The Hashmite Kingdom of Jordan certifies that Avistrep Injection Suspension manufactured by Avico is registered & freely sold in Jordan with the same name, Composition and pack (20ml, 50ml and 100ml). **Issued on**: 12-05-2019 **Letter of Authorization (Photocopy)** Arab Veterinary Industrial Co. "AVICO" P.O Box 150906 Amman 11115- Jordan & U.M. Enterprises, 18 C 3rd Floor Dolmen Estate Block-7, Shaheed e Millat Road, Karachi. Issued on: **12th of June, 2012**
	Remarks of the Evaluator [X]	• The submitted photocopy of letter of Authorization (LOA) is issued **10 years ago,** Provide valid original legalized LOA. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Submit Rs.7500/- for revision of finished product specifications. • Evidence of applied formulation/drug already approved by DRAP with **same pack size/fill volume** as applied (generic / me-too status) alongwith registration number, brand name and name of firm. ➢ 6 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions.
	Decision: Deferred for following: • **Valid original legalized LOA.** • **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Fee Rs.7500/- for revision of finished product specifications as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.** • **Evidence of applied formulation/drug already approved by DRAP with same pack size/fill volume as applied (generic / me-too status) alongwith registration number, brand name and name of firm.**	
577.	Name and address of Applicant	M/s U.M. Enterprises, Plot No. 12, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan

	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Arab Veterinary Industrial Co. ”AVICO” P.O.Box 150906, Amman 11115-Jordan
	Name and address of marketing authorization holder	M/s Arab Veterinary Industrial Co. ”AVICO” P.O.Box 150906, Amman 11115-Jordan
	Name of exporting country	Jordan
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 11472 Dated 10-07-2019
	Fee including differential fee	Rs : 1,00,000 Dated 10-07-2019
	Brand Name +Dosage Form + Strength	Avisulpha Injection
	Composition	Each 1ml Contains: Sulphadimidine Sodium…330mg (Eq. To 304mg Sulphadimidine)
	Finished Product Specification	Not mentioned
	Pharmacological Group	Antibiotic
	Shelf life	02 Years
	Demanded Price	N/A
	Pack size	100ml glass vials
	International availability	Could not be confirmed in the applied dosage form
	Me-too status	Not provided
	Detail of certificates attached	Photocopy of Legalized GMP certificate: **(Original legalized GMP certificate attached in file Trimectin Cattle Suspension (Dy. No. 26140 dated 05-12-2019)** **Certificate No:** 008342 **Certified by:** Director of Veterinary & Animal Health, Ministry of Agriculture, The Hashemite Kingdom of Jordan. **Issued on:** 25/09/2019 **Validity**: 3 years **Original Legalized free sale certificate:** Certificate No: 004816 Certified by: Ministry Of Agriculture/The Veterinary Department- Pharmacy & Drugs Control Division/ In The Hashmite Kingdom of Jordan certifies that Avistrep Injection Suspension manufactured by Avico is registered & freely sold in Jordan with the same name, Composition and pack (100ml). **Issued on**: 28-05-2019 **Letter of Authorization (Photocopy)** Arab Veterinary Industrial Co. “AVICO” P.O Box 150906 Amman 11115- Jordan & U.M. Enterprises, 18 C 3rd Floor Dolmen Estate Block-7, Shaheed e Millat Road, Karachi. Issued on: **12th of June, 2012**
	Remarks of the Evaluator [X]	• The submitted photocopy of letter of Authorization (LOA) is issued **10 years ago,** Provide legalized valid original LOA. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board.

		• Submit Rs.7500/- for revision of finished product specifications. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. ➢ 6 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions.(for both 50ml and 100ml)
	Decision: Deferred for following: • **Legalized original valid Letter of authorization/sole agency agreement between product license holder and distributor.** • **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Original valid CoPP duly attested by embassy of Pakistan.** • **Legalized original valid GMP certificateof the manufacturer.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Label in accordance with The Drugs (Labeling and Packing) Rules, 1986.** • **Demanded Pack size**	
578.	Name and address of Applicant	M/s Vety Care Pvt Ltd., Plot # 77, Street No. 6, I-10/3, Islamabad
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name and address of marketing authorization holder	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name of exporting country	**Netherlands (Holland)**
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6169 Dated 15-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 14-05-2019
	Brand Name +Dosage Form + Strength	Bravecto Spot-On Solution for dogs and Cats 500mg/1.79ml
	Composition	Each ml contains: Fluralaner…280mg
	Finished Product Specification	Not provided
	Pharmacological Group	Systemic insecticide and acaricide
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	Not mentioned
	International availability	**Bravecto USFDA approved**
	Me-too status	Not provided
	Detail of certificates attached	Photocopy of CoPP No. V2017-1051 dated 14-09-2017 issued by **US Food and Drug, Administration, USA.** The CoPP confirms free sale status of the product in **USA** as well as GMP status of the manufacturing site. Validity: 24 months Letter of Authorization/ sole agency agreement Not provided

		GMP certificate No. NL/H 15/1005102A based on inspection conducted on 06-11-2015 issued by Healthcare Inspectorate-Pharmaceutical Affairs and Medical Technology, Netherlands
	Remarks of the Evaluator [X]	• Provide valid copy of DSL • Photocopy of CoPP is provided which is **expired now but valid upon submission;** Submit original valid CoPP duly attested by embassy of Pakistan. • Provide legalized original valid GMP certificate as more than three years have elapsed since the date of last inspection of the manufacturing site. • Provide legalized original valid Letter of authorization/sole agency agreement between product license holder and distributor. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986. • Demanded Pack size is not mentioned in form-5A. ➢ 6 months accelerated and 36 months long term stability studies data has been submitted as per zone-IV-A conditions. ➢ Firm has submitted 3 separate applications with separate fee for topical solution having same strength but different fill volume. However, as per practice in vogue, a single registration number is allotted to different fill volumes of topical solution having same strength.
	Decision: Deferred for submission of following: • **Valid copy of DSL of the applicant.** • **Original, legalized & valid CoPP.** • **Notarized & valid Letter of authorization/sole agency agreement between product license holder and distributor.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size**	

579.	Name and address of Applicant	M/s Vety Care Pvt Ltd., Plot # 77, Street No. 6, I-10/3, Islamabad
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name and address of marketing authorization holder	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name of exporting country	**Netherlands (Holland)**

	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6167 Dated 15-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 14-05-2019
	Brand Name +Dosage Form + Strength	Bravecto Spot-On Solution for dogs and Cats 112.5mg/0.4ml
	Composition	Each ml contains: Fluralaner…280mg
	Finished Product Specification	Not mentioned
	Pharmacological Group	Systemic insecticide and acaricide
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	Not provided
	International availability	**Bravecto USFDA approved**
	Me-too status	Not provided
	Detail of certificates attached	Photocopy of CoPP No. V2017-1051 dated 14-09-2017 issued by **US Food and Drug, Administration, USA.** The CoPP confirms free sale status of the product in **USA** as well as GMP status of the manufacturing site. Validity: 24 months Letter of Authorization/ sole agency agreement Not provided GMP certificate No. NL/H 15/1005102A based on inspection conducted on 06-11-2015 issued by Healthcare Inspectorate- Pharmaceutical Affairs and Medical Technology, Netherlands
	Remarks of the Evaluator [X]	• Provide valid copy of DSL • Photocopy of CoPP is provided which is **expired now but valid upon submission;** Submit original valid CoPP duly attested by embassy of Pakistan. • Provide legalized original valid GMP certificate as more than three years have elapsed since the date of last inspection of the manufacturing site. • Provide legalized original valid Letter of authorization/sole agency agreement between product license holder and distributor. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is

		missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986. • Demanded Pack size is not mentioned in form-5A. ➢ 6 months accelerated and 36 months long term stability studies data has been submitted as per zone-IV-A conditions.
	Decision: Deferred for submission of following: • **Valid copy of DSL of the applicant.** • **Original, legalized & valid CoPP.** • **Notarized & valid Letter of authorization/sole agency agreement between product license holder and distributor.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size**	
580.	Name and address of Applicant	M/s Vety Care Pvt Ltd., Plot # 77, Street No. 6, I-10/3, Islamabad
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name and address of marketing authorization holder	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name of exporting country	**Netherlands (Holland)**
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6170 Dated 15-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 10-05-2019
	Brand Name +Dosage Form + Strength	Bravecto Spot-On Solution for dogs 1000mg/3.57ml
	Composition	Each ml contains: Fluralaner…280mg
	Finished Product Specification	Not claimed
	Pharmacological Group	Systemic insecticide and acaricide
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	Not mentioned
	International availability	**Bravecto USFDA approved**
	Me-too status	Not provided
	Detail of certificates attached	Photocopy of CoPP No. V2017-1051 dated 14-09-2017 issued by **US Food and Drug, Administration, USA.** The CoPP confirms free sale status of the product in **USA** as well as GMP status of the manufacturing site. Validity: 24 months Letter of Authorization/ sole agency agreement Not provided

		GMP certificate No. NL/H 15/1005102A based on inspection conducted on 06-11-2015 issued by Healthcare Inspectorate- Pharmaceutical Affairs and Medical Technology, Netherlands
	Remarks of the Evaluator [X]	• Provide valid copy of DSL • Photocopy of CoPP is provided which is **expired now but valid upon submission;** Submit original valid CoPP duly attested by embassy of Pakistan. • Provide legalized original valid GMP certificate as more than three years have elapsed since the date of last inspection of the manufacturing site. • Provide legalized original valid Letter of authorization/sole agency agreement between product license holder and distributor. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986. • Demanded Pack size is not mentioned in form-5A. ➢ 6 months accelerated and 36 months long term stability studies data has been submitted as per zone-IV-A conditions.
	Decision: Deferred for submission of following: • **Valid copy of DSL of the applicant.** • **Original, legalized & valid CoPP.** • **Notarized & valid Letter of authorization/sole agency agreement between product license holder and distributor.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size**	
581.	Name and address of Applicant	M/s Vety Care Pvt Ltd., Plot # 77, Street No. 6, I-10/3, Islamabad
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Intervet International B.V.

		Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name and address of marketing authorization holder	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name of exporting country	**Netherlands (Holland)**
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6171 Dated 15-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 10-05-2019
	Brand Name +Dosage Form + Strength	Bravecto Spot-On Solution for dogs 1400mg/5ml
	Composition	Each ml contains: Fluralaner…280mg
	Finished Product Specification	Not mentioned
	Pharmacological Group	Systemic insecticide and acaricide
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	Not mentioned
	International availability	**Bravecto USFDA approved**
	Me-too status	Not provided
	Detail of certificates attached	Photocopy of CoPP No. V2017-1051 dated 14-09-2017 issued by **US Food and Drug, Administration, USA.** The CoPP confirms free sale status of the product in **USA** as well as GMP status of the manufacturing site. Validity: 24 months Letter of Authorization/ sole agency agreement Not provided GMP certificate No. NL/H 15/1005102A based on inspection conducted on 06-11-2015 issued by Healthcare Inspectorate- Pharmaceutical Affairs and Medical Technology, Netherlands
	Remarks of the Evaluator [X]	• Provide valid copy of DSL • Photocopy of CoPP is provided which is **expired now but valid upon submission;** Submit original valid CoPP duly attested by embassy of Pakistan. • Provide legalized original valid GMP certificate as more than three years have elapsed since the date of last inspection of the manufacturing site. • Provide legalized original valid Letter of authorization/sole agency agreement between product license holder and distributor. • Evidence of approval of applied formulation in reference regulatory authorities/agencies which were declared/approved by the Registration Board in its 275th meeting. • Evidence of applied formulation/drug already approved by DRAP (generic / me-

		too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986. • Demanded Pack size is not mentioned in form-5A. ➢ 6 months accelerated and 36 months long term stability studies data has been submitted as per zone-IV-A conditions.
	Decision: Deferred for submission of following: • **Valid copy of DSL of the applicant.** • **Original, legalized & valid CoPP.** • **Notarized & valid Letter of authorization/sole agency agreement between product license holder and distributor.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size**	
582.	Name and address of Applicant	M/s Vety Care Pvt Ltd., Plot # 77, Street No. 6, I-10/3, Islamabad
	Detail of Drug Sale License	Not provided
	Name and address of manufacturer	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name and address of marketing authorization holder	M/s Intervet International B.V. Wim De Korversaraat 35, 5831 AN Boxmeer, Netherlands
	Name of exporting country	**Netherlands (Holland)**
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6168 Dated 15-05-2019
	Fee including differential fee	Rs : 1,00,000 Dated 14-05-2019
	Brand Name +Dosage Form + Strength	Bravecto Spot-On Solution for dogs and Cats 250mg/0.89ml
	Composition	Each ml contains: Fluralaner…280mg
	Finished Product Specification	Not mentioned
	Pharmacological Group	Systemic insecticide and acaricide
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	Not mentioned

	International availability	**Bravecto USFDA approved**
	Me-too status	Not provided
	Detail of certificates attached	Photocopy of CoPP No. V2017-1051 dated 14-09-2017 issued by **US Food and Drug, Administration, USA.** The CoPP confirms free sale status of the product in **USA** as well as GMP status of the manufacturing site. Validity: 24 months Letter of Authorization/ sole agency agreement Not provided GMP certificate No. NL/H 15/1005102A based on inspection conducted on 06-11-2015 issued by Healthcare Inspectorate- Pharmaceutical Affairs and Medical Technology, Netherlands
	Remarks of the Evaluator [X] • Provide valid copy of DSL • Photocopy of CoPP is provided which is **expired now but valid upon submission;** Submit original valid CoPP duly attested by embassy of Pakistan. • Provide legalized original valid GMP certificate as more than three years have elapsed since the date of last inspection of the manufacturing site. • Provide legalized original valid Letter of authorization/sole agency agreement between product license holder and distributor. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm. • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • In the finished product label the Urdu version of the following namely; (i) Name of drug (ii) dosage; and (iii) Instruction is missing. Submit label in accordance with The Drugs (Labeling and Packing) Rules, 1986. • Demanded Pack size is not mentioned in form-5A. ➢ 6 months accelerated and 36 months long term stability studies data has been submitted as per zone-IV-A conditions.	
	Decision: Deferred for submission of following: • **Valid copy of DSL of the applicant.** • **Original, legalized & valid CoPP.** • **Notarized & valid Letter of authorization/sole agency agreement between product license holder and distributor.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Demanded Pack size**	
583.	Name and address of Applicant	M/s Atzan Pharmaceuticals, 13-E, Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan
	Detail of Drug Sale License	Name: M/s Atzan Pharmaceutical Address: 13-E, Commercial Area, Aziz Bhatti Town, Sargodha, Pakistan. Validity: 14 April, 2020. Status: License to sell drugs as a Distributor (Form No.11).

	Name and address of manufacturer	M/s Vietnam Sakan Technology Development & Investment Joint Stock Company, Lot D1-D4, Dong Tho Industrial Complex, Yen Phong District, Bac Ninh Province, Vietnam
	Name and address of marketing authorization holder	M/s Vietnam Sakan Technology Development & Investment Joint Stock Company, Lot D1-D4, Dong Tho Industrial Complex, Yen Phong District, Bac Ninh Province, Vietnam
	Name of exporting country	The Socialist Republic of Vietnam
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 12409 Dated 18-07-2019
	Fee including differential fee	Rs : 1,00,000 Dated 18-07-2019
	Brand Name +Dosage Form + Strength	Amoxi 50 S Powder
	Composition	Each 100g contains: Amoxicillin Trihydrate…50g
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	24 months
	Demanded Price	Decontrolled
	Pack size	20gm, 50gm, 100gm
	International availability	N/A
	Me-too status	Not provided
	Detail of certificates attached	➢ Original Legalized Free Sale Certificate No. 351/2019/QLT-CFS issued by Ministry of Agriculture and Rural development department of Animal Health 15/78 GiaiPhong Street- DongDa- HaNoi-Vietnam Date of issuance: 03-05-2019 ➢ Original legalized GMP certificate No. 07/17/GCN-GMP issued on 06-06-2016 and valid for 5 years. (**scope of submitted GMP certificate does not cover beta lactam production line.)** ➢ Letter of Authorization/Sole Agency Certificate is not provided.
	Remarks of the Evaluator [X]	• Letter of Authorization (LOA) is not provied**,** Provide legalized valid original LOA. • Scope of submitted GMP certificate does not cover production lines of beta lactam oral powder, provide legalized original valid relevant GMP certificate. • Amoxicillin Trihydrate …50gm/100gm is mentioned in label claim on form-5A and FSC, while the referred generic product contains Amoxicillin as Trihydrate.....50gm/100gm. Submit evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration

		number, brand name and name of firm; or revise label claim in line with reference product and submit full fee of registration for revision of label claim/ master formula. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. ➢ 6 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions.
	Decision: Deferred for following: ○ **Original legalized valid Letter of Authorization (LOA)** ○ **Legalized original valid relevant GMP certificate with scope covering beta lactam production line.** ○ **Valid copy of DSL** ○ **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** ○ **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.**	
584.	Name and address of Applicant	M/s Ghazi Brothers, Ghazi House, D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi-75350, Pakistan
	Detail of Drug Sale License	Name: M/s Ghazi Brothers Address: D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi Date of issuance: 24-12-2018. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Zhummadian Huazhong Chia Tai. No.2019, Leshan Road, High Technology Development Zone, Zhumadian, Henan, China
	Name and address of marketing authorization holder	M/s Zhummadian Huazhong Chia Tai. No.2019, Leshan Road, High Technology Development Zone, Zhumadian, Henan, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6286 Dated 16-05-2019
	Fee including differential fee	**Rs : 50,000** Dated 15-05-2019
	Brand Name +Dosage Form + Strength	Farmcare 32.5% Powder
	Composition	Each 100 gram contains: Neomycin Sulphate …32.5gm
	Finished Product Specification	Chinese Pharmacopeia
	Pharmacological Group	Antibiotic
	Shelf life	2 years

	Demanded Price	Decontrolled
	Pack size	250gm, 500gm, 1Kg and 2Kg
	International availability	Not provided
	Me-too status	Could not be confirmed
	Detail of certificates attached	➢ Original Legalized Free Sale Certificate No. 191100B0/018164 issued by Animal Husbandry Bureau of Zhumadian City, Henan Province China Date of issuance: 12-03-2019 Validity: 20-02-2024
	Remarks of the Evaluator [X]	• 06 months accelerated and 36 months long term stability studies data has been submitted as per zone-IV-A conditions. **Shortcomings:** • Letter of Authorization (LOA)/ sole agency certificate is not provided**,** Provide legalized valid original LOA from product license holder. • Provide legalized original valid GMP certificate of the manufacturer. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Decision: Deferred for following: • **Legalized valid original Letter of Authorization (LOA)/ sole agency certificate.** • **Legalized original valid GMP certificate of the manufacturer.** • **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Differential fee Rs. 50,000/- for registration of imported drug.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.**	
585.	Name and address of Applicant	M/s Ghazi Brothers, Ghazi House, D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi-75350, Pakistan
	Detail of Drug Sale License	Name: M/s Ghazi Brothers Address: D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi Date of issuance: 24-12-2018. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Pucheng Chia Tai Biochemistry Co. Ltd.

		No.56, Da Shi Xi, Putan Village, Pucheng, Nanping City, Fujian Province, China
	Name and address of marketing authorization holder	M/s Pucheng Chia Tai Biochemistry Co. Ltd. No.56, Da Shi Xi, Putan Village, Pucheng, Nanping City, Fujian Province, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6287 Dated 16-05-2019
	Fee including differential fee	**Rs : 50,000** Dated 15-05-2019
	Brand Name +Dosage Form + Strength	CoxRival 12% Premix
	Composition	Each Kg contains: Salinomycin Sodium…120gm
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	25Kg
	International availability	N/A
	Me-too status	Salinafarm 120 Powder of M/s Mylab (Pvt) Ltd, Khankah Sharif, Bahawalpur. (Reg. No. 101465)
	Detail of certificates attached	➢ Photocopy of Free Sale Certificate issued by Pucheng Bureau of Agriculture ➢ Photocopy of GMP certificate No. (2017) Shou Yao GMP Zheng Zi No. 13002 issued on 20-02-2019 and valid till **16-01-2-22.** ➢ Original legalized Power of attorney dated 19-03-2019 attached in Farmcare CTC 20% Water Soluble Powder dossier.
	Remarks of the Evaluator [X]	06 months accelerated and **18 months** long term stability studies data has been submitted as per zone-IV-A conditions. **Shortcomings:** • Submitted copy of FSC, provide legalized original valid FSC. • Submitted copy of GMP certificate is expired now but valid upon submission, provide legalized original valid GMP certificate of the manufacturer. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Submit long term stability studies data as per zone-IV-A conditions upto claimed shelf life.

	Decision: Deferred for following: • **Legalized original valid FSC.** • **Legalized original valid GMP certificate of the manufacturer.** • **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Differential fee Rs. 50,000/- for registration of imported drug.** • **Long term stability studies data as per zone-IV-A conditions upto claimed shelf life (2 years).**	
586.	Name and address of Applicant	M/s Ghazi Brothers, Ghazi House, D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi-75350, Pakistan
	Detail of Drug Sale License	Name: M/s Ghazi Brothers Address: D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi Date of issuance: 24-12-2018. Date of Validity: **25-05-2020** Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Pucheng Chia Tai Biochemistry Co. Ltd. No.56, Da Shi Xi, Putan Village, Pucheng, Nanping City, Fujian Province, China
	Name and address of marketing authorization holder	M/s Pucheng Chia Tai Biochemistry Co. Ltd. No.56, Da Shi Xi, Putan Village, Pucheng, Nanping City, Fujian Province, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6288 Dated 16-05-2019
	Fee including differential fee	**Rs : 50,000** Dated 15-05-2019
	Brand Name +Dosage Form + Strength	Farmcare CTC 20% Water Soluble Powder
	Composition	Each Kg contains: Chlortetracycline HCl…200gm
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	250gm, 500gm, 1Kg
	International availability	N/A
	Me-too status	Elecylin Powder of M/s Elegance Pharmaceuticals, Rawalpindi. (Reg. No.105028)
	Detail of certificates attached	➢ Original Legalized Free Sale Certificate No. 191100B0/019936 issued by Pucheng Bureau of Agriculture and Rural Affairs, China confirms free sale status in China. Validity: 24-03-2024 ➢ Original legalized GMP certificate No. (2017) Shou Yao GMP Zheng Zi No.13002 issued on 20-02-2019 and valid till **16-01-2022** confirms GMP status

		➢ Original legalized Power of attorney dated 19-03-2019.
	Remarks of the Evaluator [X]	• 06 months accelerated (Batch No. F1109001, F1109002, F1109003) and 36 months long term (Batch No. F1202001, F1203001, F1203002) stability studies data has been submitted as per zone-IV-A conditions. **For LOD, the samples are OOS at each time point of accelerated stability studies and at 6th month time point for batch F1202001 and at 12th month time point for batches F1203001, F1203002.** **Shortcomings:** • Submitted GMP certificate is expired now but valid upon submission. Submit original valid legalized GMP certificate • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • For LOD, the samples are OOS at each time point of accelerated stability studies and at 6th month time point for batch F1202001 and at 12th month time point for batches F1203001, F1203002, clarify.
	Decision: Deferred for following: • **Legalized original valid GMP certificate of the manufacturer.** • **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Differential fee Rs. 50,000/- for registration of imported drug.** • **Clarification regarding LOD, the samples are OOS at each time point of accelerated stability studies and at 6th month time point for batch F1202001 and at 12th month time point for batches F1203001, F1203002, justify.**	
587.	Name and address of Applicant	M/s Ghazi Brothers, Ghazi House, D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi-75350, Pakistan
	Detail of Drug Sale License	Name: M/s Ghazi Brothers Address: D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi Date of issuance: 24-12-2018. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Zhummadian Huazhong Chia Tai. No.2019, Leshan Road, High Technology Development Zone, Zhumadian, Henan, China

	Name and address of marketing authorization holder	M/s Zhummadian Huazhong Chia Tai. No.2019, Leshan Road, High Technology Development Zone, Zhumadian, Henan, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6285 Dated 16-05-2019
	Fee including differential fee	**Rs : 50,000** Dated 15-05-2019
	Brand Name +Dosage Form + Strength	Tylomax 22% Granules
	Composition	Each Kg contains: Tylosin Phosphate…220gm
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	25Kg
	International availability	Not provided
	Me-too status	Could not be confirmed
	Detail of certificates attached	➢ Original Legalized Free Sale Certificate No. 191100B0/018162 issued by Animal Husbandry Bureau of Zhumadian City, Henan Province China Date of issuance: 12-03-2019 Validity: 20-02-2024 ➢ Originally legalized copy of GMP certificate No. (2014) Shou Yao GMP No.156 issued on 28-02-2019 and valid till **31-07-2019** confirms GMP status ➢ Original Legalized Power of attorney dated 12-03-2019
	Remarks of the Evaluator [X]	• 06 months accelerated and 36 months long term stability studies data has been submitted as per zone-IV-A conditions. **Shortcomings:** • Submitted copy of GMP certificate is expired now but valid upon submission, provide legalized original valid GMP certificate of the manufacturer. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Decision: Decision: Deferred for following: • **Legalized original valid GMP certificate of the manufacturer.**	

	• **Valid copy of DSL** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Differential fee Rs. 50,000/- for registration of imported drug.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.**	
588.	Name and address of Applicant	M/s Ghazi Brothers, Ghazi House, D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi-75350, Pakistan
	Detail of Drug Sale License	Name: M/s Ghazi Brothers Address: D-35, K.D.A Scheme No.1, Miran Muhammad Shah Road, Karachi Date of issuance: 24-12-2018. Status: Drug License by way of Wholesale (Form No.7).
	Name and address of manufacturer	M/s Zhummadian Huazhong Chia Tai. No.2019, Leshan Road, High Technology Development Zone, Zhumadian, Henan, China
	Name and address of marketing authorization holder	M/s Zhummadian Huazhong Chia Tai. No.2019, Leshan Road, High Technology Development Zone, Zhumadian, Henan, China
	Name of exporting country	China
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 6284 Dated 16-05-2019
	Fee including differential fee	**Rs : 50,000** Dated 15-05-2019
	Brand Name +Dosage Form + Strength	Oxypro 20% Premix
	Composition	Each Kg Contains: Oxytetracycline…200gm
	Finished Product Specification	Inhouse
	Pharmacological Group	Antibiotic
	Shelf life	2 years
	Demanded Price	Decontrolled
	Pack size	25Kg
	International availability	Not provided
	Me-too status	Could not be confirmed
	Detail of certificates attached	➢ Original Legalized Free Sale Certificate No. 191100B0/018163 issued by Animal Husbandry Bureau of Zhumadian City, Henan Province China Date of issuance: 12-03-2019 Validity: 20-02-2024 ➢ Photocopy of GMP certificate No. (2014) Shou Yao GMP No.156 issued on 28-02-2019 and valid till **31-07-2019** confirms GMP status ➢ Original Legalized Power of attorney dated 12-03-2019 attached in Tylomax 22% premix dossier.
	Remarks of the Evaluator [X]	• 06 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions.

		Shortcomings: • Submitted copy of GMP certificate is expired now but valid upon submission, provide legalized original valid GMP certificate of the manufacturer. • Provide valid copy of DSL • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.
	Decision: Deferred for following: • **Legalized original valid GMP certificate of the manufacturer.** • **Valid copy of DSL** • **Evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board.** • **Differential fee Rs. 50,000/- for registration of imported drug.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) alongwith registration number, brand name and name of firm.**	
589.	Name and address of Applicant	M/s Mustafa Brothers. 186-D, Peoples Colony No.1, Faisalabad
	Detail of Drug Sale License	Name: M/s Mustafa Brothers Address: P-186-D, Peoples Colony No.1, District Faisalabad Date of issuance:15-09-2022 Validity: 21-06-2027 Status: License to sale Drugs as a Distributor (Form No.11). (computer generated copy submitted)
	Name and address of manufacturer	Veyx-Pharma B.V., Forellenweg 16 NL-4941SJ Raamsdonksveer, The Netherlands. (Compounding, Bulk Manufacturing, primary Packaging, Batch control) Veyx Pharma GmBH Sohreweg, Schwarzenborn, Germany. (Secondary Packaging, batch release, responsible for exporting the drug)
	Name and address of marketing authorization holder	M/s Veyx Pharma GmBH Sohreweg, Schwarzenborn, Germany.
	Name of exporting country	Germany
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4680 Dated 29-04-2019
	Fee including differential fee	Rs : 100,000 Dated 29-04-2019
	Brand Name +Dosage Form + Strength	Gonavet Veyx Solution for Injection

	Composition	Each 1ml contains: Gonadorelin…50mcg
	Finished Product Specification	Ph. Eur.
	Pharmacological Group	Systemic hormonal preparations excl. sex hormone and insulin
	Shelf life	24 months
	Demanded Price	Decontrolled
	Pack size	10ml vial
	International availability	Gonavet Veyx 50 µg/ml solution for injection for cattle, pigs and horses **(approved in Germany)**
	Me-too status	Could not be confirmed
	Detail of certificates attached	➢ Original Legalized COPP No. DekR77 issued by REGIERUNGSPRASIDIUM DARMSTADT Dez. II 23.2- Pharmazie Luisenplatz 2 D-64283 Darmstadt issued on 15-11-2018, also confirms free sale status of the product. ➢ Original Legalized GMP certificate No. NL/V/17/0023 issued on 10-10-2017 is **valid upon submission but expired now.** ➢ Original Legalized distribution agreement dated 16-05-2014 between applicant and Veyx pharma GmbH.
	Remarks of the Evaluator [X]	06 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions. **Indications for use, specifying the target species:** Control and stimulation of reproduction in cattle. Treatment of ovarian-related fertility disorders or dysfunctions in cattle and horses**.** **Cattle (cows, heifers):** • Ovulation induction in case of delayed ovulation due to LH-deficiency • Induction/synchronization of ovulation within the framework of systems for timed inseminations • Stimulation of the ovaries during the puerperal period from day 12 post-partum • Ovarian cysts (due to LH-deficiency) **Horses (mares):** • Acyclia and anoestrus due to LH-deficiency ➢ The submitted GMP certificate and distribution agreement between importer and Product licence holder **is expired now but valid upon submission.**

	Decision: Approved. Registration letter will be issued after submission of original legalized valid GMP certificate and distribution agreement between importer and Product licence holder.	
590.	Name and address of Applicant	M/s Mustafa Brothers. 186-D, Peoples Colony No.1, Faisalabad
	Detail of Drug Sale License	Name: M/s Mustafa Brothers Address: P-186-D, Peoples Colony No.1, District Faisalabad Date of issuance:15-09-2022 Validity: 21-06-2027 Status: License to sale Drugs as a Distributor (Form No.11). (computer generated copy submitted)
	Name and address of manufacturer	Veyx-Pharma B.V., Forellenweg 16 NL-4941SJ Raamsdonksveer, The Netherlands. (Compounding, Bulk Manufacturing, primary Packaging, Batch control) Veyx Pharma GmBH Sohreweg, Schwarzenborn, Germany. (Secondary Packaging, batch release, responsible for exporting the drug)
	Name and address of marketing authorization holder	M/s Veyx Pharma GmBH Sohreweg, Schwarzenborn, Germany.
	Name of exporting country	Germany
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4681 Dated 29-04-2019
	Fee including differential fee	Rs : 100,000 Dated 29-04-2019
	Brand Name +Dosage Form + Strength	PGF Veyx Forte Solution for Injection
	Composition	Each 1ml Contains: Cloprostenol…250mcg
	Finished Product Specification	BP Vet specifications
	Pharmacological Group	Prostaglandin-F2α-agonist
	Shelf life	24 months
	Demanded Price	Decontrolled
	Pack size	50ml vial
	International availability	PGF Veyx forte 0.250 mg/ml solution for injection for cattle and pigs **(approved in Germany)**
	Me-too status	Estrunate Injection of M/s ICI Pakistan Ltd Karachi (Reg. No.003788)
	Detail of certificates attached	➢ Original Legalized COPP No. DekR76 issued by REGIERUNGSPRASIDIUM DARMSTADT Dez. II 23.2- Pharmazie Luisenplatz 2 D-64283 Darmstadt issued on 15-11-2018, also confirms free sale status of the product. ➢ Copy of GMP certificate No. NL/V/17/0023 issued on 10-10-2017 is **valid upon submission but expired now.** ➢ Original Legalized distribution agreement dated 16-05-2014 between applicant and

		Veyx pharma GmbH in Gonavet Veyx solution for injection dossier.
	Remarks of the Evaluator [X]	• 06 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions. • Submitted GMP certificate and distribution agreement between importer and Product licence holder **is expired now but valid upon submission.**
	Decision: Approved. Registration letter will be issued after submission of original legalized valid GMP certificate and distribution agreement between importer and Product licence holder.	
591.	Name and address of Applicant	M/s Mustafa Brothers. 186-D, Peoples Colony No.1, Faisalabad
	Detail of Drug Sale License	Name: M/s Mustafa Brothers Address: P-186-D, Peoples Colony No.1, District Faisalabad Date of issuance:15-09-2022 Validity: 21-06-2027 Status: License to sale Drugs as a Distributor (Form No.11). (computer generated copy submitted)
	Name and address of manufacturer	Veyx-Pharma B.V., Forellenweg 16 NL-4941SJ Raamsdonksveer, The Netherlands. (Compounding, Bulk Manufacturing, primary Packaging, Batch control) Veyx Pharma GmBH Sohreweg, Schwarzenborn, Germany. (Secondary Packaging, batch release, responsible for exporting the drug)
	Name and address of marketing authorization holder	M/s Veyx Pharma GmBH Sohreweg, Schwarzenborn, Germany.
	Name of exporting country	Germany
	Type of Form	Form-5A
	Diary No. & Date of R& I	Dy.No 4706 Dated 29-04-2019
	Fee including differential fee	Rs : 100,000 Dated 29-04-2019
	Brand Name +Dosage Form + Strength	Sensiblex Solution for Injection
	Composition	Each ml Contains: Denaverine HCl…40mg
	Finished Product Specification	Ph. Eur.
	Pharmacological Group	Spasmolytic agent
	Shelf life	24 months
	Demanded Price	Decontrolled
	Pack size	50ml vial
	International availability	Sensiblex 40 mg/ml solution for injection for cattle **(approved in Germany)**
	Me-too status	Could not be confirmed
	Detail of certificates attached	➢ Original Legalized COPP No. DeLR5 issued by REGIERUNGSPRASIDIUM DARMSTADT Dez. II 23.2- Pharmazie

		Luisenplatz 2 D-64283 Darmstadt issued on 06-12-2018, also confirms free sale status of the product. ➢ Original Legalized GMP certificate No. NL/V/17/0023 issued on 10-10-2017 is **valid upon submission but expired now.** ➢ Original Legalized distribution agreement dated 16-05-2014 between applicant and Veyx pharma GmbH.
	Remarks of the Evaluator [X]	• 06 months accelerated and 24 months long term stability studies data has been submitted as per zone-IV-A conditions. • Submitted GMP certificate and distribution agreement between importer and Product licence holder **is expired now but valid upon submission.**
	Decision: Approved as per policy of inspections of manufacturer abroad. Registration letter will be issued after submission of original legalized valid GMP certificate and distribution agreement between importer and Product licence holder.	

Case no. 03 Registration applications for local manufacturing of (veterinary) drugs

a. New Cases

592.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Enflox-10 Liquid
	Composition	Each ml Contains: Enrofloxacin…100mg
	Diary No. Date of R& I & fee	Dy.No 13475 dated 07-03-2019 Rs.20,000/- dated 06-03- 2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100ml, 200ml, 500ml, 1000ml: As per SRO
	Me-too status	Enroriq-10 Oral Liquid of M/S. Baariq Pharmaceuticals, Lahore. (Reg. No. 079813)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator X	▪ Liquid Syrup Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
593.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Enrocin 20 Liquid

	Composition	Each 100ml Contains: Enrofloxacin…20gm
	Diary No. Date of R& I & fee	Dy.No 13474 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100ml, 200ml, 500ml, 1000ml: As per SRO
	Me-too status	Encure-20 Solution of M/s Nawan Laboratories Pvt. Ltd., Karachi. (Reg. No. 020799)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator [X]	▪ Liquid Syrup Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
594.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Amanta Fort Powder
	Composition	Each gm contains: Amantadine HCl…980mg
	Diary No. Date of R& I & fee	Dy.No 13473 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antiviral
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100g, 200g, 500g, 1Kg: As per SRO
	Me-too status	HANSREDIN 98% POWDER of M/s D-HAANS Pharmaceuticals, Bhimber, Azad Kashmir. (Reg. No. 102207)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator [X]	▪ Dry Powder Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Deferred for review by Expert Working Group	
595.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	F.O.N-550 Powder
	Composition	Each gm contains: Florfenicol…100mg Oxytetracycline HCl…300mg Neomycin Sulphate…150mg
	Diary No. Date of R& I & fee	Dy.No 13469 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotics

	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100g, 200g, 500g, 1Kg: As per SRO
	Me-too status	Floron Oral Powder of M/s Grand Pharma Pvt. Ltd., Islamabad (Reg. No.106665)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator [X]	▪ Dry Powder Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
596.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Acrolin Liquid 100mg/100mg/40mg
	Composition	Each ml Contains: Enrofloxacin…100mg Aminophylline…100mg Guaifenesin…40mg
	Diary No. Date of R& I & fee	Dy.No 13467 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotic/Mucolytic
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100ml, 200ml, 500ml, 1000ml: As per SRO
	Me-too status	Amguflox Liquid of M/s Leads Pharma Pvt. Ltd., Islamabad (Reg. No. 088044)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator [X]	▪ Liquid Syrup Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
597.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Polidox-80 Powder
	Composition	Each 100gm contains: Doxycycline Hyclate eq To Doxycycline…80gm
	Diary No. Date of R& I & fee	Dy.No 13471 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100g, 200g, 500g, 1Kg: As per SRO

	Me-too status	Hansydox-80% Powder of M/s D-HAANS Pharmaceuticals, Bhimber, Azad Kashmir. (Reg. No. 103953)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator [X]	▪ Dry Powder Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
598.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Flotec Liquid 25g/100ml
	Composition	Each 100ml Contains: Florfenicol…25gm
	Diary No. Date of R& I & fee	Dy.No 13472 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100ml, 200ml, 500ml, 1000ml: As per SRO
	Me-too status	Interfenicol 25% Oral Solution of M/s International Pharma Labs, Lahore.(Reg. No. 082808)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator [X]	▪ Liquid Syrup Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
599.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Flucin Fort Powder
	Composition	Each 100gm contains: Doxycycline Hyclate…40gm Tylosin Tartrate…20gm Colistin Sulphate…10gm Bromhexine HCl…2gm
	Diary No. Date of R& I & fee	Dy.No 13470 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotic/Expectorant
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100g, 200g, 500g, 1Kg: As per SRO
	Me-too status	Brocotyd Powder of M/s Univet Pharmaceutical Rawalpindi (Reg. No. 058962)

	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator [X]	▪ Dry Powder Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
600.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Doxitin Powder 250/200mg
	Composition	Each gram contains: Doxycycline Hyclate…250mg Tylosin Tartrate…200mg
	Diary No. Date of R& I & fee	Dy.No 13468 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotics
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100g, 200g, 500g, 1Kg: As per SRO
	Me-too status	Trigger Water Soluble Powder of M/s Wimits Pharmaceuticals, Lahore.(Reg. No. 078313)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.
	Remarks of the Evaluator [X]	▪ Dry Powder Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
601.	Name and address of manufacturer / Applicant	M/s Biorific Pharma, Plot No.143, Industrial Triangle, Kahuta road, Islamabad
	Brand Name +Dosage Form + Strength	Dolotin Oral Powder
	Composition	Each 1000gm Contains: Doxycycline HCl…200gm Tylosin Tartrate…100gm Colistin Sulphate…30gm
	Diary No. Date of R& I & fee	Dy.No 13476 dated 07-03-2019 Rs.20,000/- dated 06-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	As per Innovator's specifications
	Pack size & Demanded Price	100g, 200g, 500g, 1Kg: As per SRO
	Me-too status	Doxi-Tol Powder of M/s Leads Pharma (Pvt) Ltd., Islamabad (Reg. No. 057053)
	GMP status	▪ Last GMP inspection is conducted on 31-10-2019 and the report concludes that firm was considered to be operating at a reasonable level of GMP compliance.

	Remarks of the Evaluator [X]	▪ Dry Powder Section (veterinary) granted vide letter No. F.1-48/2003-Lic dated 25-11-2016
	Decision: Approved. Registration letter will be issued after submission of GMP inspection report from QA&LT Division, valid within last three years.	
602.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Doragen Injection 50ml
	Composition	Each ml Contains: Doramectin…10mg
	Diary No. Date of R& I & fee	Dy.No 13765 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specification	Manufacturer‘s specifications
	Pack size & Demanded Price	10ml, 20ml, 50ml, 100ml, 1000ml: As recommended by the PRC/ (M/o NHS, R&C)/ Federal Govt.
	Me-too status	Dectomax Injectable solution of M/s Ghazi Brothers, Karachi (Reg. No. 027479)
	GMP status	cGMP certificate dated 30-07-2020 based on inspection conducted on 12-12-2019.
	Remarks of the Evaluator [X]	• Firm has revised finished product specification from inhouse to “as per innovator’s specifications” without fee submission. • Initially, multiple pack sizes (10ml, 20ml, 50ml, 100ml, 1000ml) of injectable dosage form were demanded in a single application. Now, the firm has demanded **50ml pack size**.
	Decision: Approved with innovator’s specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications and master formula (pre-approval change in in-actives) as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	
603.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Dexapred Injection
	Composition	Each ml Contains: Prednisolone…7.5mg Dexamethasone…2.5mg
	Diary No. Date of R& I & fee	Dy.No 13752 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Steroid
	Type of Form	Form 5
	Finished product Specification	As per Innovator’s specifications
	Pack size & Demanded Price	10ml, 20ml, 50ml, 100ml: As recommended by the PRC/ (M/o NHS, R&C)/ Federal Govt.
	Me-too status	Solodex Injection of M/s Breeze Pharma Pvt. Ltd., Islamabad. (Reg. No. 075674)
	GMP status	cGMP certificate dated 30-07-2020 based on inspection

		conducted on 12-12-2019.
	Remarks of the Evaluator [X]	• The firm has revised label claim in terms of salt form in line with reference product. And submitted revised formulation as mentioned below: **Each ml Contains:** **Prednisolone as acetate…7.5mg** **Dexamethasone as sodium phosphate…2.5mg** • Initially, multiple pack sizes (10ml, 20ml, 50ml, and 100ml) of injectable dosage form were demanded in a single application. Now, the firm has demanded **50ml pack size**. • Firm has not submitted fee for revision of label claim, master formula, and finished product specifications.
	Decision: Deferred for following: • **Approval of Steroid Injection section/manufacturing facility by the Central Licensing Board.** • **Indications for non-food producing animals.** • **Fee of Rs. 30,000 for revision of label claim as per notification No.F.7-11/2012-B&A/DRAP dated 13-07-2021.**	
604.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Nilzogen Injection 100ml
	Composition	Each ml Contains: Nitroxynil…340mg
	Diary No. Date of R& I & fee	Dy.No 13751 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Anthelmintic
	Type of Form	Form 5
	Finished product Specification	Manufacturer‘s specifications
	Pack size & Demanded Price	100ml, 50ml, 1000ml: As recommended by the PRC/ (M/o NHS, R&C)/ Federal Govt.
	Me-too status	Nitroxl Forte Injection of M/s Mediexcel Pharmaceuticals, Islamabad (Reg. No. 106699)
	GMP status	cGMP certificate dated 30-07-2020 based on inspection conducted on 12-12-2019.
	Remarks of the Evaluator [X]	• Firm has revised finished product specifications from manufacturer’s specification to **BP Vet specifications.** • Fee Rs.7500/- for revision of master formula, and finished product specifications. • Initially, multiple pack sizes (100ml, 50ml, and 100ml) of injectable dosage form were demanded in a single application. Now, the firm has demanded **50ml pack size**.
	Decision: Approved with BP Vet specifications. The firm shall submit fee of Rs. 7500/- for correction/pre-approval change in product specifications and master formula (pre-approval change in in-actives) as per notification No.F.7-11/2012-B&A/DRAP dated 07-05-2021.	

605.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Telmifos Injection 200mg/ml
	Composition	Each ml Contains: Toldimfos sodium…200mg
	Diary No. Date of R& I & fee	Dy.No 13766 dated 07-03-2019 Rs.20,000/- Dated 07-03-2019
	Pharmacological Group	Tonic agent; Alimentary tract and metabolism mineral supplement
	Type of Form	Form 5
	Finished product Specification	As per Innovator specifications
	Pack size & Demanded Price	10ml, 20ml, 50ml, and 100ml: As recommended by the PRC/ (M/o NHS, R&C)/ Federal Govt.
	Me-too status	**Could not be verified**
	GMP status	cGMP certificate dated 30-07-2020 based on inspection conducted on 12-12-2019.
	Remarks of the Evaluator [X]	• Initially, Toldimfos sodium…200mg/ml was mentioned in label claim while Toldimfos **as** sodium…200mg/**100**ml was mentioned in master formula; The firm has now revised the formulation as mentioned below: **Each ml Contains:** **Toldimfos as sodium…200mg** • The firm has not submitted fee for revision of master formula. • Initially, multiple pack sizes (10ml, 20ml, 50ml, and 100ml) of injectable dosage form were demanded in a single application. Now, the firm has demanded **100ml pack size**. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm is required.
	Decision: Deferred for following: • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.** • **Fee Rs. 30,000/- for revision of formulation as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**	
606.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Peprol Oral Powder 1000gm/Kg
	Composition	Each Kg Contains: Piperazine Citrate…1000gm
	Diary No. Date of R& I & fee	Dy. No 13764 dated 07-03-2019 Rs.20,000/- dated 07-03-2019
	Pharmacological Group	Antibacterial, Mucolytic agent
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 5Kg, 25Kg: As

		recommended by the PRC/ (M/o NHS, R&C)/ Federal Govt.
	Me-too status	P.C Water Soluble Powder of M/s Inshal Pharmaceutical Industries (Reg. No. 075768)
	GMP status	cGMP certificate dated 30-07-2020 based on inspection conducted on 12-12-2019.
	Remarks of the Evaluator [X]	• Firm has corrected Pharmacological group as **Anthelmintic.** **<u>Shortcomings:</u>** • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Fee Rs. 7500/- for revision of finished product specifications.
	Decision: Approved with innovator's specifications. Firm shall submit fee of Rs. 7,500 for revision of finished product specifications, as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.	
607.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Tetraflor oral powder 150mg/150mg
	Composition	Each Gram Contains: Oxytetracycline HCl…150mg Florfenicol…150mg
	Diary No. Date of R& I & fee	Dy.No 13757 dated 07-03-2019 Rs.20,000/- dated 07-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 5Kg, 25Kg: As recommended by the PRC/ (M/o NHS, R&C)/ Federal Govt.
	Me-too status	CLOXYFEN WATER SOLUBLE POWDER of M/s FIZI Pharmaceuticals and Chemical Laboratories, Lahore. (Reg. No. 103831)
	GMP status	cGMP certificate dated 30-07-2020 based on inspection conducted on 12-12-2019.
	Remarks of the Evaluator [X]	• Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Fee Rs. 7500/- for revision of finished product specifications.
	Decision: Approved with innovator's specifications. Firm shall submit fee of Rs. 7,500 for revision of finished product specifications, as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.	
608.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi

	Brand Name +Dosage Form + Strength	Oxyflor Oral Powder 150mg/300mg/1000mg
	Composition	Each Gm Contains: Neomycin Sulphate…150mg Oxytetracycline HCl…300mg Florfenicol…100mg
	Diary No. Date of R& I & fee	Dy.No 13767 dated 07-03-2019 Rs.20,000 dated 07-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 5Kg, 25Kg: As recommended by the PRC/ (M/o NHS, R&C)/ Federal Govt.
	Me-too status	FLOXYNOR ORAL POWDER of M/s FIZI Pharmaceuticals and Chemical Laboratories, Lahore. (Reg. No. 103821)
	GMP status	cGMP certificate dated 30-07-2020 based on inspection conducted on 12-12-2019.
	Remarks of the Evaluator [X]	• Firm has revised finished product specifications from manufacturer's to "as per innovator's specifications". • Initially, Florfenicol…1000mg/gm was mentioned in label claim on Form-5 while Florfenicol…100mg/gm was mentioned in master formula; the firm has now revised the formulation as mentioned below: **Each gram contains:** **Neomycin Sulphate…150mg** **Oxytetracycline HCl…300mg** **Florfenicol…100mg** • Firm has not submitted fee for correction of strength of API in label claim.
	Decision: Approved with innovator's specifications. Firm shall submit fee of Rs. 30,000 for correction/pre-approval change in composition (correction/change of strength of strength of Florfenicol), as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.	
609.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Enorfin Oral Powder 200gm/500MIU
	Composition	Each Kg Contains: Enrofloxacin…200gm Colistin Sulphate…500 MIU
	Diary No. Date of R& I & fee	Dy.No 13762 dated 07-03-2019 Rs.20,000/- dated 07-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 5Kg, 25Kg: As recommended by the PRC/ (M/o NHS, R&C)/ Federal

		Govt.
	Me-too status	Could not be verified
	GMP status	cGMP certificate dated 30-07-2020 based on inspection conducted on 12-12-2019.
	Remarks of the Evaluator [X]	• Provided following conversion of Colistin Sulphate from MIU to mg. 1mg of Colistin Sulphate contains 20,000IU **Shortcomings:** • Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Fee Rs. 7500/- for revision of finished product specifications. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Decision: Deferred for following: • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Fee Rs. 7500/- for revision of finished product specifications as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**	
610.	Name and address of manufacturer / Applicant	M/s Biogen Pharma, 8-Km Chakbeli Road, Rawat, Rawalpindi
	Brand Name +Dosage Form + Strength	Doxitin Oral Powder 500mg/100mg/30mg
	Composition	Each Gram Contains: Doxycycline Hyclate…500mg Tylosin Tartrate…100mg Colistin Sulphate…30mg
	Diary No. Date of R& I & fee	Dy.No 13756 dated 07-03-2019 Rs.20,000/- dated 07-03-2019
	Pharmacological Group	Antibiotic
	Type of Form	Form 5
	Finished product Specification	Manufacturer's specifications
	Pack size & Demanded Price	100gm, 250gm, 500gm, 1Kg, 5Kg, 25Kg: As recommended by the PRC/ (M/o NHS, R&C)/ Federal Govt.
	Me-too status	Could not be verified
	GMP status	cGMP certificate dated 30-07-2020 based on inspection conducted on 12-12-2019.
	Remarks of the Evaluator [X]	**Shortcomings:** • Original Fee challan is missing, provide original yellow copy for fee verification as per procedure adopted by the Registration Board in its 285th meeting.

		• Provide evidence of pharmacopoeial reference of finished product specification. In case, the product is non pharmacopoeial, submit product specification in the light of decision taken in 267th meeting of Registration Board. • Doxycycline Hyclate is mentioned in label claim on Form-5 while Doxycycline HCl is mentioned in master formula; clarification is required regarding salt form applied in this dossier. • Full fee of registration for revision of label claim/ master formula. • Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.
	Decision: Deferred for following clarification: • **Original yellow copy of fee challan for fee verification in light of decision of the Registration Board in its 285th meeting.** • **Clarification of applied salt form of Doxycycline whether hyclate or hydrochloride.** • **Evidence of applied formulation/drug already approved by DRAP (generic / me-too status) along with registration number, brand name and name of firm.** • **Finished product specifications in the light of decision taken in 267th meeting of Registration Board.** • **Fee Rs. 30,000/- for revision of formulation as per notification No.F.7-11/2021-B&A/DRAP dated 13-07-2021.**	

Case No.01: Registration of imported Drugs

M/s AGP Limited, B-23, C S.I.T.E, Karachi has submitted the applications dated 06th August 2021 of below mentioned four products on form-5F for registration to their name from M/s Galaxay Pharma (Private) Limited Karachi

Sr.#	Reg.#	Name of Product	Manufacturer & Product License Holder	Manufacturer & Product License Holder as per CoPP
1.	066122	Ostrodose Gel in Canister with Metering Pump	M/s Besins Manufacturing Belgium S.A., Belgium. Registered (Dated 28-10-2010, renewal dated 24-08-2020)	**Manufacturer: -** M/s Delpharm Drogenbos SA Address: Groot Bijgaardenstraat 128, Drogenbos, 1620, Belgium **Product License Holder: -** M/s Besins Healthcare Benelux S.A, Address: Avenue Louise 287-1050 Brussels, Belgium.
2.	066123	Ostrogel Gel in Tube		
3.	062214	Utrogestan 100mg Capsules (Initial Registered Dated 27-04-2010, renewal dated 10-03-2020)	Manufacturer:- M/s Cyndea Pharma, S.L., Poligono Industrial Emiliano Revilla Sanz, Avenida de Agreda, 31, Olvega 42110 (Soria) Spain Product License Holder: - M/s Besins Healthcare Benelux 287, Avenue Louise 1050 Bruxelles (Belgium) Change of manufacturing site dated 18-05-2020	**Manufacturer: -** M/s Cyndea Pharma S.L. Address: Poligono Industrial Emiliano Revilla Sanz Avenida de Agreda, 31 Olvega 42110 (Soria), Spain **Product License Holder: -** M/s Besins Healthcare S.A, Address: Avenue Louise 287-1050 Brussels, Belgium
4.	059079	Utrogestan 200mg Capsule (Registered Dated 16-10-2009, renewal dated 25-03-2019)		

M/s AGP Limited submit following documents:

i. Application on form-5F along with fee Rs 150,000 for each product.
ii. M/s. AGP Limited, B-23 S.I.T.E, Karachi submit **termination letter** from M/s Besins Healthcare Benelux 287, Avenue Louise 1050 Bruxelles (Belgium) Dated 25th May 2021.
iii. M/s. AGP Limited, B-23 S.I.T.E, Karachi submitted **authorization letter** from M/s Besins Healthcare Benelux 287, Avenue Louise 1050 Bruxelles (Belgium) for above mentioned product.

Suit No. 2707 of 2021
M/s AGP Limited & Others Versus M/s Galaxy Pharma (Private) Limited & Others
In view of above facts and circumstances, allow the application under consideration as under:

I) That the defendant No.1, its officers, employees, agents and every person working through or under it, or on his behalf from representing or claiming themselves as partners, distributors, affiliates or representatives of plaintiff No.2 and is restrained from claiming any rights in the products, i.e.,
   a) Utrogestan 100 mg soft capsule

(Micronized Progesterone 100mg)
(For Oral or Vaginal use)

b) Utrogestan 200 mg soft capsule
(Micronized Progesterone 200mg)
(For Oral or Vaginal use)

c) Oestrogel Gel (in Tube)
(Estradiol 0.6 mg/g)

d) Oestrodose Gel
(in Canister with metering pump)
(Estradiol 0.6 mg/g)

or utilizing the registration certificate of these products in any manner whatsoever.

II) As far as the importing of subject goods are concerned since it is an independent issue not arising out of the arguments, as raised, if otherwise prohibited, I am not inclined to pass any such order in this regard unless argued independently.

III) That the Drug Regulatory Authority within 15 days from the date of this order shall decide about the fate of registration of the above drugs in favour of defendant No.1 under the above facts and circumstances without asking for any NOC from defendant No.1 and submit report in this regard before this Court.

IV) In case they (Drugs Regulatory Authority) reaches to a conclusion that on account of severance of the contract, defendant No.1 is no more entitled to retain the registration of the aforesaid drugs and consequently cancel all such registrations, the application of the Besins Healthcare Distribution FZ-LLC and that of its principal be taken into consideration with immediate effect and an order be passed in this regard at the earliest with report to this Court.

Remarks:
The initial registration letter does not shows about the usage form of capsule but M/a AGP submit CoPP for both Oral and Vagianl Capsule for the product Utrogestan 100mg and 200mg Capsules.

Proceedings and decision of 321st Registration Board Meeting:

Mr. Saif-ur-Rehman Director Marketing Business Development of M/s. Galaxy Pharma Karachi appeared before the Board and submitted interim order of Honourable High Court of Sindh at Karachi in HCA No.313 of 2022 dated 21.09.2022. He also provided a copy of termination of agreement issued by M/s. BESINS Health Care Benelux, Belgium wherein M/s. BESINS Health Care, Belgium has informed that M/s Besins Healthcare (Hong Kong) Ltd has terminated the distribution agreement with M/s Galaxy Pharma (Pvt Ltd) Karachi. M/s. BESINS Health Care Benelux, Belgium further added that they have a new distribution agreement with M/s. AGP limited B-23-C SITE, Karachi.
Registration Board raised query regarding product license holder of the products in question. Mr. Saif responded that Product License Holder of said product is M/s. BESINS Health Care Belgium. However, they made a contract with M/s Besins Healthcare (Hong Kong) Ltd. So, M/s Basin Healthcare Belgium has no right to cancel the distribution agreement made between M/s Galaxy Pharma Karachi and M/s Besins Healthcare (Hong Kong). The Board further inquired about the current status of agreement between Basin Healthcare Belgium and Besins Healthcare (Hong Kong) to which Mr Saif could not respond.

Registration Board after deliberation and keeping in view the above discussion decided to send an email to M/s Basin Healthcare Belgium, Product License Holder (as per CoPP) of the below mentioned products for following clarifications:

a) Updated status of agreement between M/s Basin Healthcare, Belgium and M/s Besins Healthcare (Hong Kong) and to provide any documentary evidence if M/s Basin Heathcare Belgium has cancelled the authorization of M/s Basin Healthcare Hongkong.

b) Present authorized agent in Pakistan by the Product license holder i.e. M/s Basin Healthcare Belgium for following products:

a) Utrogestan 100 mg soft capsule

(Micronized Progesterone 100mg)
(For Oral or Vaginal use)

b) Utrogestan 200 mg soft capsule
(Micronized Progesterone 200mg)
(For Oral or Vaginal use)

c) Oestrogel Gel (in Tube)
(Estradiol 0.6 mg/g)

d) Oestrodose Gel
(in Canister with metering pump)
(Estradiol 0.6 mg/g)

As per directions of Registration Board, an email was sent to the official email (info@besins-healthcare.be) address of M/s Basin Healthcare, Belgium but the mail was undelivered and returned back. An email was sent to another official email (information@besins-healthcare.com) address of M/s Besin Healthcare UK, which reply is awaited.

Further M/s Galaxy appealed in the Honorable High Court of Sindh at Karachi vide H.C.A 313/22 against orders dated 15.09.2022 in Suit No. 2707 of 2021 for the transfer of registration of products from their name. The Honorable High Court of Sindh at Karachi vide order dated 11-10-2022 has directed DRAP to provide the opportunity of being heard to all concerned parties. Accordingly, letters for a personal hearing were issued to concerned parties dated 01-11-2022.

Proceedings of 322nd Registration Board meeting:

Mr. Shaheer Roshan Advocate counsel of M/s. Galaxy Pharma Karachi appeared before the Board. Registration Board advised to provide any document about status of current authorization from M/s Basin Healthcare Belgium (Product License Holder) in favor of M/s. Galaxy Pharma Karachi but representative of the firm was unable to provide any sort of agreement with Product License Holder. The Board further inquired about the current status of agreement between Basin Healthcare Belgium and Besins Healthcare (Hong Kong) to which Mr.Shaheer Roshan should inability to respond.

Mr. Mamoon Ch. Advocate counsel of M/s AGP Limited, Karachi and M/s Basin Healthcare Belgium informed the Board that M/s Basin Healthcare Belgium (Product License Holder) is product licensed holder for all four products and has revoked the power of attorney earlier granted to Galaxy Pharma (PVT) Ltd and has authorized M/s AGP Limited, Karachi to represent them in Pakistan as their sole authorized agent for all four products and submitted documents for consideration of Registration Board.

MARC R. FERNANDES Legal Counsel Besins Healthcare Holding Ltd. 32/F, Unit 3202, Tower 1, Enterprise Square 5, 38 Wang Chiu Road, Kowloon Bay, Hong Kong sent an email to DRAP on 05.11.2022 as follows:

First of all, our apologies for the delay response, as your e-mail got caught by an overzealous spam filter.
At any rate, please be advised with regards to the matter under consideration in the email below, I am responding on behalf of Mr. Francois Brault, as I am the Vice-Present of Legal Affair incharge of ASPAC Region. I am also a director of Besins Healthcare Holding Ltd, the ultimate holding of the group.
Firstly, we do confirm that the Distribution Agrement with Galaxy Pharma Private Limited was validly terminated by our letter dated 21May 2021, as confirmed by the evidence deposed by AGP limited.
Secondly, pursuant on an internal reorganization, Besin Healthcare (Hong Kong) Ltd. No longer exercises any trading responsibility within the company and is scheduled to be liquidated pending resolution of some outstanding issues.

We do confirm that Besins Healthcare S.A., our Belgian subsidiary which holds the regulatory authorizations for the captioned products in your email, has indeed revoked the power of attorney granted to Galaxy Pharma (PVT) Ltd. and granted a new power of attorney to AGP Limited to represent it in Pakistan who is the sole authorized agent to represent Besins Healthcare S.A. in Belgium. The full details of our authorized agent for regulatory matters and distributor are:
AGP Limited, registered under number 0088506, B-23-C,SITE, Karachi
The submissions and letters by Galaxy Pharma PVT Ltd with regards to a possible conflict around the termination of their distribution agreement are purely frivolous and aim purely at delaying the regulatory processes. The Besin Healthcare Group reserve all rights to claim compensation and seek any legal redress available against Galaxy Pharma PVT Ltd for these acts of nuisance.

Decision: Registration Board after detailed deliberation and keeping in view the above discussion decided as follows:

- **to cancel the registration of below mentioned products from M/s Galaxy Pharma (Private) Limited Karachi:**
    a. **Ostrodose Gel in Canister with Metering Pump, Registration No. 066122.**
    b. **Ostrogel Gel in Tube, Registration No. 066123**
    c. **Utrogestan 100mg Capsules, Registration No.062214**
    d. **Utrogestan 200mg Capsule, Registration No.059079**
- **Advised to evaluate cases of registration of above products submitted by M/s AGP Limited and present for consideration of the Board.**

Item No. III: Miscellaneous cases.

Registration Board while discussing the cases of M/s May & Baker Pharmaceuticals (Pvt.) Ltd. 45 Km, Thokar Multan Road, Lahore deliberated that in pursuance of the decision of Authority regarding "Borrowing of APIs for performing Product Development, R&D & stability Testing", pharmaceutical firms are availing the opportunity of loan of API for submission of Form 5F (CTD) applications. Registration Board in this context to ensure the harmony and robustness of the data submission decided as under:

- Firm shall submit the documents of loan of API to PE&R division within 15 days of such acquisition along with requisite documents and shall secure its receiving from R&I section, DRAP. This receiving shall be presented along with Form 5F at the time of dossier submission. Those firms who have already obtained such materials on loan and their product development studies are in process, are also advised to inform PE&R Division as per aforementioned procedure.
- Firm shall submit the image/picture/snapshot of the innovator/reference/comparator pack against which Pharmaceutical equivalence / Comparative Dissolution Profile studies have been performed and shall reveal the details of brand name, manufacturer, batch# and expiry date of the innovator/reference/comparator product in the section 3.2P.2.2.1 (Formulation development) of Form 5F.

Meeting ended with vote of thanks to and from the Chair.