SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Vinorelbine Karma 10 mg/ml Concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Vinorelbine (as tartarate) 10 mg/ml.
Each 1 ml vial contains a total content of vinorelbine (as tartrate) of 10 mg.

3. PHARMACEUTICAL FORM

Concentrate for solution for infusion.
Clear, colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Vinorelbine is indicated for the treatment of:
- Non small cell lung cancer (stage 3 or 4);
- As a single agent in patients with advanced breast cancer (stage 4) relapsing after or refractory to an anthracycline and texane containing regimen.

4.2 Posology and method of administration

Posology

In monotherapy vinorelbine is usually given at 25-30 mg/m^2 weekly.

In combination chemotherapy the usual dose (25-30 mg/m²) is usually maintained, while the frequency of administration is reduced e.g. day 1 and 5 every 3 weeks or day 1 and 8 every 3 weeks according to treatment protocol.

The treatment must be carried out under close haematological monitoring.
Optionally, a toxicity-related dose modification may be necessary (see Section 4.4).

The duration of treatment is determined by the physician and depends on the condition of the patient and on the chosen regimen.

- Administration in the elderly
Clinical experience has not identified relevant differences among elderly patients with regard to the response rate, although greater sensitivity in some of these patients cannot be excluded. Age does not modify the pharmacokinetics of vinorelbine (refer to sections 4.4 and 5.2).

- Administration in patients with liver insufficiency
The pharmacokinetics of Vinorelbine is not modified in patients presenting moderate or severe liver impairment. Nevertheless as a precautionary measure a reduced dose of 20mg/m^2 and close monitoring of haematological parameters is recommended in patient with severe liver impairment (refer to sections 4.4 and 5.2)

- Administration in patients with renal insufficiency

Given the minor renal excretion, there is no pharmacokinetic justification for reducing the dose of Vinorelbine in patients with renal insufficiency (refer to sections 4.4 and 5.2).

- Administration in children
Safety and efficacy in children have not been established and administration is therefore not recommended.

Method of administration

Strictly intravenous administration after appropriate dilution.
Intrathecal administration may be fatal.

Instructions for use and handling: refer to section 6.6.

It is recommended to use Vinorelbine as slow injection over 6-10 minutes after dilution in 20-50 ml of sodium chloride 9 mg/ml (0.9%) solution or glucose 50 mg/ml (5%) solution or as short infusion (20-30 min) after dilution in 125 ml of sodium chloride 9 mg/ml (0.9%) solution or glucose 50 mg/ml (5%) solution. Administration should always be followed with at least 250 ml of an isotonic solution infusion to flush the vein.

4.3 Contraindications

- Hypersensitivity to vinorelbine or other vinca alkaloids or to any of the constituents listed in section 6.1.
- Severe current or recent infection (within the last 2 weeks).
- Woman of childbearing potential not using effective contraceptive measures (see section 4.4 and 4.6).
- Lactation (see section 4.6).
- Severe current or recent infection (within the last 2 weeks).
- Neutropenia (<1500/mm³).
- Thrombocytopenia (< 100.000/mm³).
- In combination with yellow fever vaccine (see section 4.5).

4.4 Special warnings and precautions for use

Special warnings

For intravenous use only. Intrathecal administration may be fatal.

Vinorelbine should be administered under the supervision of a physician experienced in the use of chemotherapy.

Since inhibition of the hematopoietic system is the main risk associated with Vinorelbine close haematological monitoring should be undertaken during treatment (determination of haemoglobin level and the leukocyte, neutrophil and platelet counts on the day of each new administration).

The dose limiting adverse reaction is mainly neutropenia. This effect is non-cumulative, having its nadir between 7 and 14 days after the administration and is rapidly reversible within 5 to 7 days. If the neutrophil count is below 1500/$mm^3$and/or the platelet count is below 100000/mm^3, then the treatment should be delayed until recovery.

Increased myelotoxicity is to be expected for simultaneous radiation therapy of the pelvis, spine, or long bones with vinorelbine administration. The same applies for a previous radiation treatment (<3 weeks) in those regions.

If patients present signs or symptoms suggestive of infection, a prompt investigation should be carried out.

Special precautions for use

Special care should be taken when prescribing for patients with history of ischemic heart disease (refer to section 4.8).

To avoid the risk of bronchospasm and dyspnoea, especially in the combination therapy with mitomycin C, appropriate prophylaxis has to be considered. Outpatient treated patients need to be informed to call a doctor in respiratory distress.

The pharmacokinetics of Vinorelbine is not modified in patients presenting moderate or severe liver impairment. For dosage adjustment in this specific patient group, refer to section 4.2.

As there is a low level of renal excretion there is no pharmacokinetic rationale for reducing the dose of Vinorelbine in patients with impaired kidney function.
Refer to section 4.2.

Vinorelbine should not be given concomitantly with radiotherapy if the treatment field includes the liver.

This product is specifically contra-indicated with yellow fever vaccine and its concomitant use with other live attenuated vaccines is not recommended.

Caution must be exercised when combining Vinorelbine and strong inhibitors or inducers of CYP3A4 (refer to Section 4.5 – Interactions specific to vinorelbine), and its combination with phenytoin (like all cytotoxics) and with itraconazole (like all vinca-alkaloids) is not recommended.

All contact with the eyes should be strictly avoided: there is a risk of severe irritation and even corneal ulceration if the drug is sprayed under pressure. Immediate washing of the eye with sodium chloride 9mg/ml (0.9%) solution for injection should be undertaken if any contact occurs.

After prolonged treatment with Vinorelbine or in patients with increased risk neurological examination (possibly EMG controls) has to been done.

After occurrence of paralytic ileus, treatment can be continued after normalization of bowel function.

Anti-emetic therapy is recommended due to the very high incidence of nausea and vomiting.

Interstitial lung disease has been reported more frequently in the japanese population. Special attention should be exercised for this specific population.

For pregnancy, lactation and fertility please refer to section 4.6.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions to all cytostatic agents:

Due to the increase of thrombotic risk in case of tumoral diseases, the use of anticoagulative treatment is frequent. The high intra-individual variability of the coagulability during diseases, and the eventuality of interaction between oral anticoagulants and anticancer chemotherapy required, if it is decided to treat the patient with oral anticoagulants, to increase frequency of the INR (International Normalised Ratio) monitoring.

- Concomitant use contraindicated:

Yellow fever vaccine: risk of fatal generalised vaccine disease (refer to section 4.3).

- Concomitant use not recommended:

Live attenuated vaccines (for yellow fever vaccine, see concomitant use contraindicated): risk of generalised vaccine disease, possibly fatal. This risk is increased in patients already immunodepressed by their underlying disease. It is recommended to use an inactivated when exists (poliomyelitis) (refer to section 4.4).

Phenytoin: risk of exacerbation of convulsions resulting from the decrease of phenytoin digestive absorption by cytotoxic drug or loss of efficacy of the cytotoxic drug due to increased hepatic metabolism by phenytoin.

- Concomitant use to take into consideration:

Ciclosporine, tacrolimus: excessive immunodepression with risk of lymphoproliferation

Interactions specific to vinca-alkaloids:

- Concomitant use not recommended:

Itraconazole: increased neurotoxicity of vinca-alkaloids due to the decrease of their hepatic metabolism.

- Concomitant use to take into consideration:

Mitomycin C: risk of bronchospams and dyspnoea are increased, in rare case an interstitial pneumonitis was observed.

As vinca-alkaloids are known as substrates for P-glycoprotein, and in the absence of specific study, caution should be exercised when combining Vinorelbine with strong modulators of this membrane transporter (e.g. Ritonavir, Clarithromycin, Cyclosporin, Verapamil, Chinidin, or CYP3A4-inducer).

Interactions specific to vinorelbine:

- The combination of Vinorelbine with other drugs with known bone marrow toxicity is likely to exacerbate the myelosuppressive adverse effects.

  As CYP 3A4 is mainly involved in the metabolism of vinorelbine, combination with strong inhibitors of this isoenzyme (e.g. itraconazole, ketoconazole, HIV-protease-inhibitor, erythromycin, clarithromycin, telithromyin, nefazodon) could increase blood concentrations of vinorelbine and combination with strong inducers of this isoenzyme (e.g., phenytoin, phenobarbitale, rifampicin, carbamazepine, hypericum perforatum) could decrease blood concentrations of vinorelbine (refer to section 4.4).

- There is no mutual pharmacokinetic interaction when combining Vinorelbine with cisplatin over several cycles of treatment. However, the incidence of granulocytopenia associated with Vinorelbine use in combination with cisplatin is higher than associated with Vinorelbine single agent.

An increased incidence of grade 3/4 neutropenia has been suggested when intravenous vinorelbine and lapatinib were associated in one clinical phase I study. In this study, the recommended dose of intravenous form of vinorelbine in a 3-weekly schedule on day 1 and day 8 was 22.5 mg/m^2 when combined with daily lapatinib 1000 mg. This type of combination should be administered with caution.

There is evidence that Vinorelbine can enhance mucosa toxicity induced by 5-fluorouracil; in particular, when 5-fluorouracil is used in high doses and continuous infusion in combination with folinic acid. The combination of high-dose vinorelbine with mitomycin C appears in some cases to signs of increased pulmonary toxicity (bronchospasm, dyspnea). An allergic etiology is discussed.
Since occasionally mitomycin C enhance the potential pulmonary toxicity of other vinca alkaloids special care should be taken by concomitant use of Vinorelbine and mitomycin C in patients with allergic predisposition (bronchial asthma, known allergies).

4.6 Fertility, pregnancy and lactation

Pregnancy
There are insufficient data from the use of vinorelbine in pregnant women. Studies In animals have shown embryotoxicity and teratogenicity (see section 5.3). On the basis of the results of animal studies and the pharmacological action of the medicinal product, there is a potential risk of embryonic and foetal abnormalities.
Vinorelbine should therefore not be used during pregnancy, unless the indicidual awaited benefit clearly outweighs the potential risks. If pregnancy occurs during treatment, the patient should be informed about the risks for the unborn child and be monitored carefully. The possibility of genetic counselling should be considered.

Women of child-bearing potential
Women of childbearing potential must be advised to use effective contraception during treatment and three months thereafter and should inform their doctor if they become pregnant.
Vinorelbine is genotoxic. Therefore genetic counselling is recommended in case of infertility after chemotherapie.

Breast-feeding
It is unknown whether Vinorelbine is excreted in human breast milk. The excretion of Vinorelbine in milk has not been studied in animal studies. A risk to the suckling can not be excluded therefore breast feeding must be discontinued before starting treatment with Vinorelbine (refer to section 4.3).

Fertility
Men being treated with Vinorelbine are advised not to father a child during and minimally up to 3 months after treatment. Prior to treatment advice should be sought for conserving sperm due to the chance of irreversible infertility as a consequence of treatment with vinorelbine.

4.7 Effects on ability to drive and use machines

No studies of the effects on the ability to drive and use machines have been performed but on the basis of the pharmacodynamic profile vinorelbine does not affect the ability to drive and use machines. However, caution is necessary in patient treated with vinorelbine considering some adverse effects of the drug.

4.8 Undesirable effects

Adverse reactions reported as more than isolated cases are listed below, by system organ class and by frequency. *Frequencies are defined as: very common (> 1/10), common (> 1/100, < 1/10), uncommon (> 1/1,000, < 1/100), rare (> 1/10,000, < 1/1,000), very rare (< 1/10,000),* according to the MedDRA frequency convention and system organ classification.

The most commonly reported adverse drug reactions are bone marrow depression with neutropenia, anaemia, neurologic disorders, gastrointestinal toxicity with nausea, vomiting, stomatitis and constipation, Transient elevations of liver function tests, alopecia and local phlebitis.

Additional Adverse reactions from Post Marketing experience has been added according to the MedDRA classification with the frequency *Not known*

Detailed Adverse reactions information:

Reactions were described using the W.H.O classification (grade 1=G1 ; grade 2=G2 ; grade 3=G3 ; grade 4=G4 ; grade 1-4=G1-4) ; grade 1-2=G1-2 ; grade 3-4=G3-4).

Infections and infestations

Common: - Infection bacterial, viral or fungal at different localization (respiratory, urinary, GI tract…) mild to moderate and usually reversible with an appropriate treatment.

Uncommon: - Severe sepsis with other visceral failure
- Septicaemia

Very rare: - Complicated septicaemia and sometimes fatal

Not known: - Neutropenic sepsis.

Blood and lymphatic system disorders

Very Common: - Bone marrow depression resulting mainly in neutropenia (G3: 24.3%; G4: 27.8% in monotherapy), reversible within 5 to 7 days and non-cumulative over time
- Anaemia (G3-4: 7.4% in monotherapy).

Common: - Thrombocytopenia (G3-4: 2.5%) may occur but are seldom severe

Not known: - Febrile neutropenia
- Pancytopenia

Immune system disorders

Not known: - Systemic allergic reactions as anaphylaxis, anaphylactic shock or anaphylactoïd type reaction

Endocrine disorders

Not known: - Inappropriate antidiuretic hormone secretion (SIADH)

Metabolism and nutrition disorders

Rare: - - Severe hyponatraemia

Not known: - Anorexia (G1-2: 14%, G3: 1%).

Nervous system disorders

Very common: - Neurologic disorders (G 3-4: 2.7%) including loss of deep tendon reflexes
- Weakness of the lower extremities has been reported after a prolonged chemotherapy.

Uncommon: - Severe paresthesias with sensory and motor symptoms are infrequent. These effects are generally reversible.

Cardiac disorders

Rare: - Ischemic heart disease (angina pectoris, myocardial infarction, sometimes fatal)

Very rare: - Tachycardia, palpitation and heart rhythm disorders

Vascular disorders

Uncommon: - Hypotension, hypertension, flushing and peripheral coldness.

Rare: - Severe hypotension, collapse.

Respiratory system, thoracic and mediastinal disorders

Uncommon: - Dyspnoea and bronchospasm may occur in association with Vinorelbine treatment as with other vinca alkaloids.

Rare: - Interstitial pneumopathy, sometimes fatal has been reported.

Gastrointestinal disorders

Very Common: - Stomatitis (G1-4: 15% in monotherapy)
- Nausea and vomiting (G 1-2: 30.4% and G 3-4: 2.2% in monotherapy). Anti-emetic therapy may reduce their occurrence
- Constipation is the main symptom (G 3-4: 2.7% in monotherapy; G3-4: 4,1% in combination with other chemotherapeutic agents) which rarely progresses to paralytic ileus.

Common: - Diarrhoea usually mild to moderate may occur.

Rare: -Paralytic ileus, treatment may be resumed after recovery of normal bowel mobility
- Pancreatitis have been reported

Hepatobiliary disorders

Very common: -Transient elevations of liver function tests (G 1-2) without clinical symptoms were reported (SGOT in 27.6% and SGPT in 29.3%).

Skin and subcutaneous tissue disorders

Very common: - Alopecia, usually mild in nature, may occur (G3-4: 4.1% in monotherapy).

Rare: - Generalized cutaneous reactions have been reported with Vinorelbine

Not known: - Palmar-plantar erythrodysesthesia syndrome.

Musculoskeletal and connective tissue disorders

Common: - Arthralgia including jaw pain and myalgia

General disorders and administration site conditions

Very common: - Reactions at the injection site may include erythema, burning pain, vein discoloration and local phlebitis (G 3-4: 3.7% in monotherapy)

Common: - Asthenia, fatigue, fever, pain at different locations including chest pain and pain at the tumour site have been experienced.

Rare: - Local necrosis has been observed. Proper positioning of the intravenous needle or catheter and bolus injection followed by liberal flushing of the vein can limit these effects

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed below.

4.9 Overdose

Cases of accidental acute overdose have been reported in humans: such cases can result in bone marrow hypoplasia and are sometimes associated with infection, fever and paralytic ileus.
As there is no specific antidote for the overdosage of vinorelbine given intravenously, symptomatic measures are necessary in case of an overdosage, e.g.:
- Continuous control of vital signs and careful monitoring of the patient;
- Daily control of blood count to observe the need of blood transfusions, of growth factors and to detect the need of intensive care and to minimize the risk of infections;
- Measures for prevention of paralytic ileus;
- Control of circulation system and of liver function;
- Broad spectrum antibiotic therapy may be necessary in case of complications due to infections. In case of a paralytic ileus, decompression by a probe may be necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 16.1.7Antineoplastic and immunmodulating agents, vinca alkaloids,
ATC code: L 01 CA 04

Vinorelbine is an antineoplastic active substance of the vinca alkaloid family, but in contrast to all other vinca alkaloids the catharanthine portion of vinorelbine has undergone a structural modification. On the molecular level it affects the dynamic equilibrium of tubulin in the microtubular system of the cell. Vinorelbine inhibits tubulin polymerisation and binds preferentially to mitotic microtubules. Spiralisation of the tubulin is induced to a lesser degree than with vincristine. Vinorelbine blocks mitosis in phase G2-M, causing cell death in interphase or at the following mitosis.

Children
Safety and efficacy of Navelbine in paediatric patients have not been established.
Clinical data from two single arm Phase II studies using intravenous vinorelbine in 33 and 46 paediatric patients with recurrent solid tumours, including rhabdomyosarcoma, other soft tissue sarcoma, Ewing sarcoma, liposarcoma, synovial sarcoma, fibrosarcoma, central nervous system cancer, osteosarcoma, neuroblastoma at doses of 30 to 33.75mg/m^2 D1 and D8 every 3 weeks or once weekly for 6 weeks every 8 weeks, showed no meaningful clinical activity. The toxicity profile was similar to that reported in adult patients.(see section 4.2).

5.2 Pharmacokinetic properties

Distribution
After intravenous bolus injection or infusion in patients, the plasma concentration of vinorelbine is characterised by a three exponential elimination curve. The terminal elimination phase reflects a long half-life greater than 40 hours. Total clearance of vinorelbine is high (0.97-1.26 l/h/kg).
The active ingredient is widely distributed in the body with a volume of distribution ranging from 25.4-40.1 l/kg. Penetration of vinorelbine into pulmonary tissue is significant with tissue/plasma concentration ratios of greater than 300 in a study involving surgical biopsy. There is moderate binding to plasma proteins (13.5 %) but strong binding to platelets (78%). Linear pharmacokinetics have been shown for intravenously administered vinorelbine up to a dose of 45 mg/m^2.

Biotransformation
Vinorelbine is primarily metabolised by CYP3A4 of cytochrome P450. All metabolites have been identified and none are active with the exception of 4-O-deacetylvinorelbine, which is the principal metabolite in the blood. Neither sulfate nor glucuronide conjugates are found.

Elimination
Renal elimination is low (< 20% of the dose). Small concentrations of deacetyl vinorelbine have been recovered in humans, but vinorelbine is principally detected as the unchanged compound in urine.

Elimination of the active substance is mainly via the bile duct and consists of the metabolites and mainly of unchanged vinorelbine.

Special Patient Groups
Patients with renal or hepatic dysfunction
In patients with liver metastases changes only occurred in the mean clearance of vinorelbine when over 75% of the liver was affected.
In 6 cancer patients with moderate liver dysfunction (bilirubin ≤ 2 x ULN and aminotransferases ≤ 5 x ULN) treated with up to 25 mg/m² and 8 cancer patients with severe liver dysfunction (bilirubin > 2 x ULN and/or aminotransferases > 5 x ULN) treated with up to 20 mg/m², mean total clearance in the two groups were similar to that in patients with normal liver function.
These data may however not be representative for patients with reduced drug elimination capacity of the liver and therefore caution is recommended in patients with severe hepatic impairment and careful monitoring of haematological parameters required (see section 4.2 and 4.4).

The effect of kidney dysfunction on the disposition of vinorelbine has not been studied, but dose reduction is not indicated because of the low degree of renal excretion.

Elderly patients
A study with vinorelbine in elderly patients (≥ 70 years) with NSCLC demonstrated that pharmacokinetics of vinorelbine were not influenced by age. However, since elderly patients are frail, caution should be exercised when increasing the dose of vinorelbine: see section 4.2

Pharmacokinetic / pharmacodynamic relationships
A strong relationship has been demonstrated between vinorelbine blood exposure and of leucocytes or PMNs decreases.

5.3 Preclinical safety data

Acute and chronic toxicity
As a sign of overdose occurred in experimental animals to hair loss, behavioral abnormalities (fatigue, sleepiness), lung damage, weight loss and a more or less severe bone marrow hypoplasia.

In acute and chronic toxicity occurred in several animal species in a dose-dependent myelotoxicity, which extended to all the cells of the bone marrow.
Occasionally there was also atrophy of the lymphatic and spleen follocle. High doses resulted in animal studies to an increase in liver enzymes as a sign of hepatotoxicity.
Hemodynamic effects were not observed in dogs that received the highest tolerable dose. ECG studies in dogs showed only slight and non-significant disturbances of repolarization under vinorelbine as with other vinca alkaloids. In a study of primates no effect on the cardiovascular system were observed when multiple doses of vinorelbine over 39 weeks.
In the literature it has been reported sporadically on cardiovascular events such as angina pectoris and myocardial infarction treated with vinca alkaloids.

Mutagenic and carcinogenic potential
Vinorelbine induced chromosome damage, but shows in the AMES test no mutagenic potential.

In animal studies, vinorelbine induced aneuploidy and polyploidy. It can be assumed that vinorelbine might also have genotoxic effects in humans (aneuploidy and polyploidy).
The results of studies on the carcinogenic potential in mice and rats were negative, but only low doses were tested.

Reproductive toxicity
In reproduction studies in animals subtherapeutic dosages effects were observed. Determined were embryotoxic and fetotoxic effects, such as intrauterine growth retardation and delayed ossification. Lower doses that were toxic to the dams, teratogenic effects were observed (spinal fusion, missing ribs). In addition,

spermatogenesis and secretion from the prostate and seminal vesicles were reduced in rats, fertility was not restricted.

Safety pharmacology
In the performed in dogs and monkeys studies of safety pharmacology, no adverse effects found on the cardiovascular system.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections.

6.2 Incompatibilities

- Vinorelbine 10 mg/ml concentrate for solution for infusion should not be diluted with alkaline solutions (risk for precipitation).
- This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Before first opening: 2 years.

After dilution: Immediate use.
Chemical and physical in use stability has been demonstrated for 24 hours at 2-8 °C and at 25 °C.
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not normally be longer than 24 hours at 2-8 °C, unless opening and dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store in a refrigerator (2 ºC – 8 ºC).

6.5 Nature and contents of container

Glass vial type I with grey elastomer stoppers covered by blue aluminium cap with 1 ml of concentrate.

6.6 Special precautions for disposal and other handling

The preparation and administration of Vinorelbine should be carried out by trained staff. Suitable eye protection, disposable gloves, face mask and disposable apron should be worn. Eventual spillage or leakage should be mopped up.
All contact with the eye should be strictly avoided. Immediate liberal washing of the eye with sodium chloride 9 mg/ml (0.9%) solution for injection should be undertaken if any contact occurs.
On completion, any exposed surface should be thoroughly cleaned and hands and face washed.

It is recommended to infuse Vinorelbine over 6-10 minutes after dilution in 20-50 ml of sodium chloride 9 mg/ml (0.9%) solution for injection or in glucose solution for injection 5%. After administration the vein should be thoroughly flushed with at least 250 ml of isotonic solution.
Vinorelbinemust be given strictly intravenously: it is very important to make sure that the cannula is accurately placed in the vein before starting to infuse Vinorelbine. If the drug extravasates into the surrounding tissue during the administration considerable local irritation may occur. In this case, the

administration should be stopped, the vein flushed with normal saline and the remaining dose administered in another vein.
In case of extravasations, to reduce the risk of phlebitis IV glucocorticoids could be administered immediately.

6.7 DRUG PRODUCT SPECIFICATIONS

USP

7. MARKETING AUTHORISATION HOLDER

M/s Lab Diagnostic Systems (SMC) Pvt Ltd
Plot no 36-A, PSIC, SIE, Taxila, Rawalpindi

7.1. Name of Manufacturing Site

Marketing Authorization Holder in exporting country: Pharma resource GmbH Domeierstrabe 29/31 31785 Hamein Germany
Manufacturer: Thymoorgan Pharmazie GmbH Schiffgraben 3 38690 Golsar – Vienenburg Germany

8. MARKETING AUTHORISATION NUMBER(S)

101953

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30/04/2020

10. DATE OF REVISION OF THE TEXT

N/A