GUIDELINES ON HIGH ALERT MEDICATION MANAGEMENT

Document Number: **PHSR/GL/HA/010**

Document History: **1st Edition**

Effective Date: **DD-MM-YYYY**

This draft guideline is uploaded on the official website of DRAP dated 16th June, 2022, for seeking comments and suggestions from stakeholders on the draft document. Stakeholders can submit their comments and suggestions within 15 days of uploading this document using prescribed format, (further information on comments submission can access on this link. Comments and suggestions can be forwarded via email to npc@dra.gov.pk, copying at aqsa.hashmi@dra.gov.pk , or can be posted at mailing address, Director, Division of Pharmacy services, Drug Regulatory Authority of Pakistan, 3rd floor TF Complex, 7th Mauve Area, G-9/4, Islamabad

Drug Regulatory Authority of Pakistan
Islamabad-Pakistan

1. HISTORY

This is the first edition of this document.

2. APPLICATION - Guidance for Healthcare Professionals

This document is for the guidance and support of hospitals and healthcare professionals for safe prescribing, dispensing, administration and monitoring of High Alert Medication. It applies to:

i. All healthcare settings where these medicines are stored for patient use, prescribed, dispensed and/or administered. These may include: clinics, hospitals, healthcare units, diagnostic and interventional centres like Cath Labs, Pharmacies (both hospital and community pharmacies) etc.
ii. All healthcare professionals who are involved in the handling and use of these medicines e.g. doctors, pharmacists, nurses and other allied health professionals as applicable.

3. PURPOSE:

High Alert Medication (HAM) bear a heightened risk of causing significant patient harm due to error in storage, prescribing, dispensing, administration and use. These guidelines outline and recommend strategies to safely manage high alert medication and prevent risks that can be implemented by healthcare professionals during all stages of high alert medication management. The purpose of these guidelines is to:

i. Educate and sensitize healthcare professionals about the hazards associated with high alert medication.
ii. Encourage healthcare professionals and organizations to implement safety checks, risk mitigation and prevention strategies to safeguard patients' life and health.
iii. Encourage reporting of adverse events (AEs) including adverse drug reactions (ADRs) with emphasis on high alert medication and also encourage healthcare professionals and organizations to utilize this data in planning and implementing and improving healthcare practices.
iv. Educate and involve patients in the safe use of medicines.
v. Promote the culture of safety and safe use of medication in healthcare settings

Acknowledgement:-

DRAP would like to acknowledge the efforts of Pakistan Society of Health System Pharmacists (PSHP) with special thanks to Ms. Salwa Ahsan and Mr. Haris Aziz and all other members of Pakistan Society of Health System Pharmacists (PSHP) for their contribution in the development of these guidelines, endorsed by the International Pharmaceutical Federation (FIP).

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4. INTRODUCTION:

High Alert Medications (HAM) are associated with a significant risk of harm. Mishaps with high alert medication in comparison with others may or may not be more common but the consequences following medication errors can be serious to patients.

Factors like inherent risk of using HAM, vulnerable patient groups (pregnant women, paediatric patients, geriatric patients, cancer patients etc.), healthcare setting (e.g. outpatient vs inpatient settings), organizational culture, high-risk clinical scenarios (e.g. emergency and anesthesia settings) etc. could impose difficulties for healthcare professionals in ensuring patient safety while delivering health services. Accordingly, a holistic approach towards addressing medication safety is required keeping in view all the interlinked components.

As per international practices, the list of HAM in healthcare settings varies depending on the patient population treated and medicines required. DRAP has notified a tailored high-risk/high alert medication list, on the basis of medicines being used in Pakistan and internationally reported cases related to HAM.

HAM, as a whole, warrant special safeguards during the process of healthcare to reduce the risk of unnecessary patient harm associated with AEs/ADRs such as preventable medication errors. Safe use of HAM is widely dependent on / influenced by the following four factors:

i. Education and involvement of patients and the public
ii. Knowledge, skills and safe practices by healthcare professionals
iii. Safe handling and use of Medicines
iv. System design and infrastructure to support safe medication use

5. DEFINITION AND ACRONYMS:

Abuse of therapeutic good	means persistent or sporadic, intentional excessive use of therapeutic good which is accompanied by harmful physical or psychological effects;
ADR	**"***Adverse Drug Reaction*" means response to drug or therapeutic goods which is noxious and unintended that occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease or for the restoration, correction or

	modification of physiological function. A response in this context means that a causal relationship between a therapeutic good and an adverse event is at least a reasonable possibility. An adverse reaction, in contrast to an adverse event, is characterised by the fact that a causal relationship between a therapeutic good and an occurrence is suspected.
AE	**"***Adverse Event"* means any untoward medical occurrence in a patient or clinical investigation subject administered a drug or therapeutic good and which does not necessarily have a causal relationship with this treatment.
DRAP	The Drug Regulatory Authority of Pakistan
Healthcare Professionals (HCP)	means any member of the medical, dental, pharmacy, nursing professions, any allied health professional or any other person who in the course of his professional activities may prescribe, recommend, purchase, supply, sell or administer a therapeutic good including medical technologies as registered or enlisted by the Authority
High Alert Medication (HAM)	drugs that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these drugs, the consequences of an error are more devastating to patients. *Institute of Safe Medication Practices (ISMP)*
LASA	Look alike Sound Alike
Medication Error	Means any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer
Near Miss	WHO defines a near miss as "an error that has the potential to cause an adverse event (patient harm) but fails to do so because of chance or because it is intercepted" ("An error caught before reaching the patient")
NPC	National Pharmacovigilance Centre working under DRAP.
Occupational Exposure	an exposure to a therapeutic good as a result of one's professional or non-professional occupation at the workplace. It does not include the exposure to one of the ingredients during the manufacturing process before the release as a finished product at a pharma company.
Off Label Use	Refers to the use of an approved medicine under the direction

	or supervision of a healthcare professional for an unapproved indication, age group, dosage, route or form of administration.
Overdose of Therapeutic good	means administration of a quantity of a therapeutic good given per administration or cumulatively which is above the maximum recommended dose according to the registered therapeutic good information
P&TC / D&TC	Pharmacy & therapeutics Committee / Drugs & Therapeutics Committee
PV	**"**Pharmacovigilance" means the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other therapeutic good related problems.
Serious ADRs or AEs	means an untoward medical occurrence that at any dose results in patient death, is life-threatening, requires inpatient hospitalization or results in prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect or is judged to be a medically important event or reaction

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6. HIGH ALERT MEDICATIONS:

Medication errors are significant and often preventable healthcare problems. Although many medication errors may not cause grave harm to patients but risk associated with some drugs is higher than others. Errors in the administration of such drugs can have catastrophic clinical outcomes in patients.

Medications having a very narrow margin of safety require heightened vigilance, as these can cause severe patient harm when implicated in an Adverse Event. An error associated with the use of these drugs can result in significant patient injury and special precautions must be employed with their overall management. Due to this potential of risk, these drugs are identified as High Alert Medications.

7. HOW TO EFFECTIVELY USE THESE GUIDELINES?

Each individual organization and healthcare facility ha certain unique scenarios such as, the scope of services, specialties, available high alert medications (HAMs) and Look-Alike/Sound-Alike (LASA) medicines in the facility, nature and extent of use, known actual risks (through reported incidents, Adverse Events etc. specific to the facility) and potential risks (that are globally/nationally known).

Based on this knowledge, each facility needs to adopt specific HAM policies and guidelines to care for their unique patient population. A general approach should include:

1. **Assigning an independent multidisciplinary team** of healthcare professionals (physicians, pharmacists, nurses) within the facility (ideally Pharmacy & Therapeutics Committee – P&TC)

2. This team/P&TC assesses facility-specific details and parameters, and considering national HAM list, **identifies separates list of high alert and LASA medications** specific to their own facility

3. **Notify the high alert and LASA medication lists across the facility** and ensure healthcare staff involved in their handling and use are aware about and have ready access to the lists.

4. The P&TC should also develop **policies for safe use of these medicines** within their facility.

   i. The policy should highlight associated risks and briefly describe all aspects of medication management (i.e. selection, procurement, storage, prescription, dispensing, preparation, administration and monitoring).

   ii. The healthcare professionals should be made aware about the LASA and HAM policies and their respective roles in ensuring safety.

   iii. The lists and the policies must be **revised at regular intervals** (ideally: list every year and policy every 2 years)

5. P&TC in collaboration with concerned specialties (e.g. anesthesia, oncology etc.) should **develop guidelines for use of specific HAMs** (e.g. opioids or chemotherapeutics etc.) within the organization. The guidelines should address the aspects of evidence based clinical practice, standardized practices across the board, defined parameters of prescription, privileges, dispensing, preparation, administration and monitoring, mitigation of harm in case any error or toxicity is encountered etc.

6. The Healthcare facility should develop a process to **train all healthcare professionals in safe handling and use of the LASA/ HAMs** as per the organization's policy and specific guidelines ensuring that the healthcare professionals has proper orientation and awareness before new assignment of patient care activities.

7. Healthcare facility should have in place, the **process for reporting medication errors and near miss** events in the organization with special emphasis on events involving LASA and high alert medications. The reporting culture **created should be open and non-punitive** to identify/uncover the potential and actual loopholes in the healthcare system that need improvement to prevent errors and subsequent patient harm.

8. P&TC (or other assigned team) should **regularly review the medication errors and near miss reports**, with the objective to identify gaps and develop strategies to avert future recurrence or patient harm.

9. **It should also be ensured that all such strategies are uniformly implemented** and

reviewed for effectiveness in the facility and healthcare professionals are informed about the rationale.

8. HIGH ALERT MEDICATION MANAGEMENT & SAFE USE:

8.1. General Principles:

Safety must be ensured at all stages and steps of handling and dealing with high alert medication. Following are some basic principles for awareness of the healthcare professionals:

8.1.1. A **list of high alert medications (HAM)** identified from the master list and used within the facility should be prepared considering the following points;

8.1.1.1. availability of drugs and/or the volume of use in the healthcare facility

8.1.1.2. Past errors, near miss events or incidents reported with high alert medication / look-alike or sound-alike drugs in the healthcare setting

8.1.1.3. Agreement of a multidisciplinary team comprising of doctors, nurses and pharmacists (e.g. P&TC or D&TC) on drugs included in the list

8.1.1.4. Review and update of the list annually or when needed on the basis of any new LASA of HAM inclusion in inventory/formulary, or, in case of ADR

8.1.2. The approved list of LASA and HAM should be widely **disseminated to all healthcare** professionals in the facility along with information on AE reporting mechanism and available tools i.e. (Med Safety mobile application, Med Vigilance E Reporting System and Yellow reporting form).

8.1.2.1. List is displayed in prominent areas e.g. in nursing units, physician rooms, procedure rooms, medication storage areas (within or outside pharmacy) and is also freely accessible through the organization's intranet/webpage.

8.1.2.2. Newly appointed staff is given orientation about these drugs and associated hazards, while periodic refresher sessions for all healthcare professionals.

8.1.2.3. If any special training or competency assessment is required prior to prescription/administration/preparation of certain HAMs, it should be ensured and assessed properly before assigning personnel to respective job or section.

8.1.3. The organization should **develop protocols, guidelines** for safe use of HAMs, which may include prescribing through algorithms, nomograms, dose titration

protocol, reversal/rescue & resuscitation, and monitoring protocols etc.

8.1.4. HAMs and LASA drugs should be **labeled** as **HIGH ALERT MEDICATIONs, LASA** respectively as a reminder for healthcare professionals to remain vigilant in the management of the same. Be extra careful with drugs that are Look-Alike/Sound-Alike in addition to being one of the high alert medications as well.

8.1.5. Medications identified as high alert or LASA should be targeted for **specific error prevention strategies**. (*Refer to drug monographs for details under each category*)

8.1.6. HAMs and LASA are required to be stored, prescribed, dispensed, administered and monitored using **practices that ensure safety** for the patient discouraging operational shortcuts and reckless behaviour.

8.1.7. HAM and LASA must be **counterchecked** (preferably by a second independent healthcare professional) when prepared, at the time of dispensing and before administration to the patients.

8.1.7.1. A system should be established whereby one healthcare professional prepares the medication and a second counterchecks it.

8.1.7.2. All HAM issued from the pharmacy must be counterchecked and verified, for medication safety and accuracy before dispensing.

8.1.7.3. All equipment or devices used in the preparation and/or administration of drugs should be calibrated and maintained according to approved SOPs (e.g. weighing balances, laminar flow hoods, infusion pumps, syringe pumps etc.)

8.1.8. **The right to prescribe** certain HAMs should be defined by the organization e.g. chemotherapeutic drugs can be prescribed by an oncologist/hematologist and thrombolytics by Cardiologist or Neurologist Only etc.

8.1.8.1. Prescribing privileges are regularly reviewed and updated

8.1.8.2. Privileges are notified and circulated to all concerned healthcare professionals and staff involved in patient care.

8.1.8.3. Prescription privileges become part of healthcare professionals' regulations of the organizations (or equivalent records)

8.1.9. Organizations must strive to further improve provision of healthcare by

gradually implementing **international best practices.** Such as:

8.1.9.1. The appropriateness of each order is reviewed by a pharmacist before dispensing / administering.

8.1.9.2. Minimize or eliminate medication order transcription (by Nursing or other staff). Original physician order should be accessible to pharmacists for review. (Tips: use electronic physician order entry system or send duplicate/scanned copy of original order to pharmacy)

8.1.9.3. Use of electronic/computerized system for prescribing, dispensing and administration

8.1.9.4. Clinical decision support in computerized order entry systems

8.1.9.5. Barcode assisted medication administration

8.1.9.6. Use of drug libraries in smart infusion/syringe pumps

8.1.9.7. Standardized labels

8.1.9.8. Isolated and controlled storage of certain HAMs

8.1.9.9. Dispensing of diluted, ready-to-administer premixed parenteral HAMs by pharmacy

8.1.9.10. Use of Oral Syringe for liquid (oral) medication administration

8.1.9.11. Medication reconciliation at a patient's admission, transition of care and discharge etc.

8.1.10. Monitor and report Adverse Drug Reactions (ADRs), Adverse Events (ADEs), near miss and medication errors related to HAMs. Take appropriate steps to prevent recurrence in future. Healthcare Professionals and staff should be encouraged to report errors without the fear of repercussion or penalty.

8.1.11. Organizations must promote the culture of safety and accountability

8.2. Procurement:

8.2.1. All therapeutic goods should be procured from legitimate sources under warranty.

8.2.2. Strengths and brand duplications of drugs should be as limited as possible in the formulary of the healthcare facility.

8.2.3. P&TC / D&TC (or a similar multidisciplinary group) should be authorized to

take decisions on the alteration (addition or deletion of drugs) in the formulary based on scientific data (efficacy, cost and quality) and safety aspects.

8.2.4. Avoid the addition of LASA drugs in inventory if a safer option/alternate is available. In case no alternate is available, notify the end-users whenever LASA drugs are added and proactively take safety measures to avoid errors.

8.2.5. Avoid frequent changes of brand & strength and notify the end-users whenever there are changes.

8.2.6. Encourage the purchase of equipment and consumables with safety features for safe medication dispensing and administration. i.e. packs with pre-printed barcode, registered devices and equipment that are approved by DRAP, oral syringes that don't connect with invasive parenteral lines; infusion pumps with locking mechanism etc. Regular and ongoing calibration or validation (internally or through a third party) of in use equipment should be ensured.

8.2.7. At the time of receiving of stock from supplier, following points are essential to be considered:

8.2.7.1. Drugs should be safely and properly transported (maintaining storage conditions during shipment) from manufacturer to distributor, any other intermediaries and finally to the healthcare facility.

8.2.7.1.1. Temperature of the product should be maintained as per standards (or according to the manufacturer's guidelines) throughout the transportation involving transit stops and storage

8.2.7.1.2. Data Loggers (devices to constantly monitor and record temperature) for cold chain products (requiring storage at 2-8^{0}C) should be utilized for recording the data and review by the supplier and the healthcare facility

8.2.7.1.3. Genuinity of the products must be checked for the key product identification features (e.g. specific sealing tape, type and design of packaging, pack seals, holograms, barcode etc.) before accepting

8.2.7.1.4. If supplies are received in loose or unsealed cartons/packs, 100% of the supply must be checked for right product, supplied lot# and

expiry date (Risk: mix-up of other products or supply of wrong lot# or expiry that is not matching with the supply documents and the warranty)

8.2.7.1.5. SOPs should be in place for uniform procurement process addressing risk and mitigation strategies to be adopted in case the healthcare facility faces any problem as per the points mentioned above

8.2.7.2. Periodic performance of "supply chain risk assessment / audits" can also be planned to ensure the safety, efficacy and genuineness of its supplies

8.2.7.3. Purchases (both routine and emergency) must be done from authorized sources only, that should preferably be pre-approved and known to the healthcare facility

8.2.7.4. Traceability of all therapeutic goods (drugs & devices) from receiving in the facility till administration should be available for ensuring effective recall and incident management. Use of barcode technology or other electronic systems support quick actions

8.3. Storage:

8.3.1. Drugs should be stored and transported in conditions appropriate to maintain their efficacy and stability i.e. controlled conditions of (temperature, humidity and light etc.)

8.3.2. Controlled drugs (e.g. narcotics) should kept under lock and key for authorized access only.

8.3.3. Other HAMs should also be in authorized access and be protected from loss or theft across the healthcare facility

8.3.4. Drugs should be stored and used as per First Expire First Out (FEFO) principle

8.3.5. Lot (batch #) and expiry of drug should remain visible and traceable to ensure effective drug recall

8.3.6. Use cautionary label on packs and storage shelves, bins of high-alert medications and LASA drugs.

8.3.7. HAMs and LASA should be kept separately in labeled containers as indicated in monographs for each category

8.3.8. Avoid look-alike and sound-alike medications from being stored in close proximity.

8.3.9. Drugs intended for a specific route of administration must be stored in a conspicuous manner for differentiation e.g.

8.3.9.1. Oral medicines separate from intravenous

8.3.9.2. Intravenous separate from epidural or intramuscular inj.

8.3.9.3. Sustained-release or depot forms must be stored separately from immediate-release forms

8.3.9.4. Topical drugs from oral and parenteral etc.

8.3.9.5. Each type must be labeled properly on bin/shelf to alert the staff e.g. “Not for IV use” or “Epidural Use only” etc.

8.3.10. Use TALL-man lettering to emphasize differences in medication names (e.g. DOPAmine and DOBUTamine) as indicated in the monographs

8.3.11. Limit the nursing unit’s floor stock medication to standard requirement, reducing /restricting the quantity and availability of multiple strengths or dosage forms.

8.3.12. Medicines should be identified and checked with generic name in addition to their brand names while storing, picking for dispensing/administration or placing back any unused items.

8.3.13. Drugs which are not needed (hold/discontinued) should not be stored with those due for administration

8.3.14. When new stock is received or unused drugs are returned, caution must be exercised to put them back in the right place (in their designated shelf or bin). Placement in the wrong place can result in medication error when the next dispensing takes place.

8.3.15. All equipment used in monitoring and/or maintenance of storage conditions for medicines (e.g. thermos-hygrometers, dehumidifiers, data loggers etc.) must be

properly validated, calibrated and on periodic preventive maintenance (PPM).

8.4. Prescribing

8.4.1. Only authorized physicians should prescribe.

8.4.2. Identifiers like patient name and medical record # should be used for prescription to the right patient.

8.4.3. Appropriate lab tests should be ordered and reviewed periodically at baseline and during therapy.

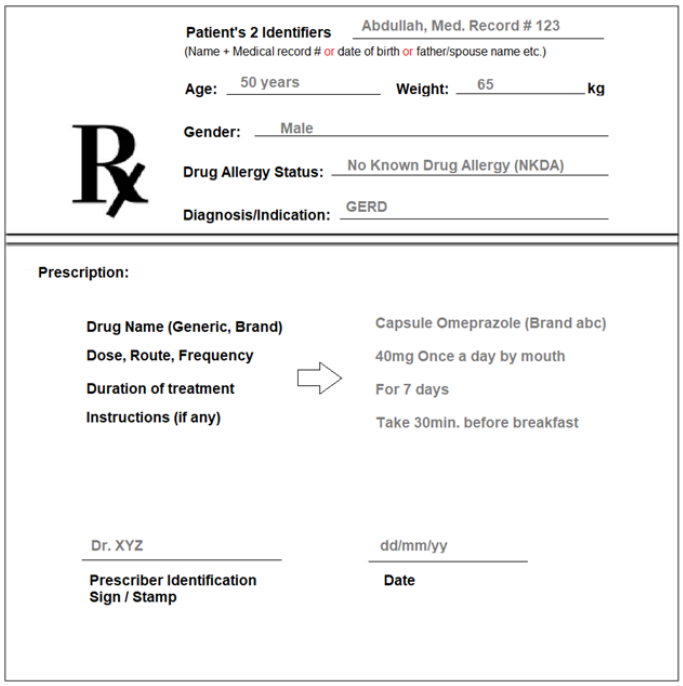
8.4.4. Prescriptions should be valid (by an authorized prescriber, with prescriber's contact and dated) with complete (proper dose, route, frequency, duration etc.) and clear (non-confusing) information. Abbreviations and jargon should be avoided.

8.4.5. Patients should be closely monitored for adequate and desired response to therapy. If any adverse reaction or event is encountered it should be recorded and reported.

8.4.6. Queries of staff or patients regarding prescriptions should be timely, politely and appropriately addressed

8.4.7. In case of drug overdose/adverse drug reaction directions for rescue or reversal agents should be immediately provided, recorded and reported.

8.4.8. The following sample for "clear and complete" prescription can be considered



Patient's 2 Identifiers: Abdullah, Med. Record # 123
(Name + Medical record # or date of birth or father/spouse name etc.)

Age: 50 years Weight: 65 kg

Gender: Male

Drug Allergy Status: No Known Drug Allergy (NKDA)

Diagnosis/Indication: GERD

Prescription:

Drug Name (Generic, Brand)	Capsule Omeprazole (Brand abc)
Dose, Route, Frequency	40mg Once a day by mouth
Duration of treatment	For 7 days
Instructions (if any)	Take 30min. before breakfast

Dr. XYZ — Prescriber Identification Sign / Stamp

dd/mm/yy — Date

8.5. Preparation

8.5.1. The most-ready to use form possible should be prepared and dispensed by the pharmacy

8.5.2. All preparations should be carried out in a clean, safe and clutter-free environment, away from distractions and contaminants

8.5.3. Specific preparation guidelines should be followed to ensure error free preparation e.g. chemo or electrolytes (refer to drug monographs for details)

8.5.4. Personnel protective equipment (PPEs) like masks, gloves, apron/gown must be worn as per the type of drug being handled

8.5.5. Hand hygiene, aseptic and safe preparation techniques should be employed in drug preparation

8.5.6. Dilutions, strengths and doses should be double checked against actual order

8.5.7. The drug should be labeled properly after preparation. The label should contain information on drug name, strength (or dilution), diluent, total volume, name and designation of person who prepared, date and time of preparation and expiry

(Note: unlabeled drugs esp. syringes/infusion are a major source of wrong drug

errors)

8.5.7.1. Standardized drug labelling formats should be developed and implemented by the P&TC/D&TC of the hospital.

8.5.8. All equipment or devices used in the preparation of medications should be clean, disinfected, calibrated and maintained according to the organization's SOP (e.g. weighing balances, laminar flow hoods, mortar & pestle, tablet cutter, droppers, measuring cups/spoons, oral syringes and other equipment etc.)

8.5.9. If multi-dose vials are used to prepare the drug, vials with leftover drug should be labelled properly with 'date and time of opening' for the next doses. Opened vials should be discarded or returned immediately on the expiry date / beyond-use-date.

8.5.10. Vial, syringes, injector pens, needles, administration devices used on one patient should not be used on other patients to avoid cross-infection

8.5.11. Sharp devices must be discarded safely in puncture-proof waste container

8.5.12. Effective measures should be adopted to prevent cross contamination and mixing of active ingredients, excipients and diluents etc.

8.6. Dispensing

8.6.1. All HAMs should be dispensed in clean, safe and clutter-free environment, away from distractions

8.6.2. Dose, route, frequency/rate of admin., dilution, allergies, relevant lab tests, indication, interactions, and contraindications should be checked while reviewing physician's order

8.6.3. If any ambiguity arises, the prescriber should be contacted to clarify before dispensing the medicines

8.6.4. In case of any changes in orders, effective and immediate communication and documentation should be assured

8.6.5. Drugs should be selected (or prepared) as per the physician's order and packed /labelled properly for dispensing.

8.6.6. Drugs should be rechecked before dispensing so that the right drug, dosage form, strength and quantity is dispensed. No medicines should leave the pharmacy without being checked and verified by a pharmacist.

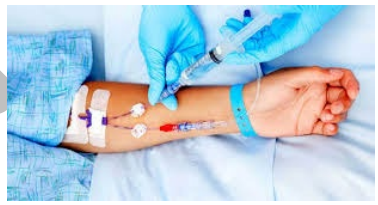
8.6.7. Verify that the drug is dispensed to the right patient by using patient identifiers like name and medical record #

8.6.8. Encourage use of technology to avoid dispensing errors e.g., barcode, printed drug labels containing patient identification, drug identification and administration instructions, auxiliary labels etc.

8.6.9. Drugs should be dispensed in the most ready-to-use form possible and minimum number of doses possible (unit dose dispensing: single dose at a time)

8.6.10. During transport appropriate storage conditions should be maintained (e.g., cold chain or spill prevention etc.) with safety measures to prevent loss or theft

8.7. Administration



8.7.1. Administration should be carried out by authorized healthcare professionals

8.7.2. Patient identifiers (like patient name and medical record #) should be used to verify administration to the right patient

8.7.3. Follow the 6 rights of safe drug administration: Right patient, Right drug, Right dose, Right time, Right route, Right documentation in charts

8.7.4. Always compare drug in hand against drug name, strength and route mentioned in physician's order before administration

8.7.5. In case of any ambiguity, the prescriber should be contacted for clarification before administering the medicines

8.7.6. In case of any changes in orders, effective and immediate communication and documentation should be assured

8.7.7. The practice of double checking or second person verification for dose, route, dilution etc. can eliminate chances of errors

8.7.8. One patient's drugs (either new or leftover) should not be used for another patient

8.7.9. Unlabeled drugs or those for which information on the contents, strength, expiry,

or dilution etc. is not known should never be used. Any unlabeled and unidentified syringes should be immediately discarded in a safe manner / as per SOPs, if found in patient care area

8.7.10. If a drug is to be prepared before administration, the preparation, calculation and dilution etc. should be completed in a clean, safe, clutter free area with minimum-to-no distractions

8.7.10.1. The drug should be properly labelled if administration is at a later time

8.7.10.2. If a multi-dose vial is used for drug preparation, it should be marked with date-of-opening, dilution concentration and the personnel's name & designation. Such vials should be discarded immediately on expiry date

8.7.11. Majority of serious administration errors occur due to administration of drug by the wrong route. Always verify the drug in hand and the source of invasive line before administration. Common errors include:

8.7.11.1. Connecting oral medicines contained in syringe (or enteral feed bags) with Intravenous (IV) cannula

8.7.11.2. Epidural or intrathecal medications given via IV route (and vice versa)

8.7.12. Verbal orders should not be given / taken for HAMs unless it's for an emergency/life-threatening situation, or during a procedure when ordering physician is scrubbed and/or performing the procedure

8.7.13. Always administer infusions with rate-controlled devices to avoid accidental free flow of drugs

8.8. Monitoring

8.8.1. Monitor the appropriate storage of drugs for safety, stability and security

8.8.2. Monitor the quantity in hand and expiry of stocks

8.8.3. Monitor the patient for the effect (or side effects) of drugs as ordered by the physician (vital signs, lab tests, physiological conditions, signs of allergy/hypersensitivity or reaction etc.)

8.8.4. If any serious condition, immediately notify the prescriber

8.8.5. Monitor for any possible errors, incidents or near-misses and report to P&TC as per the organization's SOP for education and prevention measures

8.9. Documentation, policy & procedures

8.9.1. All orders (prescriptions) should be documented in patient charts or medical records (Physician Orders) as per organization's policy.

8.9.2. Document's author (Name/ID/Stamp), date and time should be written as per the organization's policy.

8.9.3. If any correction is to be made, the original note should be struck off with a diagonal line, mentioning "Error" and a new note should be written separately. Do not over-write.

Correct way ✓	Incorrect way ☒
Rx Error ~~Inj. Furosemide 15mg Stat IV~~ Inj. Furosemide 40mg Stat IV	Inj. Furosemide ~~15~~40mg Stat IV

8.9.4. Use of pre-printed order forms (or order sets) for order or administration of high alert medicines should be encouraged. Record of the same should be maintained in patient medical record

8.9.5. Dispensing record should be available for individual doses and drugs

8.9.6. Patients' condition and progress should be documented properly in the patient chart or medical record as per the organization's policy

8.9.7. All drugs administered should be recorded in a designated place in the patient chart or medical record (Medication Administration Record) as per the organization's policy

8.9.8. All patient records should contain drugs allergy status (known or not known) and past medication history

8.9.9. Medication errors, near miss and adverse drug reactions should be documented and reported as per organization's policy for education and prevention measures

8.9.10. Drugs stored in pharmacy, store, nursing unit stock or emergency stock should be duly accounted for (i.e. record of quantity received, quantity dispensed, quantity in hand and expiry monitoring etc.is maintained) as per organization's policy

8.9.11. Storage conditions like temperature and humidity etc. of the drugs storage area

should be documented retained till a defined timeframe

8.9.12. Controlled drug record should be maintained as in compliance with the DRAP Act 2012, Control of Narcotic Substances Act 1997, Drugs Act 1976 and respective Drugs Rules.

8.10. Medical information

Healthcare facilities should ensure easy access to unbiased, evidence- based drug information resources for healthcare professionals.

Example of such resources include:

Drug Information Services, reference books, online subscriptions to drug information resources, reference charts, pocketbooks/guidelines or flyers, alerts and pop-ups in computerized medication ordering, dispensing or administration system etc.

8.11. Patient Education

8.11.1. Educating patients on safe use of medicines in general, and HAMs in particular is the shared responsibility of all healthcare professionals

8.11.2. Instructions to patients on how to use medication in a safe manner as per prescription, should be clear and understandable (written, printed, electronic or verbal).

8.11.3. Medication should be reconciled at the time of admission and upon discharge, to avoid duplications or omissions of important drugs. Patients should also be informed about the updated or current medication list

8.11.4. If any drug-food allergies (or interactions) are identified, patients or their care givers should be informed about precautionary measures (the type of medicines or foods to be avoided)

8.11.5. Use of best practices in patient education like; drug labels, auxiliary labels, pictograms, printed brochures or flyers (bilingual), use of demo devices etc. should be encouraged and recommended

8.11.6. Patients should be educated about high alert medications and how they can play their role in averting error/harm. The patient's role may include (but is not limited to):

8.11.6.1. Knowing the indication for use
8.11.6.2. Knowing the medicine name and dose they are taking
8.11.6.3. Knowing exactly when to stop the therapy and when not to
8.11.6.4. Able to identify the colour, shape of tablets/injections they are using (to avoid wrong drug administration or purchase) in case of any change in physical appearance
8.11.6.5. Knowing the administration technique and timings
8.11.6.6. Importance of doing relevant lab tests and cut-off limits
8.11.6.7. What to do in case doses are missed?
8.11.6.8. What foods or drugs to avoid?
8.11.6.9. Importance of informing other healthcare professional about using concomitant medication e.g. being on anticoagulants, and also if undergoing a procedure.
8.11.6.10. Importance of avoiding activities that could lead to adverse situations
8.11.6.11. What to do in case of emergency (e.g. overdose, bleeding or signs of thrombosis)
8.11.6.12. How to report if any serious side effect occurs

9. LIST OF HIGH ALERT MEDICATIONS:

Healthcare professionals are encouraged to actively monitor the safety of the below-mentioned high alert medications/ drugs by avoiding their inappropriate use. If any adverse drug reaction (ADR) occurs with or without inappropriate use of high alert medicines, it should be managed properly and should be reported to National Pharmacovigilance Centre, DRAP within defined timelines through one of the following channels:

- Through DRAP, MED Vigilance E-Reporting System: https://primaryreporting.who-umc.org/PK

OR

- Through Med Safety Mobile Application available both on Android and iOS platforms.

For further details on reporting refer to https://www.dra.gov.pk/wp-content/uploads/2022/04/Adverse-Events-Reporting-Guidelines-for-Healyhcare-Professionals-Edition-01.pdf

9.1. High Alert Medication List Notified by the National Pharmacovigilance Centre, DRAP.

S #	Class/Category	Drugs *
1.	**Adrenergic agonists**	IV form of Epinephrine, Phenylephrine, Norepinephrine etc.
2.	**Adrenergic antagonists**	IV form of Metoprolol, Labetalol
3.	**Anaesthetic agents**	General, Inhaled and IV form of drugs like Propofol, Ketamine, Isoflurane and Sevoflurane etc.
4.	**Antiarrhythmics**	IV form of Lidocaine and Amiodarone etc.
5.	**Antithrombotic agents**	**Anticoagulants:** Warfarin, low molecular weight heparin (Enoxaparin), Unfractionated heparin **Direct oral anticoagulants and factor Xa inhibitors:** Rivaroxaban, Fondaparinux Apixaban etc. **Thrombolytics:** Alteplase and Streptokinase.
6.	**Anti-infective**	Amphotericin, Vancomycin, Aminoglycosides.
7.	**Cardioplegic agents**	Both commercial products and compounded within hospitals
8.	**Chemotherapeutic agents**	All parenteral and oral chemo
9.	**Dextrose Hypertonic 20% and above**	Dextrose water 20% and above for parenteral use
10.	**Dialysis solutions**	Both hemodialysis and peritoneal dialysis solutions
11.	**Epidural and Intrathecal**	Bupivacaine, Ropivacaine
12.	**Hypoglycemics agents, sulfonylurea**	Oral form of Glimepiride, Glibenclamide, Glipizide etc.
13.	**Inotropic drugs**	IV form of Digoxin and Milrinone

14.	**Insulins**	All Insulins
15.	**IV electrolytes**	Undiluted Potassium Chloride for Inj, concentrate and injections of Magnesium Sulphate, Potassium Phosphate, IV form of Hypertonic saline.
16.	**Liposomal forms of drugs**	E.g. Liposomal Doxorubicin vs conventional Doxorubicin HCl
17.	**Look alike and sound alike drugs**	Each patient care facility to review and develop their own look alike (similar appearance) and sound alike (that sound similar or are read like) drugs pairs list based on their incident/ error data.
18.	**Moderate sedation agents**	IV form of Dexmedetomidine, Midazolam etc.
19.	**Moderate and minimal sedation agents for children**	Oral form of Chloral Hydrate, Midazolam, parenteral form of Ketamine etc.
20.	**Neuromuscular blocking agents**	Succinylcholine, Rocuronium, Atracurium, Cis-Atracurium etc.
21.	**Opioids**	All opioids including **oral** (liquid concentrate, immediate and sustained release formulations), Parenteral and transdermal form.
22.	**Parenteral Nutrition**	Both commercial products and compounded within hospitals
23.	**Others**	IV form of Oxytocin, Vasopressin, and Promethazine.

** Medicines and Drugs' availability status changes from time to time in market, hence, refer to the current registered and available drugs of this class in Pakistan*

Note:

Each healthcare facility must identify a list of HAMs and LASA drugs specific to their setup (please refer to the section: "How to effectively use these guidelines" for details)

** Medicines and Drugs' availability status changes from time to time in market, hence, refer to the current registered and available drugs of this class in Pakistan*

10. HIGH ALERT MEDICATIONS MONOGRAPHS:

10.1. Adrenergic agonists:

Why are these high alert?

Medication errors associated with the use of **adrenergic agonists** especially epinephrine products are a significant healthcare problem.

Medication safety problems associated with the design and use of these medicines include, drug content ratio-strength expressions such as 1:1,000 and 1: 10,000 per ampule; leading and trailing zeros when writing decimal dosage expressions; look-alike and sound-alike (LASA) drug errors with epinephrine, ephedrine and nor-epinephrine; route of administration errors such as administering IM dosage via an IV route etc. Errors involving dosage calculations and incorrect routes of administration to patients are the most significant epinephrine errors.

From 2020-2021, ISMP received a total of 16 reports involving Norepinephrine through the **ISMP National Medication Errors Reporting Program** (ISMP MERP). About one-third of these reports were hazards related to look-alike names, labeling, or packaging, for which no actual error occurred. ISMP has published seven of the reported norepinephrine errors that reached patients: four dosing errors; one wrong concentration error; one wrong drug titration error; and one accidental discontinuation of a norepinephrine infusion.

How to Ensure Safe Use of Adrenergic Agonists:

Adrenergic Agonists **Includes:** IV form of Epinephrine (Adrenaline), Phenylephrine, Norepinephrine (Noradrenaline) etc.*	
Storage	1. Primarily stored in the pharmacy 2. When in nurses' custody, must be stored in medication trolleys or patient medication cabinets under **authorized access only** 3. Availability of these drugs on floor stock of nursing or patient care units is **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance so that when needed in life saving condition it is immediately available e.g. in code trolleys/crash carts or emergency kits etc.) • **Standardize the quantity and strength** in all emergency

	kit/code trolley/crash carts across the healthcare facility • **Make dosing conversion charts available** that shows the dose as both 'mg' and 'mls' to be administered, corresponding to the age and/or weight of the patient in emergency situation • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of any of these medicines on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with Generic name of drug in **bold**, strength and labeled as "High Alert medication". 5. If any drug is **sound-alike or read-alike** with another drug, use tall-man lettering in order to correctly read/identify the drug name. See the example below: Suppose Epinephrine and Nor-Epinephrine are sound-alike or read-alike: **EPI*nephrine* 1mg/ml (1:1000) inj.** **High Alert Medicine** **NOR-EPI*nephrine* 8mg inj.** **High Alert Medicine** 6. Label epinephrine injections in mg per ml (e.g., 1 mg/mL) and to discontinue ratio strength labeling (e.g., 1:1,000 and 1:10,00) 7. Identify Medicines in your facility that are **look-like or sound-alike** with adrenergic agonists and store them apart from each other, in properly labelled bins / shelves (as shown above) 8. Identify **combination products** that contain one of the adrenergic agonists like adrenaline (epinephrine) e.g. **Lidocaine + Adrenaline** injection etc. and store them apart from plain adrenaline injections so that mix-up and wrong dispensing/administration can be avoided. 9. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration) 10. **Never leave any unlabeled syringe or infusion bag** containing adrenergic agonists in patient care area
Prescribing	1. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Check **appropriateness** of order esp. dose, as per patient weight and

	other physiological conditions such as renal function. 3. Order/prescription must be **complete and non-ambiguous**: o i.e. proper indication, patient's drug allergy status, weight as needed o Any special instructions o **Prescribe safely e.g.**: ▪ **Never use abbreviations/short forms** like Epi or Norepi, write full name ▪ **Avoid naked decimals** e.g. **.45mg** as it can be misread as **45mg** – always write **0.45 mg**. ▪ **Avoid trailing zero** e.g. **2.0mg** as it can be misread as **20mg** – always avoid trailing zero and write **2 mg** ▪ **Avoid using symbol for units** such as **5μg**, as it could be misread as **50**. Always write 5 mcg or 5 microgram ▪ **Write infusion orders** (dose expression (e.g. mcg/kg/min or mcg/mg/hr etc.), rate and diluent and concentration for infusion) very clearly and it is a best practice that prescribing should be standardized across the organization to avoid confusions ▪ Standardize the prescribing of norepinephrine infusions to either **weight-based** (mcg/kg/minute) or **non-weight-based** (mcg/minute) to reduce the risk of errors. The American Society of Health-System Pharmacists (ASHP) *Standardize 4 Safety* initiative recommends using mcg/kg/minute dosing units for norepinephrine. Some hospitals may standardize to mcg/minute dosing due to prescriber preference—either is acceptable, **but do not allow both dosing options.** ▪ When **titration of infusion** is required as per the target response, mention the **maximum (ceiling) dose** that can be reached. If patient is not giving adequate response on the defined maximum dose limit, the physician must be immediately informed ▪ It is a best practice to have a **pre-printed order form** for prescribing adrenergic agonists in critical care setting with necessary safety checks (to be filled by the doctor) 4. The **dose/rate calculation and titration** shall be done based on

	individual patient requirement and vital signs 5. Healthcare organizations must standardize to a limited number of concentrations to treat pediatric and/or adult patients. Designate weight-based limits for the most concentrated infusions, which should be reserved for patients who are fluid restricted or require larger doses of norepinephrine (to minimize bag changes). ➔ Note: Epinephrine is administered by **multiple routes** of administration. These may include IV, intraosseous (IO), intracardiac, IM, SC, endotracheal, intraocular routes, topical, and other routes. Routes of administration as well as dosages and rates of administration depend on clinical indications so very carefully write dose and clearly mention the route of administration ➔ 1 ampoule of NOREPInephrine (Noradrenaline) 4 ml contains 8 mg noradrenaline tartrate equivalent to 4 mg **NORADREnaline BASE**. The dosing is based on the noradrenaline base so confusion must be avoided while prescribing and administration ➔ The **infusion should be gradually decreased** since abrupt withdrawal can result in acute hypotension. 6. **Standing orders**: specific orders to monitor patient's response to these drugs (like vital signs, cardiac output, cardiac rate, blood pressure etc.) must be clearly mentioned. 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check** patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. It is a best practice that pharmacy dispense these drugs in most **ready**

	to administer form possible esp. IV infusions 5. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing these drugs **CAUTION HIGH ALERT MEDICINE** **Double-check** the medication before dispensing 6. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration ➔ 1 ampoule of NOREPInephrine (Noradrenaline) 4 ml contains 8 mg noradrenaline tartrate equivalent to 4 mg **noradrenaline base**. The dosing is based on the noradrenaline base so confusion must be avoided while prescribing and administration ➔ The **infusion should be gradually decreased** since abrupt withdrawal can result in acute hypotension. ➔ When **titration of infusion** is required as per the target response, mention the **maximum (ceiling) dose** that can be reached. If patient is not giving adequate response on the defined maximum dose limit, the physician must be immediately informed 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Inspect solution for injection** before administration. Do not use solutions that are pinkish to brownish in color, cloudy, or contain a precipitate or particulate matter 6. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label.

	7. **Label the lines and trace the tubing.** Label each infusion line above the pump and near the patient's access site. Also, trace the tubing by hand from the solution container to the pump, and then to the patient, for verification of the proper pump/channel and route of administration immediately before starting or changing the bag or rate of a norepinephrine infusion. 8. **Check the infusion site** frequently for free flow. Avoid extravasation into the tissues to prevent local necrosis. If blanching along the course of the infused vein occurs, consider changing the infusion site at intervals to allow the effects of local vasoconstriction to subside 9. **It is a best practice to have an established extravasation management protocol.** Nurses should receive education about the protocol, including treatment strategies and avoidance of applying cold compresses to the site, which may worsen the tissue damage. 10. It is a good practice to have a **2nd check** for dose, route, dilution by another staff 11. Infusion must always be given with rate controlled device to avoid accidental free flow of infusion. • Always follow the rate as prescribed mcg/kg/min or mcg/min 12. Never use **one patient's medicine on another** patient 13. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order review and before administering 14. **Verbal orders** must not be taken unless emergency or life threatening condition 15. **Any unused** (or hold, discontinued) high alert medicine must be immediately returned to original stock. 16. **Discontinue infusions.** If the patient is stable for 2 hours after stopping a norepinephrine infusion, consider obtaining a discontinuation order from the prescriber. Once the infusion has been discontinued, immediately disconnect the infusion from the patient, remove it from

	the pump, and discard it to prevent inadvertent administration. Infusions paused for more than 2 hours should also be disconnected from the patient. 17. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or organization's policy • Vital signs, hemodynamic status, BP, pulse, cardiac output etc. 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Counsel family as and when indicated

Ref:

1. Analysis Identifies Multiple Common Causes of Norepinephrine Errors, March 24, 2022, https://www.ismp.org/resources/analysis-identifies-multiple-common-causes-norepinephrine-errors
2. Medication Safety: Epinephrine/Adrenaline problems, Corrections, and Applications, 2020;https://www.ivtnetwork.com/article/medication-safety-epinephrineadrenaline-problems-corrections-and-applications
3. EMC Nonadrenaline (Norepinephrine), https://www.medicines.org.uk/emc/product/4115/smpc#gref
4. ASHP IV adult continuous infusion guidelines version 1.01, Nov 2016, https://www.ashp.org/-/media/assets/pharmacy-practice/s4s/docs/s4s-proposed-standard-concentrations-adult-continuous-infusions.ashx

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.2. Adrenergic Antagonists (IV Bet Blockers):

Why are these high alert?

Beta-blockers are prescribed frequently, in an evidence-based manner, to manage prevalent conditions such as atrial fibrillation, ischemic heart disease, hypertension and heart failure. As a result, a large number of patients admitted to the hospital are on established beta blocker therapy. Abrupt withdrawal of beta-blockers is harmful, producing problematic tachycardias, in particular atrial fibrillation with rapid ventricular rate and subsequent hypotension, as well as potentially increasing myocardial oxygen demand and ischemia.

Intravenous (IV) administration of Beta Blockers comes with risks involved. Concerns include the potential for hypotension, bradycardia and A-V nodal conduction delay. In most hospitals, the administration of IV beta-blockers to inpatients is limited to the wards with cardiac monitoring.

How to Ensure Safe Use of IV Beta Blockers:

Adrenergic Antagonists (Beta Blockers) **Includes:** Injection Metoprolol, Labetalol etc.*	
Storage	1. Primarily stored in the pharmacy 2. When in nurses' custody, must be stored in medication trolleys or patient medication cabinets under **authorized access only** 3. Availability of these drugs on floor stock of nursing or patient care units is **discouraged**. • **Keep injectable forms only if absolutely necessary** (e.g. in operating rooms (ORs), ER or interventional areas like Cath lab etc.) • **Only Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC)** of the hospital should authorize stocking of any of these opiates on patient care units (outside pharmacy) ➔Note: Limiting access to these products is a strong deterrent to inadvertent use or misuse. 4. When stored in healthcare facility, **bins should be labelled** with Generic name of drug in **bold**, brand, strength. 5. If any IV Beta Blocker is **Look-Alike**, **sound-alike or read-alike** with another drug, or its own strength or with its oral counterparts, use recommended techniques to properly differentiate them e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of auxiliary/colored labels etc. 6. **Drug discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration) 7. **Never leave any unlabeled syringe or infusion bag** in patient care area
Prescribing	1. To be **prescribed by a senior physician** trained and knowledgeable about the dosing and monitoring protocol, and safety concerns associated with IV Beta Blockers

	2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. It is recommended that IV Beta Blocker are prescribed and used as per **standard protocol or guidelines** defined by the organization including: • Dose range, maximum dose, frequency/rate of administration, standard dilution and duration of treatment as per the indications, including use in special population like very young or very old • Special dosing protocols e.g. intermittent vs continuous infusion etc. • Contraindications for use • Co-morbid conditions that can be exacerbated or affected by use of IV Beta Blockers (e.g. underlying heart disease, diabetes, thyroid disorders, asthma etc.) • When switching from IV to Oral; Gap between last IV dose and first oral dose • Dose Titration as per response and Tapering protocol • Standard monitoring protocol before, during and after stopping infusion (e.g. continuous cardiac monitoring; ECG, Blood pressure, Heart rate and Bronchospasm etc.) • Protocol to manage adverse effects like hypotension, bradycardia, heart block etc. • Prompt availability of rescue agents in case above mentioned adverse drug effects are observed 4. Check **appropriateness** of order esp. dose, rate of administration, as per patient age and weight, other physiological conditions such as renal function 5. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Any special instructions • **Prescribe safely e.g.**: o **Never use abbreviations or short forms.** E.g. Meto 5 mg IV stat: it does not specify the actual drug intended and can be confused between metoprolol and metoclopramide etc. o **Avoid naked decimals** e.g. **.5 mg** as it can be misread as **5mg** – always write **0.5 mg**. o **Avoid trailing zero** e.g. **15.0mg** as it can be misread as **150mg** – always avoid trailing zero and write **15 mg** 6. **Standing orders**: specific orders to be written: • To monitor patient's response to these drugs (like cardiac and hemodynamic monitoring); including when and how frequently to be done. • When to hold infusion (specify cut-off values for heart rate and/or blood pressure) • When and how to use rescue agents in case of serious adverse reactions to IV Beta Blockers 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to

	medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check** patient parameters (like allergy, contraindications, renal function, weight, etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. **Double-check** the medication before dispensing 5. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Inspect solution for injection** before administration. Do not use solutions that are have discoloration, are cloudy, or contain a precipitate or particulate matter 6. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. • Staff administering these drugs must be knowledgeable about the organization's guideline (see prescribing point # 3) on the use of Beta Blockers 7. Never use **one patient's medicine on another** patient 8. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order review and before administering 9. **Verbal orders** must not be taken for IV Beta Blockers unless there is an emergency or life threatening situation, or for stopping or holding the administration 10. **Any unused** (or hold, discontinued) high alert medicine must be immediately returned to original stock. 11. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to

	medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or organization's protocol • Cardiac/hemodynamic monitoring, vital signs and signs of toxicity or adverse drug reactions 2. Raising the patient into the upright position within 3 h of IV Beta Blockers administration should be avoided since excessive **postural hypotension** may occur. 3. Monitor **Co-morbid conditions** that can be exacerbated or affected by use of IV Beta Blockers (e.g. underlying heart disease, diabetes, thyroid disorders, asthma etc.) 4. **Monitor blood glucose levels.** In insulin-dependent diabetics, beta-blockers can prolong, enhance, or alter the symptoms of hypoglycemia, while hyperglycemia appears to be the major risk in noninsulin-dependent diabetics. 5. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 6. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Not applicable - Counsel family as and when indicated

Ref:

1. Safety of intravenous metoprolol use in unmonitored wards: a single-centre observational study 2015, *https://onlinelibrary.wiley.com/doi/pdf/10.1111/imj.12842 -*
2. Lopressor Injection, *https://www.rxlist.com/lopressor-injection-drug.htm#medguide*
3. Labetalol Injection, *https://www.medicines.org.uk/emc/product/10831/smpc#gref*

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.3. Anaesthetic agents:

In general, anesthetics are medications that induce and maintain a state of unconsciousness. They cause anterograde amnesia, meaning that a patient does not remember the events that follow their administration. This class of medications create amnesia for surgery. These can be given either by IV injection or inhaled as a gas. Propofol is the most commonly used IV general anesthetic. Ketamine is mainly used for pediatric anesthesia. The main disadvantage is hallucination, nightmare and other transient psychotic disorders.

The Anesthesia mishaps are well reported in literature and efforts must be done to avoid medication errors related to anesthesia drugs as they can have serious consequences. Some common issues identified with these errors include: human factors including haste, inattention/carelessness, fatigue, distraction, poor labeling and failure to check or read the label, lack of labeling standardization with ASTM color-coded syringe standards. Poorly designed medication dispensing systems/carts, labels and fonts, vial sizes, and unaddressed embedded human factors constraints, including the existence of confusing drug names and look-alike/Sound-Alike dissimilar drugs, are the most common causes of medication errors worldwide. The anesthesiologist working alone to draw up, dilute, label, and administer medications with little or no oversight is a contributory factor. 'Syringe swap' is also a common error identified internationally with anesthesia drugs.

The most common medications associated with errors in the operating room (OR) were propofol, phenylephrine, fentanyl, neuromuscular-blocking agents and opioids.

How to Ensure Safe Use of Anesthetic Agents:

Anesthetic Agents include*: Inhaled forms: Isoflurane and Sevoflurane etc.* IV forms: Propofol, Ketamine etc.* ☛ Also see the section on: Moderate sedation	
Storage	1. Primarily stored in the pharmacy 2. Availability of these drugs on floor stock of nursing or patient care units is **not recommended**. • Healthcare facility can allow the storage of selected drugs in operating areas where anesthesia is administered. This decision should be guided by the evidence, and need, as per the type and nature of the procedures performed. i. Anesthetic drugs must be stored in **authorized access only** ii. Anesthetic room drug cupboards must be locked when the operating theatre is unoccupied.

	• **Only Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC)** of the hospital should authorize stocking of any of these drugs on patient care units (outside pharmacy) 3. When these drugs are stored in healthcare setting, **storage bins should be labelled** with name of drug in **bold**, strength, warning: "High Alert medication". Brand names can be used for reference purpose after the generic name. See the example below: 4. If any of these drugs are **sound-alike, read-alike or look-alike**, use tall-man lettering, highlight its strength, brand name, color or shape etc. in order to correctly read/identify the drug name. 5. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing anesthetic drugs **CAUTION HIGH ALERT MEDICINE** 6. **Medicines discontinued or hold by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock immediately (to avoid any accidental administration). 7. Never leave any **unlabeled syringe or infusion bag** in patient care area 8. **Appropriate resuscitation resources and reversal agents** are readily accessible and accompanied by a clear indication for when they should be used, their order of use, directions for administration near the point of use, and a protocol or coupled order set that permits emergency administration.
Prescribing	1. Only an **Anesthetist or practitioner trained in moderate-deep sedation** and advance life support, as determined by the organization, should prescribe these drugs 2. Prescribers are aware of routine and rare emergencies, their management, proper functioning of the resuscitative and monitoring equipment, patient monitoring and assessment parameters and coordination of staff roles before, during and after anesthesia. 3. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 4. Check **appropriateness & clarity** of order esp. dose, rate, route of administration. 5. Order/prescription must be **complete and non-ambiguous**: ☛ i.e. proper indication, patient's drug allergy status, weight as needed ☛ Drug name, dose, rate, route, frequency, dilution etc. ☛ Any special instructions ☛ **Never use abbreviations**: E.g. • Keta is not safe, always write full name "Ketamine" • Avoid naked decimals e.g. **.2mg** as it can be misread as **2mg** – always write **0.2 mg**. • Avoid trailing zero e.g. **250.0mcg** as it can be misread as **2500mcg** – always avoid trailing zero and write **250 mcg** • **Avoid using symbol for units** such as **50μg**, as it could be misread as **500**. Always write **50 mcg** or 50 microgram **Some important considerations while prescribing:**

	6. The physician planning anesthesia conducts a **Preoperative anesthesia evaluation** of the patient that is based on predefined criteria for assessment approved by the healthcare facility a. Preoperative anesthesia evaluation allows for obtainment of indicated laboratory tests, imaging procedures, or additional medical consultations when warranted. b. **Complete history** should be attained with attention to any new, ongoing, or worsening medical conditions, previous personal or familial adverse reactions to general anesthetics, assessment of functional cardiac and pulmonary states, and allergy and medication history. 7. During anesthesia and patient recovery, **supplemental oxygen and age-/size-appropriate equipment and medications that may be needed to RESCUE** or resuscitate a sedated patient are readily accessible, regardless of the location of the procedure or recovery 8. **Protocols and order sets exist and are used to RESCUE** a patient who has entered a higher level of anesthesia than intended 9. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#). 2. The drug name, dose, rate, route, frequency, dilution, duration of therapy must be carefully checked and ensure that the right medicine is ordered 3. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 4. **Check necessary info**, patient parameters (like allergy, weight, contraindications, renal function etc.) and drug parameters (dose, rate, route, concentration for infusion, duration, duplications, interactions etc.) during order/prescription review while dispensing 5. It is best practice to affix **caution stickers** / **auxiliary labels** while dispensing and storing these drugs (see storage section for detail) 6. **Double-check** the medication before dispensing 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration. Some additional error reduction strategies include:

	• Reading the label before any drug being drawn up or injected • Ensuring legibility and that label details meet agreed-upon standards • Always labeling syringes • Standardized and organized drug trays/workspaces in as many work locations as possible • Drug labeling should always be confirmed with an additional staff or through a barcode reader. • Use of drug library in smart infusion pumps 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Verbal order:** During a procedure, drug names and doses communicated verbally by the prescriber are read back (or repeated back, if conditions do not allow immediate transcription of the verbal order) to the prescriber for verification before administration 6. **Drugs dilution** shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label if not to be administered immediately. 7. **Any unused** (or hold, discontinued) anesthetic agents must be immediately returned to original stock or pharmacy or discarded as indicated 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or hospital surgical /procedure protocol 2. After the procedure, patients are **monitored in a recovery area** staffed with **practitioners who are trained** to monitor and recover sedated patients 3. **Predefined criteria** for adults (e.g., Aldrete Scoring System, Post-Anesthetic Discharge Scoring System), and for neonates and/or pediatric patients if applicable (e.g., ability to remain awake for at least 20 minutes in a quiet environment), exist to determine when a patient has approached a pre-sedation state and can be discharged from the facility or no longer requires post-procedure recovery monitoring. 4. A **longer period of monitoring** beyond meeting predefined criteria (as per point 3) is required for patients who have received a long-acting sedative and/or have an anatomical airway problem or underlying medical condition that might compromise blood pressure or ventilation (e.g., sleep-disordered breathing), or if the ability of the responsible adult to observe the patient after discharge is limited. 5. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 6. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)

Patient Education	1. Patients must be briefed about the procedure, pain control and possible risks before the procedure (informed consent to be taken as per organizational protocol where needed) 2. Patients who are discharged post-procedure are accompanied by a responsible adult who agrees to drive the patient home; and staff reasonably confirm that a responsible adult will be available to observe the patient for the remainder of the day. 3. Guidelines should be given anesthesiologist that patient should not have any food or drink after midnight on the day of your procedure. 4. Patient should be instructed not to use certain drugs before surgery. 5. Patient should have been instructed to take any of oral medications, with only a sip of water. 6. If a patient is a smoker, he should be informed to stop smoking for full day prior to surgery.

Ref:

1. Medication Safety in Anesthesia: Epidemiology, Causes, and Lessons Learned in Achieving Reliable Patient Outcomes, Cooper, R, 2019, https://journals.lww.com/anesthesiaclinics/fulltext/2019/05730/medication_safety_in_anesthesia__epidemiology,.9.aspx
2. Medication Safety in Anesthesia: Risks and Opportunities, Caitlin Aberle, https://nyschp.memberclicks.net/assets/docs/EventsEducation/webinar/NYSCHP%20January%20Webinar%20Anesthesia%20Medication%20Safety%20Grand%20Rounds%20-%20Caitlin%20Aberle.pdf
3. Medication safety in the operating room: literature and expert-based recommendations, J.A. Wahr, January 2017, https://www.bjanaesthesia.org.uk/article/S0007-0912(17)30113-7/fulltext
4. https://www.aegisanesthesiapartners.com/common-medications-used-anesthesia/
5. https://emedicine.medscape.com/article/1271543-overview#a2
6. https://www.uofmhealth.org/health-library/rt1592#:~: Monitoring
7. BNF Adult 73rd Edition
8. https://anaesthetists.org/Portals/0/PDFs/Guidelines%20PDFs/Guideline_storage_drugs_anaesthetic_rooms_2016 (Storage)
9. https://www.aarh.org/patient-education/

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10.4. Antiarrhythmics:

Why are these high alert?

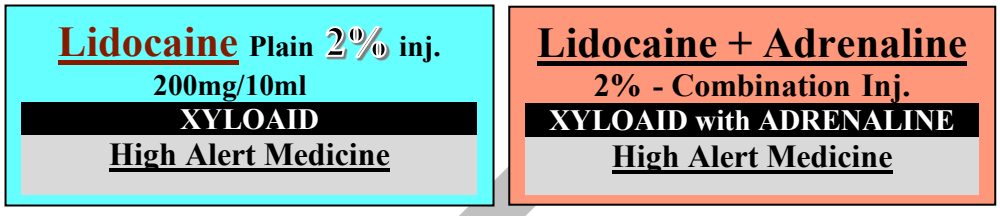
Although antiarrhythmic drugs remain the first and most frequently used approach to therapy for arrhythmias, there is growing concern about their safety. Organ toxicity may occur with some of these drugs. However, the most serious problems are cardiac side effects including conduction abnormalities, worsening of congestive heart failure, and aggravation of arrhythmia.

Antiarrhythmic drugs are drugs with a narrow therapeutic window, and there is a small plasma concentration interval between the lowest effective dose and the first toxic dose, that is, between undertreatment and the toxic or proarrhythmic effect.

Errors have been reported with antiarrhythmic drugs leading to serious patient harm. The main causes of errors include; toxicity due to wrong dose or rate of infusion, failure to properly monitor patient, serious drug-drug interactions or mix-ups between drugs that resulted in inadvertent administration of an antiarrhythmic drug.

How to Ensure Safe Use of Antiarrhythmic:

Antiarrhythmic: **Includes:** IV forms of Lidocaine (Lignocaine) and Amiodarone etc.*	
Storage	1. Primarily stored in the pharmacy 2. When in nurses' custody, must be stored in medication trolleys or patient medication cabinets under **authorized access only** 3. Availability of these drugs on floor stock of nursing or patient care units is **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance so that when needed in life saving condition it is immediately available e.g. in code trolleys/crash carts or emergency kits etc.) • **Standardize the quantity and strength** in all emergency kit/code trolley/crash carts across the healthcare facility • **Make dosing conversion charts available** that shows the dose as both 'mg' and 'mls' to be administered, corresponding to the age and/or weight of the patient in emergency situation • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of any of these medicines on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with Generic name of drug in **bold**, strength and labeled as "High Alert medication". 5. If any drug is **Look-Alike**, **sound-alike or read-alike** with another drug, its own strength or with its oral counterparts, use recommended techniques to properly

<table>
<tr>
<td></td>
<td>differentiate them e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc.
See the example below:
Suppose Lidocaine (plain) and Lidocaine + Adrenaline (combination) injections can be confused with each other, so labels the bins using colors and bold names as follows:
 

6. Identify combination products that contain adrenergic agonist like adrenaline (epinephrine) with local anesthetic e.g. Lidocaine + Adrenaline injection, and store them apart from plain adrenaline injections and plain lidocaine injections so that mix-up and wrong dispensing/administration can be avoided.
7. Identify different strengths of antiarrhythmic injections that can be confused with each other e.g. Lidocaine 1% inj. vs 2% injection. Reserve higher strengths for specific areas or indications only, and avoid dispensing the other strength in those area/cases (and vice versa).
• Avoid keeping multiple strengths in inventory/formulary to minimize risk of error.
8. Drugs discontinued or changed by doctor must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration)
9. Never leave any unlabeled syringe or infusion bag containing antiarrhythmics in patient care area</td>
</tr>
<tr>
<td>Prescribing</td>
<td>1. Must verify correct patient before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#)
2. Check appropriateness of order esp. dose, as per patient weight and other physiological conditions such as renal function.
3. Order/prescription must be complete and non-ambiguous:
o i.e. proper indication, patient’s drug allergy status, weight as needed
o Any special instructions
o Prescribe safely e.g.:
▪ Never use abbreviations/short forms like Epi or Norepi, write full name
▪ Avoid naked decimals e.g. .45mg as it can be misread as 45mg – always write 0.45 mg.
▪ Avoid trailing zero e.g. 2.0mg as it can be misread as 20mg – always avoid trailing zero and write 2 mg
▪ Avoid using symbol for units such as 5μg, as it could be misread as 50. Always write 5 mcg or 5 microgram
▪ Write infusion orders (dose expression (e.g. mcg/kg/min or mcg/mg/hr etc.), rate and diluent and concentration for infusion) very clearly and it is a best</td>
</tr>
</table>

	practice that prescribing should be standardized across the organization to avoid confusions ▪ When **titration of infusion** is required as per the target response, mention the **maximum (ceiling) dose** that can be reached. If patient is not giving adequate response on the defined maximum dose limit, the physician must be immediately informed ▪ It is a best practice to have a **pre-printed order form** for prescribing in critical care setting with necessary safety checks (to be filled by the doctor) 4. The **dose/rate calculation and titration** shall be done based on individual patient requirement and vital signs ➔ Note: Epinephrine is administered by **multiple routes** of administration. These may include IV, intraosseous (IO), intracardiac, IM, SC, endotracheal, intraocular routes, topical, and other routes. Routes of administration as well as dosages and rates of administration depend on clinical indications so very carefully write dose and clearly mention the route of administration ➔ 1 ampoule of NOREPInephrine (Noradrenaline) 4 ml contains 8 mg noradrenaline tartrate equivalent to 4 mg **NORADRenaline Base**. The dosing is based on the noradrenaline base so confusion must be avoided while prescribing and administration ➔ The **infusion should be gradually decreased** since abrupt withdrawal can result in acute hypotension. 5. **Standing orders**: specific orders to monitor patient's response to these drugs (like vital signs, cardiac output, cardiac rate, blood pressure etc.) must be clearly mentioned. 6. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check** patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. It is a best practice that pharmacy dispense these drugs in most **ready to administer form possible** esp. IV infusions 5. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing these drugs = **CAUTION HIGH ALERT MEDICINE** 6. **Double-check** the medication before dispensing 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to

	medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration ➔ 1 ampoule of NOREPInephrine (Noradrenaline) 4 ml contains 8 mg noradrenaline tartrate equivalent to 4 mg **noradrenaline base**. The dosing is based on the noradrenaline base so confusion must be avoided while prescribing and administration ➔ The **infusion should be gradually decreased** since abrupt withdrawal can result in acute hypotension. ➔ When **titration of infusion** is required as per the target response, mention the **maximum (ceiling) dose** that can be reached. If patient is not giving adequate response on the defined maximum dose limit, the physician must be immediately informed **Amiodarone infusion safety:** ➔ To prevent local reactions (phlebitis), **do not use concentrations exceeding 3 mg/ml** ➔ Repeated or continuous infusions via peripheral veins may lead to **local reactions (inflammation).** ➔ Whenever repeated or continuous infusions are intended, administration via a central line is recommended. ➔ **Central venous route** is preferable. If it is not readily available, **peripheral venous route**, using a large peripheral vein with a flow is very as important. Or possibly, by a slow injection over a minimum of 3 minutes, followed by administration of 200 ml of infusion fluid. Do not give other medicinal substances in the same syringe with amiodarone. Amiodarone can cause severe irritation of the vein, therefore adequate rinsing after bolus injection must be ensured. ➔ Due to the presence of benzyl alcohol, amiodarone intravenous administration is **contraindicated** in neonates, infants and children up to 3 years old. 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Inspect solution for injection** before administration. Do not use solutions that are pinkish to brownish in color, cloudy, or contain a precipitate or particulate matter 6. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. 7. **Check the infusion site** frequently for free flow. Avoid extravasation into the tissues to prevent local necrosis. If blanching along the course of the infused vein occurs, consider changing the infusion site at intervals to allow the effects of local vasoconstriction to subside 8. It is a good practice to have a **2nd check** for dose, route, dilution by another staff

	9. Infusion must always be given with **rate controlled device** to avoid accidental free flow of infusion 10. Never use **one patient's medicine on another** patient 11. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order review and before administering 12. **Verbal orders** must not be taken unless emergency or life threatening condition 13. **Any unused** (or hold, discontinued) high alert medicine must be immediately returned to original stock. 14. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or organization's policy • Vital signs, hemodynamic status, BP, pulse, cardiac output etc. • Inj. Amiodarone should only be used in a special care unit under continuous monitoring (ECG and blood pressure). 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Counsel family as and when indicated

Ref:

1. Antiarrhythmic drugs–clinical use and clinical decision making: a consensus document from the European Heart Rhythm Association (EHRA) and European Society of Cardiology (ESC) – 2018, https://academic.oup.com/europace/article/20/5/731/4846844#116518918
2. Wrong-Time Error With High-Alert Medication, 2016, https://psnet.ahrq.gov/web-mm/wrong-time-error-high-alert-medication
3. Amiodarone injection, emc, https://www.medicines.org.uk/emc/product/8739/smpc#gref

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.5. Antithrombotic agents / Anticoagulants / Thrombolytics:

Why are these high alert?

Anticoagulants and Thrombolytics are classified as high-alert medications, and if errors occur in dosing, monitoring or inappropriate administration, there is a real risk of **bleeding** ranging from minor bruises/bleed up to severe bleeding leading to death. However, on the other side if the dose is subtherapeutic, then there is a risk of clotting i.e. **thrombosis** which carries far greater risk of morbidity and mortality than hemorrhage. Therefore, a therapeutic balance is to be maintained and monitored closely to avoid any of the above grave consequences. Common mistakes that occur with this class of high alert medicines include: inadequate monitoring, failure to monitor effects of drug, failure to check duplications, omissions, failure to stop anticoagulants before procedure/surgery, overdose etc.

How to Ensure Safe Use of Anticoagulants/Thrombolytics:

<table>
<tr><td colspan="2"><u>Anticoagulants</u>
Includes: Warfarin (PO), Heparin (inj.), Enoxaparin (inj.), Fondaparinux (inj.), Rivaroxaban (PO), Apixaban (PO) etc.*

<u>Thrombolytics</u>
Includes: Alteplase (inj.) and Streptokinase (inj.) etc.*</td></tr>
<tr><td>Storage</td><td>1. Primarily stored in the pharmacy
2. When in nurses' custody, must be stored in medication trolleys or patient medication cabinets under authorized access only
3. Availability of these drugs on floor stock of nursing or patient care units is discouraged.
• Keep only if absolutely necessary (e.g. in case pharmacy is closed or at distance so that when needed in life-saving condition it is immediately available)
• Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC) of the hospital should authorize stocking of any of these medicines on patient care units (outside pharmacy)
4. When stored in pharmacy and/or at patient care unit floor stock, bins should be labelled with Generic name of drug in bold, strength and form (inj./tab) and labeled as "High Alert medication". See the example below:
HEPARIN 25000 UNITS/vial
INJECTION
<u>High Alert Medicine</u>
5. If any drug is sound-alike or read-alike with another drug, use tall-man lettering in order to correctly read/identify the drug name. See the example below:
Suppose Rivaroxaban and Abixaban are read-alike:</td></tr>
</table>

	rivaROXAban 10mg **TABLET** **High Alert Medicine** | **aPIXAban 5mg** **TABLET** **High Alert Medicine** 6. Usually, Heparin **vials can be saved and reused** for 28 days at room temperature once opened (refer to brand specific manufacturer's recommendations). • **Once opened:** always mention **date of opening, expiry/beyond use date**, patient name, MR# and staff initials on the label • **Discard** the leftover quantity when the expiry/beyond use date is reached 7. **Medicines discontinued or changed by a doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration) 8. **Never leave any unlabeled syringe or infusion bag** containing any anticoagulants or antithrombotic in patient care areas
Prescribing	1. Before starting therapy, perform **bleeding risk assessment** and check **contraindications** that can lead to severe bleeding (e.g. in-situ epidural catheter, active hematoma or bleeding, clotting disorder, drug allergy or serious drug-drug interaction etc.) 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. Check **baseline INR/APTT/Platelet count, Hb, Creatinine etc.** and repeat periodically while on therapy 4. Check **appropriateness** of order esp. dose, as per patient weight and other physiological conditions such as renal function. 5. Check if a patient is already on, or has received any **other anticoagulant**, antithrombotic or thrombolytic drug recently. • If yes keep appropriate gap as applicable, or discontinue one of these to avoid duplicate effect (leading to enhanced bleeding risk). • Also, if bridging is required b/w 2 anticoagulants, specify clearly in the prescription / order 6. It is a best practice to have a **pre-printed order form** for prescribing anticoagulants with these necessary safety checks (to be filled by the doctor) 7. These should **not** be ordered on **PRN/ need basis** 8. **Review the order** upon the availability of fresh INR / APTT (as per nomograms) and adjust dose as indicated (continue, hold temporarily or discontinue) 9. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Drug name, dose, route, frequency, duration of therapy • Anticoagulant orders should not stop unless purposefully kept on hold by doctor • Any special instructions (e.g. target INR or target APTT) • Never use abbreviations. E.g.: ▪ Heparin ***5000U*** intravenous infusion can be misunderstood as 50000. Therefore, write 5000 '**units'** and not 'U' –or-

	▪ Heparin *IV250* units can be misunderstood as **10250** or **14250** units; write "Heparin 250 units **IV** infusion" ▪ The abbreviation NoAC, NOAC, or No-AC (intended to mean novel or new oral anticoagulant, or non-vitamin K1 oral anticoagulant) is **not** used when referring to direct oral anticoagulants to avoid misunderstanding as "No anticoagulant." 10. The **dose/rate calculation and titration** shall be done based on individual patient requirement and lab value 11. **Intravenous Heparin Infusion** is sometimes indicated; the hospitals using infusion must have written protocol/nomogram in place and relevant doctors, nurses and pharmacists should be trained to safely use it. 12. **Standing orders**: it is highly recommended that the doctor mentions the following whenever these drugs are prescribed: • **Name of lab test**, how frequently to be repeated and what is the target level (for nursing staff, pharmacists and patients) • In case of bleeding, mention the **name, dose, route of reversal agent** (Vitamin K or Protamine etc.) to be used (for nursing staff) 13. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check necessary labs** (INR/APTT/PT), patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing • If INR/APTT is **high**, take necessary action to avoid bleeding (e.g. hold dose/drug after discussing with prescriber) • If INR/APTT is **low**, take necessary action to avoid thrombosis (e.g. increase dose or offer bridging therapy where indicated, after discussing with prescriber) 4. It is a best practice that pharmacy dispense these drugs in most ready to administer form possible esp. IV infusions 5. For patients already on anticoagulants, **review the previous orders/dose** whenever a fresh order is received so that accidental overdose/duplications can be prevented. Guide nurse and/or patient accordingly to avoid confusions 6. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing these drugs **CAUTION HIGH ALERT MEDICINE** 7. Double-check the medication before dispensing

	8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or the patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. 5. Never rub the sub-cut injection site after administration as it can result in hematoma 6. It is a good practice to have a **2nd check** for dose, route, dilution by another staff 7. Infusion must always be given with **rate controlled device** to avoid accidental free flow of infusion 8. Never use **one patient's medicine on another** patient (leftover or new) 9. **Check INR and APTT** result before and during administration as per doctor's orders 10. **Hold the dose** if a level is too high or if the patient starts to bleed. Restart only if and as ordered by doctor 11. **Timely administer the reversal agents** in event of bleeding as per doctor's (standing) orders 12. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 13. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary labs (INR/APTT/PT), patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order review and before administering 14. **Any unused** (or hold, discontinued) high alert medicine must be immediately returned to original stock. 15. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or nomogram 2. **Vital signs** are monitored as applicable and patient must be observed for any signs of over /under dose dosage (esp. **bleeding or thrombosis**) 3. **Blood specimens for INRs** are drawn at a standard time each day, enabling the results to be available before warfarin doses are prescribed

	4. The hospital provides stat **laboratory test results 24 hours per day and 7 days** per **week** to ensure safe and timely monitoring of antithrombotic therapy. 5. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 6. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	It is highly recommended that printed patient instructions, preferably in two languages (English and Urdu, or any local language) should be developed for anticoagulants in order to guide patients in a uniform manner. Patients must be educated about: Why these medicines are high alert and how patients can play their role in averting error/harm. The patient's role may include (but not limited to): 1. Knowing the **indication** for use 2. Know medicine **name and dose** they are taking 3. Exactly know **when to stop** the therapy and when not to 4. Able to identify the **color, shape of tablets/injections** they are using (to avoid wrong drug administration or purchase) 5. Know the **administration technique and timings** 6. Importance of **doing relevant lab tests** and cutoff limits 7. What to do in case **doses are missed** 8. What **foods or drugs to avoid** 9. Importance of **informing other healthcare professional** about being on anticoagulants, and also if undergoing a procedure. 10. Importance of **avoiding activities** that could lead to bleeding 11. What to do in case of **emergency** (e.g. overdose, bleeding or signs of thrombosis) 12. How to report if they experience any **serious side effect** 13. **Medication reconciliation** (taking past medication history and comparing with current medicines list) at the time of admission and discharge is recommended to avoid omissions/errors/duplication

Ref: *https://surveys.ismp.org/s3/2017-ISMP-Medication-Safety-Self-Assessment-for-Antithrombotic-Therapy*

**Medicines' availability status changes from time to time in the market, hence refer to the current registered and available products of this class in Pakistan*

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10.6. Anti-infectives

Why are these high alert?

Aminoglycosides (e.g. amikacin, gentamicin, streptomycin and tobramycin) and the glycopeptide antibiotic, vancomycin etc. may cause damage to hearing or the kidneys in a dose-related, type A adverse drug reaction. Individuals at particular risk are those with pre-existing renal impairment, older persons, obese individuals, patients with cystic fibrosis, neonates and children, particularly when high doses are administered. Since the major route of excretion of these medications is by filtration through the kidney, any nephrotoxicity caused by the medications can further reduce their renal clearance, resulting in a vicious cycle of increasing renal damage and reduced excretion of the offending agent.

Amphotericin B is used in the treatment of severe fungal infections and is available in several formulations. Lipid-based forms of the medication appear to have less severe toxicity, but the conventional form of the medication may be inadvertently substituted at an inappropriate dose, risking possible severe cardiotoxicity, including cardiorespiratory arrest. Conventional Amphotericin B can lead to acute kidney injury, electrolyte imbalance and severe infusion-related adverse reactions etc.

How to Ensure Safe Use of Anti-Infectives:

Anti-Infectives **Includes:** Vancomycin, Amphotericin B (Conventional as well as Liposomal), Aminoglycosides etc.*	
Storage	1. Primarily stored in the pharmacy 2. When in nurses' custody, must be stored in medication trolleys or patient medication cabinets under **authorized access only** 3. Availability of these drugs on floor stock of nursing or patient care units is **not recommended**. • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of any of these medicines on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with Generic name of drug in **bold**, brand, strength. 5. If any drug is **sound-alike or read-alike** with another drug, or its own strength or with its lipid-based formulation, use recommended techniques to properly differentiate them e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of auxiliary/colored labels etc.

	6. **Drug discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration) 7. **Never leave any unlabeled syringe or infusion bag** in patient care area 8. Vials of some of the anti-Infectives are **stable after opening** for certain time period (refer to manufacturer's recommendations for individual drug detail). • Such opened vials must be properly labeled with drug name, concentration (if reconstituted), date of opening, name/sign of staff and date of expiry. • Opened, labeled vials must be stored within defined temperature limits (room or refrigerator) as applicable to specific drugs • Opened vials must be discarded when their expiry date has reached.
Prescribing	1. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. It is recommended that these anti-infectives are prescribed and used as per **standard protocol or guidelines** defined by the organization including: • Dosing nomogram, route, frequency and duration of treatment as per the indications or criteria for use, including use in special population like neonates or pre-term babies • Special dosing protocols e.g. intraventricular use or continuous infusion etc. • Serum drug levels monitoring protocol where indicated and target serum level ranges • Adjusted doses in case of renal impairment and/or if patient is on hemodialysis etc. • Standard dilutions, diluent, rate for infusion and need of pre-medications (where applicable) to avoid infusion related adverse events • Protocol to manage infusion related adverse events • Required monitoring protocol (i.e. lab test e.g. serum creatinine, electrolytes, serum drug levels, and body function test like audiology etc.) to rule out or manage toxicity 3. Check **appropriateness** of order esp. dose, as per patient weight, other physiological conditions such as renal function, and follow the culture-sensitivity tests to guide about the choice of anti-infectives used 4. Order/prescription must be **complete and non-ambiguous**: o i.e. proper indication, patient's drug allergy status, weight as needed o Any special instructions o **Prescribe safely e.g.**: ▪ **Never use abbreviations/short forms** ▪ **Avoid naked decimals** e.g. **.5 mg** as it can be misread as **5mg** – always write **0.5 mg**. ▪ **Avoid trailing zero** e.g. **15.0mg** as it can be misread as **150mg** – always avoid trailing zero and write **15 mg** ▪ Most of these drugs can be administered via more than one routes e.g. IV, Intraventricular, Nebulization, Ophthalmic etc. carefully prescribe the respective doses and clearly mention the route of administration to avoid any error or confusion

	5. **Standing orders**: specific orders to be written to monitor patient's response to these drugs (like blood counts, culture reports, renal function, serum drug levels, fever etc.); including when and how frequently to be done 6. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check** patient parameters (like allergy, contraindications, renal function, weight, etc.) and drug parameters (dose, route, frequency, duplications, interactions, serum drug levels etc.) during order/prescription review while dispensing 4. It is a best practice that pharmacy dispense these drugs in most **ready to administer form possible** 5. **Double-check** the medication before dispensing 6. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Inspect solution for injection** before administration. Do not use solutions that are have discoloration, are cloudy, or contain a precipitate or particulate matter 6. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. • Concentration of infusion and rate of administration must not deviate from standard as it can lead to serious infusion related Adverse Events • Staff administering these drugs must be knowledgeable about the organization's guideline (see prescribing point # 2) on the use of anti-infectives 7. Never use **one patient's medicine on another** patient 8. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber

	• Otherwise, nursing staff to check necessary patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order review and before administering 9. **Verbal orders** must not be taken for anti-infectives 10. **Any unused** (or hold, discontinued) high alert medicine must be immediately returned to original stock. 11. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or organization's policy 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Counsel family as and when indicated

Ref:

Medication Safety in High-risk Situations Technical Report - World Health Organization 2019, https://apps.who.int/iris/bitstream/handle/10665/325131/WHO-UHC-SDS-2019.10-eng.pdf?sequence=1&isAllowed=y

**Medicines' availability status changes from time to time in the market, hence refer to the current registered and available products of this class in Pakistan*

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10.7. Cardioplegic agents

This is a Greek word where: *Cardio* means Heart and *-plegia* means Paralysis. Hence Cardioplegia is a pharmacological therapy administered during cardiac surgery to intentionally and temporarily arrest (stop) the heart. Cardioplegia is an essential component of cardiopulmonary bypass and with the primary goal to reduce myocardial oxygen demand by creating electrical quiescence and cooling the heart to reduce the ischemic effects of being on bypass. The use of cardioplegia, in addition to being cardioprotective, also provides a relatively bloodless and motionless surgical field.

Cardioplegic solution primarily exerts this function due to its high concentration of Potassium Chloride (which itself is a well-known high alert medication) and other high-risk components. Its incorrect use can lead to serious consequences and even patient death hence it is designated as a High Alert Medication. The risks involved are its inadvertent or wrong use, which can happen as a result of:

- Confusing product packaging (look-alike drugs)
- Wrong route of administration
- Insecure storage of drugs/open access to staff
- Not confining to only authorized staff related to cardiothoracic surgery (Perfusionist, Surgeon), etc.

How to Ensure Safe Use:

Cardioplegics include: Both commercially available ampules/vials and those compounded within a pharmacy	
Storage	1. Primarily stored in the pharmacy 2. **In surgical areas,** vials of concentrated potassium chloride or high-dose potassium **Cardioplegic solutions** are sequestered in sealed kits or locked storage areas, or placed in labeled lidded containers and obtained immediately before use; and once the procedure has been completed, there is an effective process in place to return unused products to their secure locations or dispose of the partially empty vials or bags ☛ Must be stored under **authorized access only** 3. Availability of Cardioplegics is only allowed under the following conditions: • **Cardiothoracic Surgery Operating Room** (under authorized staff access only i.e. perfusionist or cardiac surgeon etc.) • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize the stocking of Cardioplegics in the designated operating room(s)

	4. When stored in a healthcare facility, **bins should be labelled** with a generic name in **bold** and labeled as "High Alert Medication". 5. Cardioplegics (commercially available) **look-alike** with other commercially available injectable products: see picture below:  6. To avoid errors with **Look-Alike**, **sound-alike, or read-alike** appearance, use all possible recommended techniques for proper differentiation e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference, and use of auxiliary/colored labels, etc. ☛ Remember any accidental mix-up between these products **can lead to serious patient harm or death.** ☛ Each healthcare facility **must review the possible look-alike or sound-alike products** with that of Cardioplegic in particular (and other high alert medicines in general) in their stocks, to take proactive measures to prevent any accident and patient harm 7. **Leftovers** must be discarded immediately after the procedure, while **unused** vials/ampules must be returned to stock without any delays (to avoid any accidental administration) 8. **Never leave any unlabeled syringe or infusion bag** containing a Cardioplegic in the patient care area/theater
Prescribing & Use	1. The **perfusionist** is the main individual responsible for delivering Cardioplegic by keeping track of the flow rate, volume, temperature, components, and timing of each dose. o There is an important interplay between the cardiothoracic surgeon, anesthetist and perfusionist just prior, during, and coming off of bypass. o Prophylactic measures are taken to reduce the complications of Cardioplegia, such as frequent blood sampling by the perfusionist and notifying the surgeon and anesthesiologist of derangements while treating abnormalities as they present. 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. Check **appropriateness** of dose, rate, volume etc. as per patient weight and other physiological conditions and nature of procedure. 4. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.

Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check** patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. **If a Cardioplegic is compounded within pharmacy;** it must be done by trained staff under the supervision of a qualified pharmacist. The composition must be standardized and approved by the concerned authority (Cardiac Surgery). Calculation or compounding errors must be avoided by all means. All preparations must be done aseptically in designated area and labelled properly after preparation. 5. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing Cardioplegics **CAUTION HIGH ALERT MEDICINE** 6. **Double-check** before dispensing 7. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **check drug in hand** against drug name, strength before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Inspect solution for injection** before administration. Do not use solutions that are discolored, cloudy, or contain a precipitate or particulate matter 6. It is administered directly into the **coronary vessels** after the heart has been isolated from the systemic circulation • Prevent accidental administration in to systemic circulation 7. Never use **one patient's medicine on other** patient 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per surgeon's orders, cardiac surgery procedure or organization's policy: 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization.

	3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Not applicable

Ref:

1. Cardioplegia; Catalina et.al; https://www.ncbi.nlm.nih.gov/books/NBK554463/
2. Accidental systematic administration of 1 litre of cardioplegia solution during paediatric cardiac surgery; D F Newington, https://pubmed.ncbi.nlm.nih.gov/33937778/

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.8. Chemotherapeutic agents

Why are these high alert?

Chemotherapeutic Agents are defined a drug as "hazardous" based on its qualitative toxicity, including its carcinogenicity, mutagenicity, reproductive and developmental toxicity, or other acute toxicity /bleed up to severe bleeding leading to death. These drugs are nonselective in their action, in that they exhibit their effects in both cancerous and noncancerous cells in most organs and body tissues. Known effects in treated patients include hepatic and renal toxicity, cardiac toxicity, hematopoietic toxicity, pulmonary toxicity, immunotoxicity, ototoxicity, dermal toxicity, and particular injury to tissues with a rapid turnover rate.

How to Ensure Safe Use of Chemotherapeutic Agents:

<table>
<tr><td colspan="2">➔ Includes <u>all</u> dosage forms (i.e. parenteral, oral, ophthalmic, bladder instillation solutions etc.) of cytotoxic (chemotherapeutic) drugs
➔ Includes <u>both</u> indications i.e. <u>cancer</u> (like breast, colon, lung, blood cancers etc.) and <u>non-cancer</u> indications (like rheumatoid arthritis - RA, ectopic pregnancy, Systemic Lupus Erythematosus – SLE etc.)
<u>Some major drugs/classes are:</u>
• Alkylating agents: Nitrogen mustards such as Chlorambucil, Cyclophosphamide, Ifosfamide, Temozolomide etc.*
• Antimetabolites:5-fluorouracil (5-FU), 6-mercaptopurine (6-MP), Cytarabine, Capecitabine, Fludarabine, Gemcitabine, Methotrexate (MTX) etc.*
• Anthracyclines: DOXOrubicin, DAUNOrubicin etc.*
• Topoisomerase inhibitors: Topotecan, Irinotecan, Etoposide etc.*
• Plant alkaloids: Paclitaxel, Docetaxel, Vinca alkaloids such as vinBLASTine, vincristine etc.*</td></tr>
<tr><td>Storage</td><td>1. Primarily stored in the pharmacy
2. When in nurses' or physician custody, these must be stored in medication trolley or medication fridge as appropriate depending on the storage requirements of these drugs
3. Availability of these drugs on floor stock of nursing or patient care units is not recommended.
• Only Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC) of the hospital should authorize stocking of any of these drugs on patient care units (outside pharmacy)
4. When these drugs are stored in healthcare setting, storage bins should be labelled with name of drug in bold, strength, warning: "High Alert medication". Brand names can be used for reference purpose after the generic name. See the example below:</td></tr>
</table>

If any of these drugs are **sound-alike, read-alike or look-alike**, use tall-man lettering, highlight its strength, brand name, color or shape etc. in order to correctly read/identify the drug name.

Suppose **vinBLASTine** and **vinCRISTine** are read alike:

vinCRISTine	**vinBLASTine**
2mg/2ml	**10mg/vial**
High Alert Medicine	**High Alert Medicine**
Caution: Cytotoxic Drug	**Caution: Cytotoxic Drug**

7. Store both conventional and lipid based chemo drugs apart from each other and label the bins properly *(see lipid based drugs section for details)*
8. It is a good practice to paste **caution stickers** (High Alert Medicine – Caution Chemotherapy)

CAUTION HIGH ALERT MEDICINE

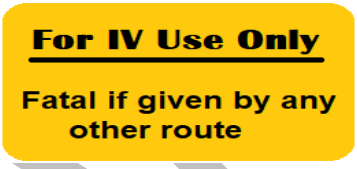
8. **Medicines discontinued or hold by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock immediately (to avoid any accidental administration).
9. Never leave any **unlabeled syringe or infusion bag** in patient care area
15. Cytotoxic agents should not be stored in close proximity with non-chemo drugs.
16. The **cytotoxic waste** should handle safely separate from routine (non-hazardous, non-infectious) waste as per the organizational guidelines
17. Personnel should be **educated** on the hazards posed by chemo drugs and trained in the use of Personnel Protective Equipment (**PPEs**), including a respirator for use in the event of breakage or a spill.
    - **Spill kits** must be readily available in the storage area, and all concerned personnel must be trained to perform spill cleanup.
    - The contents of spill kit must be **standardized** across the facility
    - Facility should have a written chemo/hazardous drugs handling, waste disposal and spill management **guidelines** and staff are **trained** accordingly.

18. The storage area must have appropriate **ventilation**.
19. Proper storage should be done to prevent accidental fall/drop and breakage of these drugs. Never keep breakable (glass) units close to the edge of racks/shelves, may use

<table>
<tr><td></td><td>deep bins to securely stock units. The baskets/trolleys used to carry the bulk stock of chemo must also be safe and able to prevent breakage or leakage.
20. Medicines discontinued or changed by doctor must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration)</td></tr>
<tr><td>Prescribing</td><td>1. Prescribing privileges of cytotoxics should be restricted to practitioners who are deemed qualified by the institution (e.g. through credentialing and privileging framework).
• The restriction should include prescribing for cancer as well as for non-cancer indications.
2. Informed consent is to be taken from patients prior to starting chemotherapy
3. Must verify correct patient before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#)
4. Check appropriateness & clarity of order esp. dose, rate, route of administration.
5. Order/prescription must be complete and non-ambiguous:
• i.e. proper indication, patient’s drug allergy status, weight as needed
• Drug name, dose, rate, route, frequency, dilution, duration of therapy
• Any special instructions
• Never use abbreviations: E.g.
o Cyclo 100mg IV is not safe, always write full name “Cyclophosphamide”
o Avoid naked decimals e.g. .2mg as it can be misread as 2mg – always write 0.2 mg.
o Avoid trailing zero e.g. 250.0mcg as it can be misread as 2500mcg – always avoid trailing zero and write 250 mcg
• If an acronym is used to identify the chemotherapy protocol, the acronym is defined in the order, and each medication is prescribed individually, with the dose and schedule designated for each.
o For example: CMV for bladder cancer is defined as CISplatin 100 mg/m2/day on Day 2, methotrexate 30 mg/m2/day on Day 1 and Day 8, vinBLAStine 4 mg/m2/day on Day 1 and Day 8.)
• Drug doses should be expressed clearly in terms of amount to be taken per dose/per day to prevent misinterpretation.
o E.g. oral chemotherapy doses to be described as amount of medication to be taken per dose and not as total daily dose, in divided doses; see example below, intended dose is 200mg 3 times a day:
<table><tr><th>Correct ✓</th><th>Incorrect ☒</th></tr><tr><td>Drug XYZ
Dose = 200mg every 8hrly</td><td>Drug XYZ
Dose = 600mg daily, q8rly</td></tr></table>o Chemotherapy drugs for specific days are written explicitly: E.g., orders should be written as “Day 1, 2, 3,” and never as “Days 1-3,” which can be misunderstood as days 1 and 3;</td></tr>
</table>

	And: orders are written as "Daily for 21 consecutive days and stop for 7 consecutive days," and never as "Days 1-21, stop for Days 22-28"). ○ **Prescribing total chemotherapy doses for whole, entire cycle is not allowed:** E.g., order for 400 mg/m2 on day 1, 2, 3, and 4, **not** as: 1,600 mg/m2 over 4 days; or fluorouracil 750 mg/m2 continuous infusion on day 1, 2, 3, 4, and 5, **not** 3,750 mg/m2 continuous infusion over 5 days • It is a universal safe practice that prescribers **include the patient-specific dose and the mg/kg, mg/m^2, units/m^2, AUC**, or other dosing method used to calculate the patient-specific dose for all chemotherapy orders E.g., for a 1.67 m^2 patient: 240 mg/m^2; dose = 400 mg 6. It is best practice that calculated chemotherapy doses with a decimal point that are less than 10 mg are **rounded** to the nearest tenth, and doses greater than or equal to 10 mg are rounded to the closest whole number 7. **Standardized regimen**: specific medication order forms should be developed and employed for medication prescribing. They can decrease potential errors by organizing treatment information in a clear, consistent and uniform format. 8. **Electronic prescribing systems** i.e. computerized prescriber order entry (CPOE) should be implemented where possible to further enhance the adjust dose as indicated (continue, hold temporarily or discontinue) safety of cytotoxic prescriptions. This will help eliminate interpretation errors from illegible handwriting, enable standardization of orders involving cytotoxics, control user access to restrict prescribing to specific specialties/designations and provide additional safety checks that are not possible with paper orders 9. **Standing orders**: it is highly recommended that doctor mention the following whenever these drugs are prescribed: • **Name of lab or diagnostic test** (e.g. electrolytes, serum creatinine, LFTs, serum drug levels, Echo etc.) ○ When to be done, how frequently to be repeated and what is the target level • Complete and clear orders for **Pre-chemo drugs**, **chemo adjuvants**, required **hydration** and **rescue agents** as indicated 10. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing and Preparation	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. The drug name, dose, rate, route, frequency, dilution, duration of therapy must be carefully checked and ensure that the right medicine is ordered 3. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 4. **Check necessary info**, patient parameters (like allergy, weight, height, BSA, AUC, contraindications, renal function etc.) and drug parameters (dose, rate, route,

concentration for infusion, duration, duplications, interactions etc.) during order/prescription review while dispensing
    - A system is in place (electronic or manual) to document, track, and communicate the lifetime cumulative dose of chemotherapy as appropriate (e.g., anthracyclines, bleomycin).
5. It is highly recommended that all chemo drugs are premixed, diluted and dispensed in ready-to-use form by pharmacy
    - Chemotherapy is prepared, dispensed, and administered only within facility-**defined timeframes** when adequate resources and trained staff are available to review the order, assess the patient, prepare and check the chemotherapy, and administer the chemotherapy without feeling rushed
    - The **total volume** to be infused is expressed on the pharmacy label
    - **vinCRIStine** is dispensed in a minibag of a compatible solution (e.g., 25 mL for pediatric patient, 50 mL for adults); and vinCRIStine doses are **never** dispensed and/or administered in a syringe
    - Vinca alkaloids and bortezomib are dispensed with a prominent warning label that reads: **FOR INTRAVENOUS USE ONLY—FATAL IF GIVEN BY OTHER ROUTES**



6. All **mixing and preparation** of cytotoxic drug (any dosage form) should be performed in one centralized area in a specially designated class II, type B biological safety cabinet that is exhausted through a hepa (high-efficiency particulate air) filter to the outside atmosphere in a manner that prevents recirculation into any inside area.
    - Type B biological safety cabinet should be equipped with a continuous monitoring device to permit confirmation of adequate airflow and cabinet performance.
    - Biological safety cabinets should remain in operation 24 hours per day, 7 days per week, as recommended by the manufacturer
7. Prepared cytotoxic drugs should be placed in a closed, leak-proof plastic bag (e.g. Ziploc type plastic bag) for safe transportation and to contain any leaks, if happens

8. **Proper PPEs** must be worn and changed regularly as per the institutional guidelines
9. **Aseptic techniques** must be followed while preparing sterile chemo drugs

	10. For dispensing of **oral chemo for outpatient setting,** the number of tablets/capsules dispensed should be the exact quantity required for a single cycle of treatment. (Additional quantity (whole pack size) should not be dispensed) 11. It is best practice to affix **caution stickers** / **auxiliary labels** while dispensing and storing these drugs (see storage section for detail) 12. **Double-check** the medication against physician order before dispensing 13. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against the doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. Before administering chemotherapy, a nurse conducts and documents (e.g., with initials or electronically) an INDEPENDENT DOUBLE CHECK of the prescriber's dosing method (e.g., mg/kg, mg/m2, units/m2, or AUC) and calculated dose as per the protocol or treatment plan, using the patient's BSA, weight, or AUC. 6. **Verbal order:** must never be taken for chemo drugs except to hold or discontinue chemotherapy. 7. **Maintain most current/recent** Weight, height, body surface area and drug allergies status in the patient record 8. **Drugs dilution** in wards shall be done by a trained pharmacist /nursing staff and concentration with date, time of preparation is mentioned on the label. 9. In areas in which chemotherapy drugs are administered must have the following equipment available and routinely checked, where appropriate, to ensure suitability (e.g. within expiry date) and function: o Resuscitation equipment o Drugs for the management of emergencies – cardiac arrest and anaphylaxis o Extravasations kit o Cytotoxic spillage kit o Access to running water (to wash accidental exposure) o Disposal equipment e.g. appropriate sharps bins o Copies of relevant policies and guidelines 10. **Any unused** (or hold, discontinued) chemo must be immediately returned to original stock or pharmacy – or discarded as per hospital policy **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. During chemotherapy administration, monitor the patient's ability to tolerate hydration regimens, electrolyte abnormalities, possible tumor lysis syndrome, control

	of nausea, vomiting, and other acute side effects via patient interview and routine monitoring of chemicals and vital signs. 2. Monitor for phlebitis or signs of extravasation 3. Common side effects of chemotherapy are hematological, such as anemia, thrombocytopenia, and neutropenia. OPSs can monitor absolute neutrophil counts and platelet and hemoglobin levels to assure blood parameters are within acceptable limits for the next cycle of chemotherapy. 4. Patients may need IV support or nutritional support during or between cycles of chemotherapy, due to nausea/vomiting, prolonged mucositis, enteritis, diarrhea, significant weight loss, cancer cachexia, and dysgeusia. 5. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 6. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Patients must be educated about: 1. New chemotherapy patients with a review of all the **patient's medications**, including prescriptions, over-the-counter, vitamins, alternative therapy, and herbal products, for drug–drug interactions, duplicate therapy, and potential side effects 2. Counseling can also include **patient expectations** at clinic visits, education on adverse effects, compliance with supportive care medications, and any lifestyle modifications, such as contraception, diet, and fall-prevention precautions. 3. Patients may also need education on proper **handling and storage of oral agents**. Medication-information brochure is provided that guides about **limiting exposure** of care-giver by using non-absorbable gloves, aprons, and how to dispose of hazardous waste including patient's excreta (vomit/urine/stool) and soiled linen/clothes etc. 4. Patients should be advised to **avoid crushing or manipulating the dosage form** without consulting an oncology Physician or pharmacist. Importance of **doing relevant lab tests** during chemotherapy.

Ref:

1. https://www.ismp.org/sites/default/files/attachments/2018-01/EntireAssessmentWorkbook.pdf: ISMP Medication Safety Self-Assessment ® for High-Alert Medications - 2017
2. Safe handling of cytotoxics: guideline recommendations (nih.gov) (Dispensing and preparation) safe-handling-chemotherapy-drugs.pdf, national-guidelines-on-high-alert-medications.pdf
3. safe-handling-chemotherapy-drugs.pdf, https://www.england.nhs.uk/mids-east/wp-content/uploads/sites/7/2018/04/guidelines-administration-chemotherapy-for-malignant-disease-v2-1-0.pdf (Administration)
4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4324350/ (Dispensing &Preparation)
5. https://www.dovepress.com/role-of-pharmacists-in-optimizing-the-use-of-anticancer-drugs-in-the-c-peer-reviewed-fulltext-article-IPRP (Monitoring, patient education)

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.9. Dextrose hypertonic 20% and above

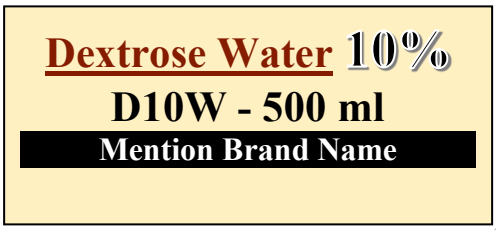
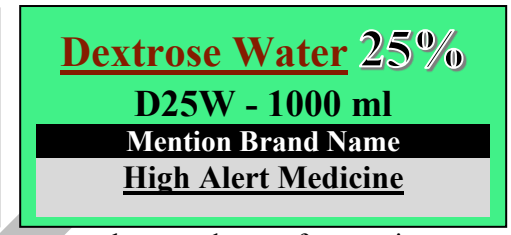
Glucose 20% and above concentrations are hypertonic solutions (*in vitro tonicity*) which provide source of calories in a minimal volume of water. In Pakistan, Dextrose water 25% (commonly called D25W) is available, so the same will be referred for details (unless more hypertonic strengths become available in the future).

D25W is frequently used in both adults and children to restore blood glucose concentrations in the treatment of hypoglycemia resulting from insulin excess, or other causes. D25W is frequently used in the parenteral nutrition as a source of carbohydrates. It may also be used to provide temporary relief from the symptoms of cerebral edema and from hypoglycemic coma. Hyperosmotic Glucose with or without insulin may also correct hyperkalemia in renal failure.

Hypertonic Dextrose Injection 20% and above is a high alert medication because of its accidental substitution for lower Dextrose solutions and the potential harm associated with rapid infusion including fluid overload, altered electrolytes, congested states and pulmonary edema.

How to Ensure Safe Use of Dextrose 20% & above:

Dextrose water 20% and above **Includes:** Dextrose water 25% 25ml vials and infusion bottles of 500-1000ml etc.*	
Storage	1. Primarily stored in the pharmacy 2. When in nurses' custody, must be stored in medication trolleys or patient medication cabinets under **authorized access only** 3. Availability of D25W on floor stock of nursing or patient care units is generally **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance so that when needed in life saving condition it is immediately available e.g. when urgent reversal of hypoglycemia is intended.) • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of D25W on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with Generic name and strength in **bold** and labeled as "High Alert medication". 5. D25W can be confused with other strengths of Dextrose containing infusions such as Dextrose 5% or 10% etc. Or smaller vials of 20-25ml can be confused with vials of other products like Normal Saline, Sodium Bicarbonate or Potassium chloride etc., available in similar pack size. Efforts must be done to avoid accidental substitution or mix-ups between these products. 6. To avoid errors with **Look-Alike**, **sound-alike or read-alike** appearance, use recommended techniques for proper differentiation e.g. tall-man lettering, bold

	labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc. See the example below: Suppose **Dextrose 10%** and **Dextrose 25%** can be confused with each other, so labels the bins using colors and bold names as follows:   7. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration) 8. **Never leave any unlabeled syringe or infusion bag** containing hypertonic dextrose in patient care area
Prescribing	1. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Check **appropriateness** of order esp. dose, as per patient weight and other physiological conditions such as glucose level and calorie requirements. 3. Order/prescription must be **complete and non-ambiguous**: o i.e. proper indication, patient's drug allergy status, weight as needed o Any special instructions o **Prescribe safely e.g.**: ▪ **Never use abbreviations/short forms** like DW, write full name and strength "Dextrose water 25%" ▪ **Avoid naked decimals** e.g. **.1 gm** as it can be misread as **1 gm** – always write 0.1 gm. ▪ **Avoid trailing zero** e.g. **2.0 gm** as it can be misread as **20 gm** – always avoid trailing zero and write **2 gm** ▪ **Write infusion orders very clearly** (dose expression e.g. gm or ml per min or gm or ml per hour etc., rate and duration for infusion) and it is a best practice that prescribing should be standardized across the organization to avoid confusions ▪ **D25W prescribed as a part of parenteral nutrition;** please read the section on Total Parenteral Nutrition for details 4. The **dose/rate calculation and titration** shall be done based on individual patient requirement blood sugar levels 5. **Standing orders**: specific orders to monitor patient's response to dextrose 25% (like vital signs or blood glucose levels etc.) must be clearly mentioned. 6. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.

Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check** patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing hypertonic dextrose **CAUTION HIGH ALERT MEDICINE** 5. **Double-check** before dispensing 6. **D25W prescribed as a part of parenteral nutrition;** please read the section on Total Parenteral Nutrition for details 7. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Inspect solution for injection** before administration. Do not use solutions that are discolored, cloudy, or contain a precipitate or particulate matter 6. **Drugs dilution** in wards shall be done by a trained nursing staff using aseptic techniques. Mention concentration with date, time of preparation on the label. 7. It is a good practice to have a **2nd check** for dose, route, dilution by another staff 8. The **maximum rate** at which dextrose can be infused without producing glycosuria is 0.5 g/kg of body weight per hour (usual range; 0.24-0.36 gm/kg/hr) 9. When concentrated dextrose infusion is **abruptly withdrawn**, it is advisable to follow with the administration of 5% or 10% dextrose to avoid rebound hypoglycemia. 10. Dextrose solution with concentration higher than 12.5% **should be administered via central line** 11. Concentrated dextrose solutions **should not be administered subcutaneously or intramuscularly.** 12. **Check the infusion site** frequently for free flow. Avoid extravasation into the tissues 13. Infusion must always be given with **rate controlled device** to avoid accidental free flow of infusion

	14. Never use **one patient's medicine on another** patient 15. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order review and before administering 16. **Verbal orders** must not be taken unless emergency or life threatening condition 17. **Any unused** (or hold, discontinued) high alert medicine must be immediately returned to original stock. 18. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or organization's policy • Vital signs, blood glucose level etc. • Electrolyte deficits, particularly in serum potassium and phosphate, may occur during prolonged use of concentrated dextrose solutions. Blood electrolyte monitoring is essential, and fluid and electrolyte imbalances should be corrected. Essential vitamins and minerals also should be provided as needed. 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Counsel family as and when indicated Inform patients, caregivers, or home healthcare professionals of the following risks of Dextrose Injection: • Hyperglycemia and hyperosmolar hyperglycemic state • Hypersensitivity reactions • Risk of infection • Vein damage and thrombosis • Fluid overload and electrolyte imbalance

Ref:

1. https://www.pfizer.ca/sites/default/files/201711/2017.09.21_Dextrose_PS_E_205097.pdf (storage)
2. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/017521s069lbl.pdf (prescribing & patient education)
3. https://www.icumed.com/media/8137/en-2527.pdf (administration &monitoring)

4. https://www.medicoverhospitals.in/medicine/dextrose

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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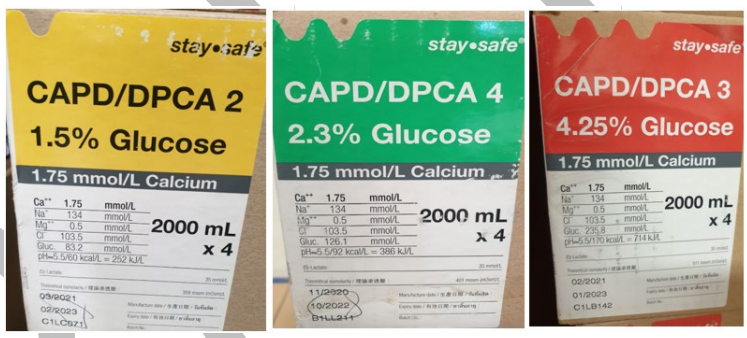
10.10. Dialysis solutions

- **Hemodialysis** removes small solutes (potassium, blood urea nitrogen [BUN], creatinine, etc.) from patients, using a system in which the patient's blood is pumped through a semipermeable membrane (the dialyzer) and the dialysis solution (dialysate) flows countercurrent to the blood, resulting in the movement (diffusion) of solutes.
- **Peritoneal dialysis** is a type of dialysis that uses the peritoneum in a person's abdomen as the membrane through which fluid and dissolved substances are exchanged with the blood.
- **Dialysis fluids** are solutions of electrolytes, glucose, amino acids formulated in concentrations similar to those of extracellular fluid or plasma. They are either intended for hemodialysis (HD) or peritoneal dialysis (PD).

Potential sources for errors exist throughout dialysis, including contamination of the dialysate and/or the water used to make the dialysate, use of an incorrect dialysate for a given patient, ill-fitting lines connecting the dialyzer, dialyzer leaks, and issues with the patient's access (arteriovenous fistula, graft, or venous catheter), Hemolysis, the transmission of infection, and the accumulation of toxins have all been reported. In some cases, incorrect dialysis solution or contaminated water was the source of the adverse event; in others, human error contributed. Also to note that both HD and PD solutions come in different strengths and compositions, therefore caution is exercised to ensure use of correct solution/strength to avoid patient harm.

How to Ensure Safe Use of HD and PD solutions:

Dialysis solutions include*: **HD solution**: Hemodialysis concentrate, and Hemodialysis concentrate Low Potassium **PD solution**: PD 1.5% Dextrose, PD 2.3% Dextrose, PD 4.25% Dextrose	
Storage	1. Primarily stored in the pharmacy 2. When in patient care unit, must be stored in **authorized access only** 3. Availability of dialysis solutions on floor stock of nursing or patient care units is **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance. Or in main dialysis unit) • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of dialysis solutions on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with name and strength in **bold** to avoid mix-ups. 5. To avoid errors with **Look-Alike**, **sound-alike or read-alike** appearance against any other drug available in the inventory, use recommended techniques for proper

	differentiation e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc. See the example below: ☛ Normal and low potassium solutions should be kept apart to avoid mix-ups and wrong dispensing or usage  ☛ PD Solutions may be available in differently colored labels, the same should be used as a second check to avoid wrong drug use and/or dispensing  6. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration)
Prescribing	1. To be **prescribed by** physicians with nephrology training 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. It is recommended that Dialysis (HD or PD) as a procedure, is conducted as per **standard protocol or guidelines** defined by the organization including the safe handling and use of dialysis solutions ☛ The potential for adverse events and medical errors in dialysis units is high due to the procedure itself, the need for medications, the risk for falls, risk of infection/contamination and the comorbidities of the patient population etc. 4. Ensure **appropriateness** of order as per patient age, weight, other physiological conditions like serum electrolytes and fluid status etc. 5. Order/prescription must be **complete and non-ambiguous** 6. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.

Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check** patient parameters (like allergy, contraindications, renal/hepatic function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing dialysis solutions **CAUTION HIGH ALERT MEDICINE** 5. **Double-check** before dispensing 6. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Before administration always **check solution in hand** against name and strength prescribed 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Not to be administered by IV route** 6. Never use **one patient's solution on another** patient 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. **Resuscitation equipment**, supplemental oxygen must be readily accessible wherever dialysis is being performed 2. After dialysis sessions, hemodynamic shifts can lead to transient hypotension (low blood pressure) and dizziness. The **fall risk** in hemodialysis patients is higher than in the general population. Assessment of fall risk, exercise programs to increase muscle strength, reducing the use of neuropsychiatric medications, and avoiding hypotension in dialysis patients may all reduce fall risk 3. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 4. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future

	(Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Patients receive verbal and up-to-date written information at an appropriate reading level and in their preferred language about their dialysis procedure, types, risks, purpose, do's and don'ts to ensure they remain in best of their condition (especially in case of home dialysis, patients should be adequately educated in both written and verbal form)

Ref:

1. Renal Association Clinical Practice Guideline on Haemodialysis; https://bmcnephrol.biomedcentral.com/articles/10.1186/s12882-019-1527-3
2. National Kidney Foundation; https://www.kidney.org/atoz/content/dialysisinfo (patient education)
3. Dangerous Dialysis, Jean L. Holley, 2010, https://psnet.ahrq.gov/web-mm/dangerous-dialysis
4. Maintaining Safety in the Dialysis Facility, Alan S. Kliger, 2015, https://cjasn.asnjournals.org/content/10/4/688

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.11. Epidural & Intrathecal

- An **epidural** is a procedure that involves injecting a medication either an anesthetic or a steroid etc. into the space around spinal nerves known as the epidural space.
- **Intrathecal administration** is a route of administration for drugs via an injection into the spinal canal, or the subarachnoid space so that it reaches the cerebrospinal fluid (CSF) (also referred to as neuraxial block or neuraxial anaesthesia)

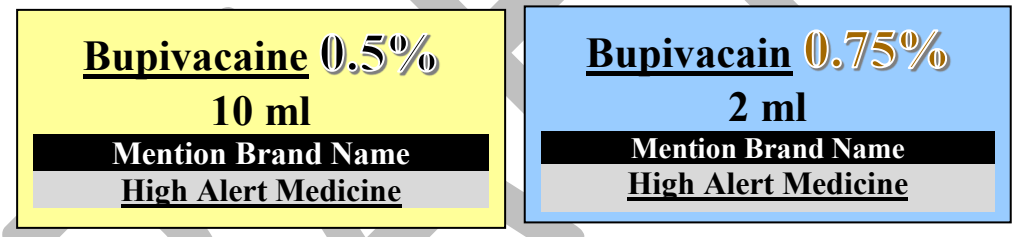
Several risks have been associated with Epidural/Intrathecal injections and infusions, particularly the wrong route of administration. The most common errors include: erroneous infusions of epidural medications particularly epidural infusions containing bupivacaine by the intravenous (IV) route of administration. The administration of IV bupivacaine can quickly lead to cardiotoxicity. A boxed warning for bupivacaine notes that it can cause significant disturbances in cardiac rhythm and contractility that are resistant to typical resuscitation efforts. Thus, making these drugs mix-ups particularly deadly. Likewise, medications intended for IV administration particularly morphine and vincristine etc. have been accidentally given via the epidural or intrathecal route, also leading to fatal outcomes.

☛ Hence extreme caution is to be exercised and procedures should be in place to safeguard against the accidental administration of IV drugs by the epidural/Intrathecal route and the administration of epidural/ Intrathecal drugs by the IV route.

Unlike many unavoidable threats to patient safety, those involving epidural–IV mix-ups are well understood and can be prevented by IV and epidural syringe and tubing connections incompatible with each other. In addition to this we encourage all staff members to evaluate the risks in their organizations and to implement safety procedures.

How to Ensure Safe Use of Epidural/Intrathecal (Neuraxial) Drugs:

Neuraxial Drugs include: This includes continuous infusions of epidural analgesia/anesthesia with opioids and/or local anesthetics (including epidural PCA); single injections of epidural or intrathecal opioids and/or local anesthetics; and combination intrathecal injection and epidural continuous infusion. Examples of neuraxial opioids include: morphine, fentanyl. Examples of neuraxial local anesthetics include: bupivacaine, ropivacaine, lidocaine. **Note**: For intrathecal chemotherapeutics; please refer to the concerned section on chemotherapeutic agents	
Storage	1. Primarily stored in the pharmacy 2. When in nurses' custody, must be stored in medication trolleys or patient medication cabinets under **authorized access only**

	3. Availability of neuraxial drugs on floor stock of nursing or patient care units is generally **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance. Or in procedure areas or operating rooms where such administrations are commonly done) • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of neuraxial drugs on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with Generic name and strength in **bold** and labeled as "High Alert medication". 5. To avoid errors with **Look-Alike**, **sound-alike or read-alike** appearance against any other drug available in the inventory, use recommended techniques for proper differentiation e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc. See the example below: Suppose **Bupivacaine** is available in different strengths, and can be confused with each other, so labels the bins using colors and bold names as follows:  6. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration) 7. **Never leave any unlabeled syringe or infusion bag** containing these drugs in patient care area
Prescribing	1. To be **prescribed by a senior physician** trained and knowledgeable about the dosing, monitoring protocol and safety concerns associated with epidural/intrathecal drugs 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. It is recommended that neuraxial drugs are prescribed and used as per **standard protocol or guidelines** defined by the organization including: o When appropriate and available, agents for epidural administration that may be **less cardiotoxic** than bupivacaine, such as ropivacaine o How to identify and treat **local anesthetic toxicity or opioid overdose**. o Dosing regimens for neonates and pediatric patients are adapted for age and weight with **maximum doses** clearly defined in protocols to minimize the risk of cumulative opioid and local anesthetic toxicity o **Patient monitoring parameters**, frequency and procedure for emergency resuscitation

	○ Placement of epidural/intrathecal **lines** and their **clear demarcation** from that of other systemic (IV) lines ○ **Labelling of infusion bags/syringes** containing neuraxial agents to highlight the route of administration "Epidural" or "Intrathecal" ○ **Protocol for anticoagulants** while patient is on epidural drugs (to prevent spinal hematoma) ○ Restriction to use other pain medications, central nervous system (CNS) depressants, or epidural drugs without the consent of an anesthesia practitioner 4. Check **appropriateness** of order esp. dose, rate of administration, as per patient age and weight, other physiological conditions such as renal/hepatic function 5. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Any special instructions • **Prescribe safely e.g.**: ○ **Clearly write route of administration** ○ **Never use abbreviations or short forms.** E.g. **"**Bupi" or "IT": write full form i.e. 'Bupivacaine' or 'Intrathecal' ○ **Avoid naked decimals** e.g. **.5 %** as it can be misread as **5%** – always write **0.5 %** ○ **Avoid trailing zero** e.g. **5.0ml** as it can be misread as **50ml** – always avoid trailing zero and write **5 ml** 6. **Standing orders**: specific orders to be written: • To monitor patient's response to these drugs (see monitoring section); including when and how frequently to be done. • When to hold infusion • When and how to use rescue agents in case of serious adverse reactions/toxicity 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. It's a good practice that all epidural/intrathecal drugs are prepared by pharmacy and dispensed in most ready-to-use form possible ○ **Preparations** must be done by trained staff under supervision of qualified pharmacist. Medicines are prepared aseptically in designated area and labelled properly before dispensing. Calculation or compounding errors must be avoided by all means ○ All bags and syringes of neuraxial opioids and/or local anesthetics, and their overwraps if applicable, are **labeled with a prominent** auxiliary warning

	(e.g., For Epidural Use Only; For Intrathecal Use Only) in a large font size (e.g., greater than 20 point) on both sides of the bag or syringe.  ○ The pharmacy dispenses epidural infusions with an **epidural administration set/tubing** or connects the epidural tubing to the bag prior to dispensing the infusion. ○ **Intrathecal drugs** should be dispensed in overwraps that help differentiate these syringes and bags from other drugs intended for IV administration. 4. **Check** patient parameters (like allergy, contraindications, renal/hepatic function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 5. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing neuraxial drugs **CAUTION HIGH ALERT MEDICINE** 6. **Double-check** before dispensing 7. In **low-volume-use areas**, the epidural agent should be dispensed immediately before it is used, and the drug should be handed to an authorized clinician. 8. In **high-volume-use areas** (e.g., labor and delivery), the epidural medication should be immediately placed in the appropriate storage location. ☛ Epidural drugs should not be left in medication rooms for the clinical staff to put away, and they should not be sent in pneumatic tubes to the units. 9. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. **Equipment** used for neuraxial drugs insertion and infusion (infusion pumps (including syringe pumps) is standardized throughout the facility so that it is familiar to all practitioners administering or supervising administration. • **Dual-channel infusion pumps** are <u>not</u> used for simultaneous administration of IV and epidural infusions. • Infusion pumps used to administer medications and solutions via different routes of administration (e.g., IV and epidural) are <u>not</u> stacked on the **same pole.** • Placing IV pumps and epidural pumps on **opposite sides of the patient's bed** can help maintain the separation of the two infusion systems 2. Administration sets with **yellow-striped tubing** and without injection ports are used for all epidural infusions, and not for any other purpose; ☛ A tube or catheter should always be traced from the patient to the point of origin. End of the tubing closest to the patient is clearly labeled "Epidural.

	3. Epidural infusion lines and central venous access **lines are secured on opposite sides** of the patient's back or chest 4. All bags and syringes of neuraxial opioids and/or local anesthetics, and their overwraps if applicable, are labeled with a **prominent auxiliary warning** (e.g., For Epidural Use Only; For Intrathecal Use Only) in a large font size (e.g., greater than 20 point) on both sides of the bag or syringe. • The epidural and IV bags in the pumps should **always be hung with the labels facing out** so that they can be read. Pharmacy labels should be applied to accommodate loading syringes or bags in a pump with the labels facing out. 5. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 6. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 7. Always **check drug in hand** against drug name, strength before administration 8. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 9. An **independent double-check** is important at the bedside of all individuals receiving epidural medications and IV opioids to verify the patient, pump settings, line attachment, drug, dosage, and concentration. • The receiving nurse and the transferring nurse should be required to verify pump settings and line attachments during shift changes and patient transfers 10. Never use **one patient's medicine on other** patient 11. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. **Resuscitation equipment**, supplemental oxygen, and naloxone are readily accessible wherever neuraxial opioids and/or local anesthetics are administered; and the **naloxone** is accompanied by clear indications for when it should be used, directions for preparation and administration near the point of use, and a protocol or coupled order set that permits emergency administration • **Lipid emulsion** is readily accessible wherever neuraxial opioids and/or local anesthetics are administered; and the lipid emulsion is accompanied by clear indications for when it should be used, directions for administration near the point of use, and a protocol or coupled order set that permits emergency administration. 2. **Patients receiving a neuraxial opioid or a local anesthetic/opioid combination** are monitored at defined frequencies for the following: level of sedation; pain score; degree of motor or sensory block (if applicable); adequacy of ventilation (e.g., respiratory rate, depth and quality of respirations, capnography); pulse rate; and blood pressure (or as defined in organizational protocol) 3. **Patients receiving neuraxial local anesthetics (without an opioid)** are monitored at defined frequencies for the following: pain score; degree of motor or sensory block; adequacy of ventilation (e.g., respiratory rate, depth and quality of

	respirations); pulse rate; and blood pressure. (or as defined in organizational protocol) 4. **Fetal heart rate** patterns are monitored at facility-defined frequencies by a qualified practitioner immediately before, during, and after administration of neuraxial analgesia during labor and delivery. 5. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 6. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Patients receive verbal and up-to-date written information at an appropriate reading level and in their preferred language about the signs and symptoms of an epidural abscess or post-dural puncture headache and what to do if it occurs since patients may be discharged before the onset of symptoms.

Ref:

1. Reducing the Risk of Deadly Mixups With Epidural and Intravenous Drugs; Matthew Grissinger, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3474426/ accessed on 14/2/2022
2. https://www.ismp.org/sites/default/files/attachments/2018-01/EntireAssessmentWorkbook.pdf: ISMP Medication Safety Self-Assessment ® for High-Alert Medications - 2017

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.12. Hypoglycaemic agents, sulfonylurea

Why are these high alert?

The risk of drug-induced severe hypoglycemia (e.g., blood glucose less than 2.8 mmol/L) exists with both insulin and oral hypoglycemic agents such as those that stimulate the body's release of insulin (sulfonylureas [e.g., glyburide (glibenclamide), gliclazide, glimepiride, chlorpropamide, tolbutamide] and metiglinides [e.g., repaglinide and nateglinide]). Oral hypoglycemic agents have been identified as high-alert medications, but still very few healthcare practitioners (doctors, nurses, pharmacists) considered them as high-alert medications.
Cases of unexpected hypoglycemia due to the inadvertent administration of insulin or an oral hypoglycemic agent to nondiabetic patients have been reported in the literature. It has also been highlighted that patients who were admitted to the hospital for treatment of hypoglycemia and who denied any use of a hypoglycemic agent had received such medication inadvertently. Although all of the case reports highlighted in the literature involved the inadvertent administration of a hypoglycemic agent to nondiabetic patients, medication errors can lead to hypoglycemia in diabetic patients as well.

How to Ensure Safe Use of hypoglycemic agents/sulfonylureas:

Sulfonylureas Include*: Oral form of gliMEPride, gliBENclamide (glyburide), gliPIZIde, gliCLAZide etc.*	
Storage	1. Store within pharmacy until dispensed 2. When in nurse's custody, should be stored in medication cabinets / trolleys under restricted access 3. Availability of these medicines on floor stock of nursing or patient care units is **not allowed**. 4. Majority of errors reported in literature depict that sulfonylureas were not the intended medicine and were accidently dispensed in place of any other drug and led to severe hypoglycemia and/or death. In these incidents, similarities within generic or brands names of the 2 drugs involved were found, that led to the confusion and wrong dispensing. Therefore, it is imperative that while storing these sulfonylureas (**SUs**) or oral hypoglycemic agents (**OHGAs**) following safety points should be considered: • Review how oral hypoglycemic agents are stored in the pharmacy and ensure they are **optimally stored for differentiation**. • **Limit the number of brands and strengths** for each SU or OHGA an organization has in its inventory/formulary (lesser the brands – lesser with be chances of mix-ups or wrong dispensing) • Identify **similar sounding generics or brand names (sound-alike or read-alike)** available in inventory and ensure these are not confused with SUs/OHGAs, by storing them apart and properly labeling them • Identify **similar appearing products (look-alike)** available in inventory and ensure these are not confused with SUs/OHGAs, by storing them apart and properly labeling them

	• Store **regular release and delayed/sustained released forms** of SU/OHGAs separately to avoid mix-ups and wrong dispensing 6. It is a good practice to paste **caution stickers** (High Alert Medicine) on the bins/shelves containing SUs/OHGAs **CAUTION HIGH ALERT MEDICINE** 10. **If SU/OHGAs are discontinued or hold by doctor,** must be stored away from active medicines due for administration, and returned to pharmacy/stock (to avoid any accidental administration).
Prescribing	1. Must **verify correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Check **appropriateness & clarity** of order esp.: dose, route, frequency etc. 3. **Write the drug's name clearly (both brand and generic)** to avoid any confusion with similar sounding or read-alike names of other drugs. It is a best practice to add indication "for diabetes" along with medicine name so that dispensing staff is aware about correct drug to be dispensed 4. Carefully choose between **regular release and delayed/sustained released forms** of SU/OHGAs to avoid wrong prescription 5. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Any special instructions • **Prescribe safely e.g.**: i. Never use abbreviations/short forms ii. Avoid naked decimals e.g. **.2mg** as it can be misread as **2mg** – always write **0.2 mg**. iii. Avoid trailing zero e.g. **2.0mg** as it can be misread as **20mg** – always avoid trailing zero and write **2 mg** 6. **Standing orders**: it is highly recommended that doctor mention the following whenever insulin is prescribed: • **Name of lab test (e.g. random or fasting blood glucose level)**, how frequently to be repeated and what is the target level (for nursing staff and patients) • In case of hypoglycemia (give cutoff value), mention the **name, dose and route of reversal agent** to be used (e.g. Dextrose 10 or 25% IV or fast-acting carbohydrates given orally as indicated) (for nursing staff) 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Since majority of errors reported in literature depict that sulfonylureas were not the intended medicine and were accidently dispensed in place of any other drug and led to severe hypoglycemia and/or death. In these incidents, similarities within generic or brands names of the 2 drugs involved were found, that led to the confusion and wrong dispensing.

	Therefore, it is imperative that while dispensing these sulfonylureas (**SUs**) or oral hypoglycemic agents (**OHGAs**) following safety points should be considered: • **Verify that patient is diabetic** before dispensing (check patient record, written diagnosis on prescription, ask patient or prescriber directly. Also check if there are other diabetes medicines on the prescription as well) • **Double check** the medicine before dispensing against the prescription to avoid any wrong drug dispensing • **Involve patient in the verification process** so the s/he acknowledges that prescribed medicines are for controlling their blood sugar. (If a patient is not diabetic, s/he will definitely raise concern and wrong dispensing can be prevented at that point) • Carefully choose between **regular release and delayed/sustained released forms** of SU/OHGAs to avoid wrong dispensing • Dispense **patient-specific unit doses** of these agents whenever possible. 2. Must **verify correct patient** before preparation and dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#). 3. Medicine orders will be **reviewed for appropriateness** and completeness. In case of incorrect, ambiguous or incomplete order, hold dispensing and clarify the order with the prescriber. Always confirm – never assume. ☛ Check necessary patient parameters (like diagnosis, allergy, contraindications, renal function etc.) and drug parameters (dose, rate, route, duration, duplications, interactions etc.) during order/prescription review 4. It is best practice to affix **caution stickers** / auxiliary labels while dispensing (see storage section for detail) 5. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare medicine** in hand against actual doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Verify** that patient is diabetic before administration 6. **Check blood glucose levels** and if patient is already hypoglycemic, hold the dose of SU/OHGA and confirm with prescriber. • Treat the hypoglycemia if it is below the safe limit as mentioned in physician standing order or as per organization's protocol • Severe toxicity may require additional reversal agents like Octreotide to be used, and must be administered as per physician orders • Restart the dose as directed by physician

	7. **Any unused** (or hold, discontinued) drugs must be immediately returned to original stock or pharmacy 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner
Monitoring	1. It is to be carried out as per physician orders or hospital protocol; but generally includes: fasting/random blood glucose levels at regular interval, signs of hypo or hyper glycemia, meals and nutrition status esp. NPO (nothing per oral) or if meals/nutrition are skipped 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future 4. Hospitalized patient who experienced hypoglycemia with SU/OHGAs should be observed for at least 24 hours before can be safely discharged to home (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	It is highly recommended that printed patient instructions, preferably in two languages (English and Urdu, or any local language) should be developed for SU/OHGAs in order to guide patients in a uniform manner. Patients must be educated about: Why these medicines are high alert and how patients can play their role in averting error/harm. The patient's role may include (but not limited to): 1. Knowing the **indication** for use 2. Know the **dose, timings, name and strength** (esp. sustained/delayed release forms) of drug they are using 3. Exactly know **when to stop** the therapy and when not to 4. Able to identify the **color, shape, strength of tablets** they are using (to avoid wrong drug administration or purchase) 5. Which types of tablets **must not be chewed or crushed** (sustained/delayed release forms) 6. Importance of **checking blood glucose** and cutoff limits. How to use glucometer 7. What to do in case **doses are missed?** 8. Importance of **regular meal intake** 9. What **foods or drugs** can affect diabetes control? 10. **Signs and symptoms** of hypoglycemia 11. Keeping source of **fast-acting carbohydrate** in easy reach to combat hypoglycemia 12. Importance of **informing other healthcare professional** about being on SU/OHGAs 13. What to do in case of **emergency**

	14. How to report if they experience any **serious side effect** 15. **Medication reconciliation** (taking past medication history and comparing with current medicines list) at the time of admission and discharge is recommended to avoid omissions/errors/duplication

Ref:

1. ISMP Canada Safety Bulletin 2007, https://www.ismp-canada.org/download/safetyBulletins/ISMPCSB2007-01Hypoglycemia.pdf
2. Sulfonylurea agent poisoning, https://www.uptodate.com/contents/sulfonylurea-agent-poisoning#H7 -

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10.13. Ionotropic medicines

Inotropic medications like Milrinone are high alert because of the risk of cardiac arrhythmias and hypotension associated with the use of the drugs. Appropriate monitoring is required. While, Digoxin is a high-alert medication because of the narrow therapeutic serum range (0.8-2.0 ng/mL. The toxic level is >2.4 ng/mL); the therapeutic endpoint is difficult to quantify and digoxin toxicity may be life-threatening.

Medication errors associated with digoxin include miscalculation of doses esp. for pediatrics, drug-drug interactions and insufficient monitoring of digoxin levels. Fortunately, approximately 50% of digoxin toxicity cases are preventable, which should motivate us to improve the treatment outcomes of digoxin, reduce the incidence rate of digoxin toxicity, and minimize the related medical costs.

How to Ensure Safe Use of Inotropes:

Inotropes include*: Digoxin oral/injection forms, Milrinone injection	
Storage	1. Primarily stored in the pharmacy 2. When in patient care unit, must be stored in **authorized access only** 3. Availability of inotropes on floor stock of nursing or patient care units is generally **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance. Or in critical care, emergency or resuscitation units) • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of inotropes on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with brand and generic name and strength in **bold** to avoid mix-ups. 5. To avoid errors with **Look-Alike**, **sound-alike or read-alike** appearance against any other drug available in the inventory, use recommended techniques for proper differentiation e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc. See the example below: ☛ *Digoxin* and *Thyroxin* names can be confused (Sound-Alike or Read-Alike); hence must be clearly differentiated, written/typed and labeled to avoid mix-ups ☛ Both drugs are also look-alike; exercise caution to avoid dispensing/administration of wrong drug

	 6. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration)
Prescribing	1. To be **prescribed by** physicians with cardiology and/or critical care training 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. It is recommended that both digoxin and Milrinone are prescribed as per **standard protocol or guidelines** defined by the organization including at least: indications for use, contraindications & precautions, factors that can lead to error and their preventive measures, administration protocol, monitoring protocol and management of overdose/toxicity 4. Ensure **appropriateness of order** as per patient age, weight, other physiological conditions like serum electrolytes, fluid status and concomitant (possibly interacting) drugs etc. 5. Order/prescription must be **complete and non-ambiguous** i.e.: o Proper indication, patient's drug allergy status, weight, age as needed o Any special instructions o **Prescribe safely e.g.**: o **Clearly write name, dose and route of administration** o **Never use abbreviations or short forms.** E.g. **"Dig**": write full form i.e. 'Digoxin' o **Avoid naked decimals** e.g. **.25 mcg** as it can be misread as **25 mcg** – always write **0.25 mcg** o **Avoid trailing zero** e.g. **5.0 mcg** as it can be misread as **50 mcg** – always avoid trailing zero and write **5 mcg** o **Avoid using symbol for units** such as **5μg**, as it could be misread as **50**. Always write **5 mcg** or **5 microgram** 6. **Standing orders**: specific orders to be written: o To monitor patient's response to these drugs (see monitoring section); including when and how frequently to be done. o When to hold infusion / dose o When and how to use rescue agents in case of serious adverse reactions/toxicity 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.

Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check patient parameters** (like allergy, contraindications, renal/hepatic function, weight, age etc.) and **drug parameters** (serum drug levels (digoxin), dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. **Hold dose and first confirm with doctor** if digoxin serum level is high ☛ Samples for digoxin TDM are required to be taken at least eight hours after the last dose or ideally immediately before the next dose ☛ If loading dose is not given the steady state is usually achieved in 5-7 days so levels should be drawn at that time 5. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing inotropes **CAUTION HIGH ALERT MEDICINE** 6. **Double-check** before dispensing 7. **Ask patient about any possible signs of toxicity** when they visit pharmacy to purchase/refill digoxin prescription ☛ Initial toxicity symptoms may include: Anorexia, Vomiting, Diarrhea, visual disturbances, irregular heart beat 8. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Before administration always **check medicine in hand** against name and strength prescribed 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. Accidental overdose of Milrinone/digoxin can cause patient harm or death. Have second staff independently check original order, dose calculations, and infusion pump settings • Use smart infusion pump drug library to prevent dosing and rate related errors 6. Never use **one patient's medicines on other** patient 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.

<table>
<tr><td>Monitoring</td><td>
<table>
<tr><th>Milrinone</th><th>Digoxin</th></tr>
<tr><td>• Continuous blood pressure and heart rate monitoring for the duration of the infusion (Slow or discontinue if BP drops excessively) and Monitor fluid balance and electrolytes at least daily.
• Monitor ECG continuously during infusion. Arrhythmias are common and may be life threatening.
o The risk of ventricular arrhythmias is increased in patients with a history of arrhythmias, electrolyte abnormalities, abnormal digoxin levels, or insertion of vascular catheters.
• Monitor electrolytes and renal function frequently during administration.
o Correct hypokalemia prior to administration to decrease the risk of arrhythmias.
o Monitor platelet count during therapy.</td><td>• Withhold dose and notify doctor if pulse rate is <60 bpm in an adult, <70 bpm in a child, or <90 bpm in an infant.
• Notify promptly of any significant changes in rate, rhythm, or quality of pulse.
• Pediatrics: Heart rate varies in children depending on age, ask physician to specify at what heart rates digoxin should be withheld.
• Monitor BP periodically in patients receiving IV digoxin.
• Monitor ECG during IV administration and 6 hr after each dose. Notify doctor if bradycardia or new arrhythmias occur.
• Observe IV site for redness or infiltration; extravasation can lead to tissue irritation and sloughing.
• Before administering initial loading dose, determine whether patient has taken any digoxin in the preceding 2–3 wk.
• Hypokalemia, hypomagnesemia, or hypercalcemia may make the patient more susceptible to digoxin toxicity (correct electrolytes if there is any abnormality)</td></tr>
</table>
1. Assess patient for resolution of signs and symptoms of heart failure (HF) (peripheral edema, dyspnea, rales/crackles, weight gain) and improvement in hemodynamic parameters (increase in cardiac output and cardiac index, decrease in pulmonary capillary wedge pressure).
2. Any adverse drug reaction (ADR) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization.
3. Any medication error or near miss related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future
(Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
</td></tr>
<tr><td>Patient Education</td><td>It is highly recommended that printed patient instructions, preferably in two languages (English and Urdu, or any local language) should be developed for Digoxin in order to guide patients in a uniform manner. Patients must be educated about:
Why these medicines are high alert and how patients can play their role in averting error/harm. The patient's role may include (but not limited to):
1. Knowing the indication for use
2. Know medicine name and dose they are taking
3. Exactly know when to stop the therapy and when not to</td></tr>
</table>

	4. Able to identify the **color, shape of tablets/injections** they are using (to avoid wrong drug administration or purchase) 5. Know the **administration technique and timings** 6. Importance of **doing relevant lab tests** and cutoff limits (Digoxin serum level) 7. Monitoring of pulse rate and symptoms of Digoxin toxicity 8. What to do in case **doses are missed** 9. What **foods or drugs to avoid** 10. Importance of **informing other healthcare professional** about being on anticoagulants, and also if undergoing a procedure. 11. Importance of **avoiding activities** that could lead to bleeding 12. What to do in case of **emergency** (e.g. overdose, bleeding or signs of thrombosis) 13. How to report if they experience any **serious side effect** **Medication reconciliation** (taking past medication history and comparing with current medicines list) at the time of admission and discharge is recommended to avoid omissions/errors/duplication**.**

Ref:

1. Davis's Drug Guide (Digoxin, Milrinone); https://www.drugguide.com/ddo/view/Davis-Drug-Guide/51218/all/digoxin; https://nursing.unboundmedicine.com/nursingcentral/view/Davis-Drug-Guide/51505/all/milrinone
2. Improvement of Adequate Digoxin Dosage: An Application of Machine Learning Approach, Ya-Han Hu, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6120286/
3. NHS Acute Sector sample guidelines for Therapeutic Drug Monitoring in Adults https://www.nhsgrampian.org/globalassets/foidocument/foi-public-documents1---all-documents/nhsgtdma.pdf

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.14. Insulins

Why are these high alert?

Insulins are classified as high-alert medications, meaning that it has the potential to cause detrimental patient harm when used in error. If given as an excessive dose, insulin may cause life-threatening seizures and coma due to hypoglycemia, while an under-dose of insulin may lead to life-threatening ketoacidosis or hyperosmolality related to hyperglycemia.

Errors related to insulin mostly occur in their dose, time of insulin administration (basal = once or twice daily vs bolus = with/pre meals three times a day), or with inadequate/lack of monitoring of glucose levels or nutrition status of patient, identifying hypoglycemia but delay in treating it, holding basal insulin dose if glucose level was found in range at the time of administration, or poor communication between the transition of care within the hospital, at the time of admission or at discharge etc.

How to Ensure Safe Use of Insulins:

Insulins **Rapid, Short, Ultra-short, Intermediate and Long-Acting or Ultra-Long Acting Insulin:** Regular insulin, pre-mixed insulin e.g. 70/30, Mix-25, Mix-50 etc., NPH insulin, long acting insulin (Glargine, Detemir, Degludec etc.*)	
Storage	1. Primarily stored in the pharmacy in **cool temperature** (refrigeration) i.e. 2-8^{0}C. **Do not freeze** 2. Vial/pens **once opened**, can be stored at room temperature. Opened vials/pens must be discarded after 28 days, or as mentioned in the product leaflet (package insert) 3. Once the vial/pen is opened, always mention **date of opening, expiry/beyond use date**, patient name, MR# and staff initials on the label and affix to the vial/pen (not at the removable cap). Discard when the date is reached as per point # 2 4. Insulin pen of one patient should not be used on another patient even when the needle is changed 5. When in nurses' custody, must be stored in medication trolleys (opened vials/pens) or in medication refrigerator (unopened vial/pen) under **authorized access only** 6. Availability of these drugs on floor stock of nursing or patient care units is **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance so that when needed in life saving condition it is immediately available) • **Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC)** of the hospital should authorize stocking of any insulins on patient care units (outside pharmacy)

<table>
<tr>
<td></td>
<td>
No insulin other than Regular insulin should be placed in floor stock (that also if approved by D&TC/P&TC)
7. When stored in healthcare setting, storage bins should be labelled with name of drug in bold, highlight the type of insulin and strength and label as “High Alert medication”. Brand names can be used for reference purpose after the generic name. See the example below:

Glargine (Lantus) 100 UNITS/ml
Long Acting Insulin
<u>High Alert Medicine</u>

Humalog Mix-25
Short Acting Insulin
<u>High Alert Medicine</u>

8. Store same type of insulins together to avoid mix-ups, i.e. Bolus/Prandial Insulin (i.e. rapid or short acting) in one shelf, while Basal Insulin (i.e. intermediate or long acting) in separate shelf within fridge.
9. If any insulin is sound-alike or read-alike with another insulin, use tall-man lettering, type of insulin or its strength to be made bold on bin label or use vial/pen’s colors as identifier in order to correctly read/identify the drug name. See the example below:
Suppose Humalog-Mix 25 and Humalog-Mix 50 are read-alike, but both packs are of different color (Mix 25 = yellow and Mix 50 = Orange/red) so you can label the bin as per their color to avoid mix-ups/wrong dispensing:

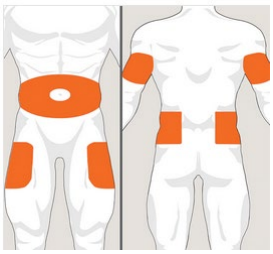
Humalog MIX-25
Short Acting Insulin
<u>High Alert Medicine</u>

Humalog MIX-50
Short Acting Insulin
<u>High Alert Medicine</u>

Some examples of Tallman lettering for read alike/sound-alike insulin e.g., HumaLOG, HumuLIN, NovoLOG
10. Insulin discontinued or changed by doctor must be stored away from active medicines due for administration, and sent back to pharmacy, returned to stock or discarded without any delays (to avoid any accidental administration)
11. Never leave any unlabeled syringe or infusion bag containing insulin in patient care area
</td>
</tr>
<tr>
<td>Prescribing</td>
<td>
1. An endocrinologist or practitioner trained in insulin management, as determined by the organization, should prescribe insulin
2. Must verify correct patient before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#)
3. Check baseline labs (fasting, random glucose, Glucose Tolerance Test, HbA1C etc.) and repeat periodically while on therapy
Check potassium level if Insulin is being used for managing hyperkalemia
4. Check appropriateness of order esp. dose, as per patient weight, total insulin requirement per day and daily division of doses b/w bolus and basal insulin types.
</td>
</tr>
</table>

	5. If patient is already on insulin therapy and either **dose or insulin type is changed**, it should be clearly communicated to the nurse and/or patient so that double/wrong administration can be prevented 6. Check if patient is already on, **other medicines or have conditions that can** effect glucose level and adjust insulin dose as indicated: • Some common drugs that can cause **hyperglycemia** are: gatifloxacin, β-blockers, thiazide diuretics, atypical antipsychotics (SGAs), prolonged/high dose corticosteroids, cyclosporine and tacrolimus etc. • Some common drugs that can cause **hypoglycemia** are: gatifloxacin, β-blockers, sulfonylureas, Indomethacin etc. 7. It is a best practice to have a **pre-printed order form** for prescribing Insulins with necessary safety checks as mentioned above (to be filled by the doctor) 8. These should **not** be ordered on **PRN/ need basis**. If **sliding scale insulin** is needed, it should be used for minimum possible time period in hospitalized patients, as per standard diabetes management guidelines. 9. **Intravenous Insulin Infusion** (of regular Insulin) are sometimes indicated; hospitals using these must have written protocol in place and relevant doctors, nurses and pharmacists should be trained to safely use it. 10. **Review order** as per patient's blood sugar levels and adjust dose as indicated (continue, hold temporarily or discontinue) 11. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Drug name, dose, route, frequency, duration of therapy • Any special instructions (e.g. target HbA1C or blood glucose level) • Never use abbreviations: E.g. • Insulin Glargine 20U Sub-cut once a day, can be misunderstood as **200**. Therefore, write Insulin Glargine 20 Units Sub-cut once a day **(write 'units'** and not 'U') • Regular Insulin IV20 units can be misunderstood as **1020** or **1420** units; write "Regular Insulin 20 units **IV** infusion" 12. The **dose/rate calculation and titration** shall be done based on individual patient's requirement and lab value 13. **Standing orders**: it is highly recommended that doctor mention the following whenever insulin is prescribed: • **Name of lab test (e.g. random or fasting blood glucose level)**, how frequently to be repeated and what is the target level (for nursing staff and patients) • In case of hypoglycemia (give cutoff value), mention the **name, dose and route of reversal agent** to be used (e.g. Dextrose 10 or 25% IV or fast-acting carbohydrates given orally as indicated) (for nursing staff) 14. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.

Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check necessary labs** (HbA1C, blood glucose level etc.), patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. If patient is hypoglycemic or hyperglycemic, **discuss with doctor** before dispensing 5. For patients already on insulin, **review the previous orders/dose** whenever a fresh order is received so that accidental overdose/duplications can be prevented. Guide nurse and/or patient accordingly to avoid confusions 6. It is a best practice that pharmacy dispenses insulin in **most ready to administer** form possible esp. IV infusion 7. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing insulins **CAUTION HIGH ALERT MEDICINE** 8. **Double-check** the medication before dispensing 9. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. 6. Infusion must always be given with **rate controlled device** to avoid accidental free flow of infusion 7. It is a good practice to have a **2nd check** for dose, route, dilution by another staff 8. An insulin pen cartridge is never used as a vial 9. Never use **one patient's insulin pen on another** patient 10. Always administer insulin on specified times (pre/with meal, on sliding scale or at bedtime), never change the dose or timings on your own 11. **Hold the needle** in place in sub-cut administration for 5-10 seconds to avoid leaking of insulin from injection site**. Rotate** subcutaneous injection sites;

	 12. Keep a record of patient's **nutrition status** e.g. NPO (nil per os = nil by mouth), skipped meals, receiving any IV source of glucose or enteral/parenteral nutrition etc. or not, and inform doctor if there is any change in the status (as insulin dose might need to be adjusted) 13. **Regularly check blood glucose levels** as per doctor's orders and if below cut-off (hypoglycemia) must not delay the administration of glucose (IV or oral as per doctor's order) 14. **Hold dose** if patient is in severe hypoglycemia. Restart only if and as ordered by doctor 15. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary labs, patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order review and before administering 16. **Any unused** (or hold, discontinued) insulin must be immediately returned to original stock or pharmacy 17. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or hospital protocol 2. **Vital signs** are monitored as applicable and patient must be monitored for hyper or hypoglycemia 3. Watch out for **hypokalemia** 4. Monitor the **nutrition status** of the patient 5. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 6. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)

Patient Education	It is highly recommended that printed patient instructions, preferably in two languages (English and Urdu, or any local language) should be developed for insulins in order to guide patients in a uniform manner. Patients must be educated about: Why Insulin are high alert and how patients can play their role in averting error/harm. The patient's role may include (but not limited to): 1. Knowing the **indication** for use 2. How to **store** insulin (opened vs un-opened) and when to discard 3. Know the **dose, timings and name** of Insulin they are using 4. Exactly know **when to stop** the therapy and when not to 5. Able to identify the **color, shape, strength of vials or pens** they are using (to avoid wrong drug administration or purchase) 6. Know the **administration technique** (vial and pens). Common errors reported with insulin pens include: not inverting and rolling insulin pens to properly mix the insulin, injection technique errors (e.g., not keeping pen needle under the skin for 6 seconds to prevent leakage from the injection site), misreading the dose, and measurement errors, such as twisting the dosing dial back down to zero instead of pressing the injection button on a pen to administer a dose etc. 7. Importance of **checking blood glucose** and cutoff limits. How to use glucometer 8. What to do in case **doses are missed?** 9. Importance of **regular meal intake** 10. What **foods or drugs** can affect diabetes control? 11. **Signs and symptoms** of hypoglycemia 12. Keeping source of **fast-acting carbohydrate** in easy reach to combat hypoglycemia 13. Importance of **informing other healthcare professional** about being on insulin 14. What to do in case of **emergency** 15. How to report if they experience any **serious side effect** 16. **Medication reconciliation** (taking past medication history and comparing with current medicines list) at the time of admission and discharge is recommended to avoid omissions/errors/duplication

Ref:

ISMP Guidelines for Optimizing Safe Subcutaneous Insulin Use in Adults, 2017,
https://www.ismp.org/sites/default/files/attachments/2018-09/ISMP138D-Insulin%20Guideline-090718.pdf

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.15. IV electrolytes / Concentrated Electrolytes for IV Use:

Why are these high alert?

Concentrated electrolytes especially Potassium Chloride, Magnesium Sulfate, Potassium Phosphate and Hypertonic Saline (greater than 0.9% concentration); all for IV use, are linked to serious patient harm and deaths when used in error. For example, Intravenous (IV) administration of a concentrated potassium solution (≥ 2 mEq/mL) is considered to be a pharmaceutical "never event". "Never events" are defined as "patient safety incidents that result in serious patient harm or death, and that can be prevented by using organizational checks and balances." The World Health Organization has focused on high-risk situations, such as these pharmaceutical "never events" and the use of high-alert concentrated electrolytes, as 1 of 3 key areas in its Third Global Patient Safety Challenge, "Medication Without Harm".

How to Ensure Safe Use of Concentrated Electrolytes:

<table>
<tr><td colspan="2"><u>Concentrated Electrolytes:</u>
Commercially available: Potassium Chloride vials, Magnesium Sulfate ampules (for IV use) etc.*
Compounded by pharmacy: Potassium Phosphate, Hypertonic Saline (for IV use) etc.*</td></tr>
<tr><td>Storage</td><td>1. Primarily stored in the pharmacy
2. When in nurses' custody, these must be stored in medication trolleys and under authorized access only
3. Availability of these drugs on floor stock of nursing or patient care units is strictly discouraged.
• Keep concentrated forms only if absolutely necessary (e.g. in specific type of operating rooms (ORs), labour room, or in crash cart/code trolley only)
• Only Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC) of the hospital should authorize stocking of any of these electrolytes on patient care units (outside pharmacy)
➔Note: Limiting access to these products is a strong deterrent to inadvertent use.
4. When stored in healthcare setting, storage bins should be labelled with name of drug in bold, strength, warning: "Must be diluted before use" and "High Alert medication". Brand names can be used for reference purpose after the generic name. See the example below:</td></tr>
</table>

Potassium Chloride inj.
1mEq/ml
Must Be Diluted Before Use
High Alert Medicine

5. If any drug is **sound-alike or read-alike** with another, use tall-man lettering, highlight its strength, color or shape etc. in order to correctly read/identify the drug name. See the example below:
   Suppose ***Magnesium Sulfate inj. is available in 2 strengths*** as depicted below, and confusion or mix-ups can occur between the two, so label the bin highlighting their strengths and volume of ampule, also can color code the labels to differentiate them further:

Magnesium Sufate inj.	**Magnesium Sufate inj.**
1 gm/2ml	**5 gm/10ml**
Must Be Diluted Before Use	**Must Be Diluted Before Use**
High Alert Medicine	**High Alert Medicine**

   Examples of Tallman lettering for read alike/sound-alike drugs e.g.,
   Potassium **CHLORIDE** vs ***Potassium*** **PHOSPHATE**
6. It is a best practice to label each ampule/vial of these electrolytes with **auxiliary colored sticker** (see sample below), so that individual vial/ampule bears warning *"must be diluted before use" and "High Alert Medicine"* to avoid wrong administration.

   ➔The auxiliary label should be affixed to the neck of vial/ampule so that the actual printing on the vial/ampule's body is not obscured esp. the drug name and strength (see the picture).
7. **Medicines discontinued or hold by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock immediately (to avoid any accidental administration). This includes both intact vials/ampules, filled syringes and diluted infusions.

<table>
<tr><td></td><td>8. In surgical areas, vials of concentrated potassium chloride or high-dose potassium cardioplegic solutions are sequestered in sealed kits or locked storage areas, or placed in labeled lidded containers and obtained immediately before use; and once the procedure has been completed, there is an effective process in place to return unused products to their secure locations or dispose of the partially empty vials or bags
9. Never leave any unlabeled syringe or infusion bag containing concentrated electrolytes in patient care area
10. To respond to emergencies caused by magnesium sulfate overdoses, a standard protocol has been established that guides the administration of a RESCUE agent (i.e., calcium gluconate) after prescriber notification; and the RESCUE agent is easily accessible, along with directions for use, in all clinical areas where high-dose magnesium sulfate is administered.</td></tr>
<tr><td>Prescribing</td><td>1. Organizations should have written electrolyte replacement protocols in place and concerned staff (doctors, nurses and pharmacists) are trained to use it
2. Oral route is a preferred and safer route of electrolyte replacement and should be used if clinically indicated. IV route should be switched to oral route as soon as it is feasible to do so.
3. Must verify correct patient before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#)
4. Check appropriateness, completeness & clarity of order esp. dose, dilution (concentration of infusion), rate, route of administration and duration of treatment E.g.
<table>
<tr><td>Potassium Chloride</td><td>40 mEq in 500ml normal saline (NS0.9%)</td><td>infuse over 8 hours</td><td>@ 62.5ml/hour</td><td>through peripheral IV line</td></tr>
<tr><td>Drug</td><td>Concentration</td><td>Duration</td><td>Rate</td><td>Route</td></tr>
</table>
Some important considerations while prescribing are:
➔ Certain concentrations of infusion esp. for Potassium Chloride and Hypertonic Saline require Central line for administration.
➔Certain concentrations of Potassium Chloride infusion require cardiac monitoring during infusion
➔ Certain concentrations for infusions should be restricted for use in critical care setting only
➔ Small volume single or intermittent IV infusions are never referred to as “bolus”, since “Bolus” doses might be misinterpreted as direct, undiluted, and/or rapid IV administration
➔ Practitioners use a standard, facility-defined dosing unit of measure (e.g. gm vs. mEq vs mMole) to prescribe
5. Baseline serum electrolyte levels must be checked before starting the therapy and thereafter periodically (specific order to be written).
• Stop IV electrolyte replacement (or shift to oral maintenance dose as appropriate) according to the serum electrolyte levels</td></tr>
</table>

	6. It is a best practice to have a **pre-printed order form** for prescribing electrolytes with necessary safety checks as mentioned above (to be filled by the doctor) 7. These should **never** be ordered on **PRN/ need basis** 8. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Drug name, dose, rate, route, frequency, dilution, duration of therapy • Any special instructions • Never use abbreviations: E.g. i. MST 1gm in 100ml NS0.9% IV stat. MST was intended for magnesium sulfate but can be misunderstood as any other drug e.g. morphine sulfate. Therefore, always write full name ii. Avoid writing chemical names e.g. KCL, $MgSO_4$ iii. Avoid naked decimals e.g. **.5**gm as it can be misread as **5**gm – always write **0.5**gm. iv. Avoid trailing zero e.g. **5.0**gm as it can be misread as **50**gm – always avoid trailing zero and write **5**gm 9. The **dose/rate calculation and titration** shall be done based on individual patient's requirement and lab values 10. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) **2.** It is a best practice that pharmacy dilutes the concentrated electrolytes in standard dilutions and dispense in **pre-mixed, ready to use form. When diluted in pharmacy:** • The **calculation** i.e. mEq (or mls) to be added in the given volume of diluent (e.g. NS0.9% or Dextrose 5%) must be verified and ideally double checked. • Only **compatible diluent** must be used to avoid any precipitation etc. • The prepared infusion must be inverted several times (at least 8-10 times) to allow **uniform mixing** of electrolyte with diluent. (Reason: Potassium Chloride tends to settle down when added in diluent, and if not mixed, a more concentrated solution will reach to patient first when infusion is started. This can result in serious harm/death) • Prepared infusion must be properly labeled with: i. Drug name ii. Concentration (%, gm/ml, mEq/ml or mMole/ml) iii. Total volume of preparation iv. Diluent name (e.g. NS0.9% or D5W) – (for other than hypertonic saline) v. Date of preparation and Date/time of expiry vi. Route (central or peripheral)

	3. Pharmacist to check the presence of **central line** and patient being in **critical care unit** if certain high dose/concentrations are ordered 4. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 5. **Check necessary info**, patient parameters (like serum electrolyte level, allergy, weight, contraindications, renal function, central vs peripheral line etc.) and drug parameters (dose, rate, route, concentration for infusion, duration, duplications, interactions etc.) during order/prescription review while dispensing 6. It is best practice to affix **caution stickers** / **auxiliary labels** while dispensing and storing these drugs (see storage section for detail) 7. **Double-check** the medication before dispensing 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. If a concentrated electrolyte is prepared and diluted in patient care unit: • The **calculation** i.e. mEq (or mls) to be added in the given volume of diluent (e.g. NS0.9%) must be verified and ideally double checked. • Only **compatible diluent** must be used to avoid any precipitation etc. • The prepared infusion must be inverted several times (at least 8-10 times) to allow **uniform mixing** of electrolyte with diluent. (Reason: Potassium Chloride tends to settle down when added in diluent, and if not mixed, a more concentrated solution will reach to patient first when infusion is started. This can result in serious harm/death) 6. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. 7. Infusion must always be given with **rate controlled device** to avoid accidental free flow of infusion 8. It is a best practice to have a **2nd check** for dose, route, dilution by another staff 9. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary labs, patient parameters (like serum electrolyte level, allergy, contraindications etc.) and drug parameters

	(dose, rate, route, duration, duplications, interactions etc.) during order review and before administering 10. **Any unused** (or hold, discontinued) concentrated electrolyte must be immediately returned to original stock or pharmacy (or discarded as appropriate) 11. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or hospital protocol • **Vital signs, serum electrolyte levels, fluid balance, signs of toxicity/over dose, signs of phlebitis or extravasation** etc. should be monitored • Certain concentrations of Potassium Chloride infusion require **cardiac monitoring** during infusion and hence must be administered with proper cardiac monitoring 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Not applicable – counsel family as and when indicated.

Ref:

1. ISMP Canada Safety Bulletin 2019, *https://www.ismp-canada.org/download/safetyBulletins/2019/ISMPCSB2019-i1-ConcentratedElectrolytes.pdf ;*
2. ISMP Medication Safety Self-Assessment ® for High-Alert Medications – 2017, *https://www.ismp.org/sites/default/files/attachments/2018-01/EntireAssessmentWorkbook.pdf:*

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.16. Look-alike and Sound alike drugs

Look-Alike Sound-Alike (LASA) medications involve medications that are visually similar in physical appearance or packaging (see pictures below) and names of medications that have spelling similarities and/or similar phonetics or Read-Alike effect. Therefore, LASA drugs are sometimes also referred to as LASARA drugs.

For example:

Digoxin *Thyroxin*	*Dobutamine* *Dopamine*	*Epinephrine* *Norepinephrine*	*Lasix* *Losec*
Angised *Ansaid*	*Filgrastim* *Peg-Filgrastim*	*Vincristine* *Vinblastine*	*Lamisil* *Lamnet*

How to Ensure Safe Use of LASA drugs:

It includes*:

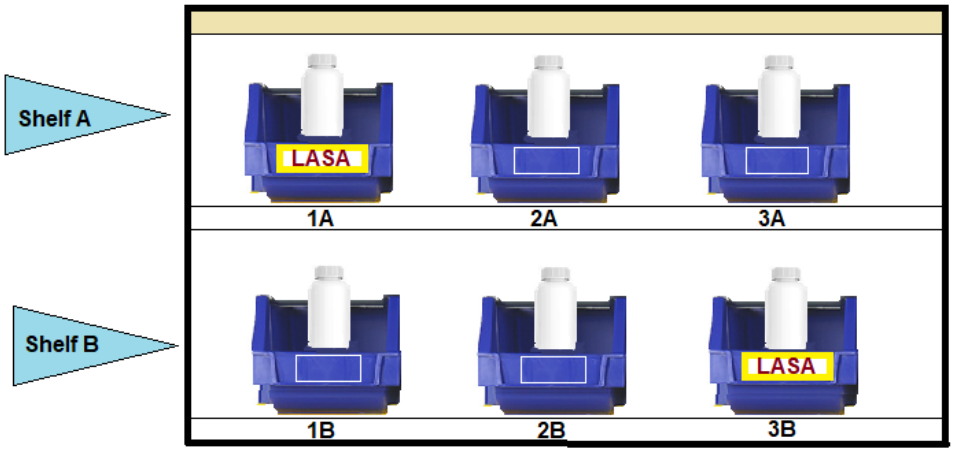
- Internationally established LASA drugs that are known to cause medication mix-ups and errors (review which of these are available in your facility)

• Your healthcare facility to generate its own LASA Drugs List by periodically performing review of available error-prone drugs due to similar designs, packaging, names and phonetics. • Also, review reported incidents, errors and near-miss in your organization and evaluate if their contributing factor involves any LASA drugs	
Selection and Procurement	1. Healthcare facility should generate a **list of LASA drugs** specific to their facility in close coordination with main stakeholders i.e. pharmacy, nursing, physicians and other healthcare staff routinely involved in the handling of medicines • In LASA drugs' list, **LASA pairs** must be identified (i.e. which drug Looks-Alike or is Sounds-Alike with which drug?) • LASA list must be **regularly revised** (preferably annually, plus as and when any incident related to LASA drugs is encountered –or- when any new LASA medicine is added in the inventory/formulary) • List is **widely disseminated** and available in easy access of all concerned healthcare staff 2. Medications considered for **formulary/inventory addition** should be evaluated for LASA status. • Healthcare facility can **deny the addition** if the product is LASA, provided that other safer options are available. • In case no option is available, actions must be taken to **proactively prevent errors** (e.g. special labeling, separate storage, identifying specific locations for keeping stocks, discussion with vendor for change in packaging, restricted number of strength/Stock Keeping Units (SKUs) etc.) • **Awareness** to be made among all stakeholders (doctors, nurses and pharmacists etc.) about the error potential and harms associated with inadvertent use of LASA medications and preventive measures taken • **Alert** is given to all healthcare staff if any brand, form, strength etc. is changed, and also if any new drug with LASA status is added in inventory/formulary • Staff to be encouraged to **report mix-ups or confusions** between products during handling, so that actions for minimizing the errors can be taken. This may also include replacing with alternate products that have minimum similarity in names and/or packaging 3. **Limiting the variations:** If a drug is available in multiple strengths (e.g. 250mg, 500mg and 1000mg) or dosage forms (e.g. inj. oral, rectal etc.), carefully review which of these are absolutely required for patient care and must be available in inventory. ☛ Goal is to keep minimum possible dosage forms and strengths of same drug to prevent mix-ups or errors 4. **Limiting the duplications:** duplication of multiple brands of same generic must be kept to a minimum in inventory in order to prevent mix-ups or errors
Storage	1. Availability of LASA drugs pairs on floor stock of nursing or patient care units is **discouraged**. • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of drugs on patient care units (outside pharmacy) in general, and LASA drugs pair in particular

- Area staff exactly knows that which LASA drug pairs are in their stock and what caution is applicable to them

2. When stored in healthcare facility, **bins should be labelled** with brand and generic name and strength in **bold** to avoid mix-ups. (see individual drug monographs for details)
3. Medicines in par levels are to be stored in **alphabetical order (generic name wise),** with LASA drug pairs are stored apart from each other.
4. Brand names should not be used as primary or only source of product identification, rather; they can be used as a reference only in addition to generic name. (Because brands may change from time to time due to temporary or permanent shortage of existing brands)
    - Shelf Location should preferably be marked (e.g. either A, B, C or 1, 2, 3) and drugs are placed in designated place on the shelf only, so that mix-ups or wrong placement in shelf/bin is prevented. LASA drugs are boldly labelled.
    - Oral, injectable and topical/dermals products should be stored separated from each other.

    See following fig. as example:



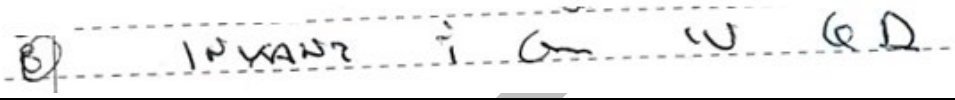
5. To avoid errors with **Look-Alike**, **sound-alike or read-alike** appearance against any other drug available in the inventory, use recommended techniques for proper differentiation e.g.
6. Tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc.
7. See individual drug monographs for details

DexMEDETOmidine
200 mcg/2ml ***(Precidex)***
High Alert/LASA Medicine

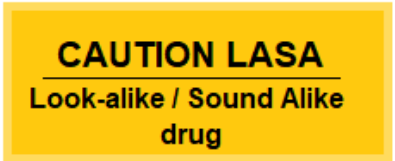
8. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration)

	9. **When new stock is received or unused drugs are returned** from patient care areas, drug name and strength must be carefully checked before placing back in the shelf/bin. Goal is to avoid placement of drugs in the wrong location (shelf or bin)
Prescribing	1. **Prescribers must be aware and educated** about the risks involved with Look-Alike, Sound-Alike and Read-Alike drugs 2. **Selection of medication in computerized medication order entry** system must be done carefully. Drugs starting with same letters such as **EPInephrine** or **EPIrubicin** can be confused. ☛ Always type at least first 4 letters to narrow down the list of drugs ☛ Be careful if using brand name for drug selection. E.g. **TRA***nsamine* (Transexamic acid) can be confused with **TRA***curium* (Atracurium) and deadly error can occur ☛ Do not select and enter the drug until full drug name, dosage form (inj. vs oral) and strength is read and verified from the list 3. **Verbal orders** must be limited to urgent, lifesaving situations only. Healthcare facility should have a written verbal order policy and concerned staff are trained on it. ☛ If verbal order is given, pronounce clearly so that misunderstanding at the order receiving end can be averted ☛ READ BACK policy to be followed by the person receiving the order 4. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 5. Ensure **appropriateness of order** as per patient age, weight and other physiological conditions. 6. Order/prescription must be **complete and non-ambiguous** i.e.: ☛ Proper indication, patient's drug allergy status, weight, age as needed ☛ Any special instructions ☛ **Prescribe safely e.g.**: ○ **Clearly write name, dose, route and rate of administration** ○ **Never use abbreviations or short forms.** Always write full form ○ Prescriptions must be written legibly so that it can be clearly understood ○ It's a best practice to add **indication/purpose for use and both generic and brand names** in the prescription to avoid misinterpretation of medicine name, e.g.: ✓ *Tablet* ***Lasix 40mg*** *(Furosemide) by mouth once a day (for blood pressure)* ✓ *Capsule* ***Losec 40mg*** *(Omeprazole) by mouth once a day (for gastric acidity)* 7. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#)

2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume.
   - ☛ If dose, route, frequency or diagnosis is not matching with the name of drug interpreted/read by pharmacy, there is a high likelihood that an error in either prescribing or interpretation of the drug name has occurred.
   - ☛ Never proceed without confirmation, see example below:

Prescription	
	
Pharmacy interpretation 1	**Pharmacy interpretation 2**
IV VANC (i.e. Vancomycin) 1 gm IV QD	Invanz (i.e. Ertapenem) 1 gm IV QD
Clues	
1. Normal dose of Vancomycin in adults is 1gm q12hrly – not 1gm QD (once daily) 2. Patient's renal function, serum creatinine was also in normal range, therefore renal adjusted dose of Vancomycin is also ruled out 3. Ertapenem normal adult dose is 1gm QD 4. Culture/sensitivity report checked and found infection that does not require coverage of gram positive organisms (i.e. no indication of Vancomycin)	
Discussed with prescriber	
• It was confirmed that INVANZ was prescribed • Correct drug was dispensed	

3. **While filling or before preparation**, drugs must never be identified on the basis of medication storage bin/shelf alone, as wrong drug could have been placed there.
   - ☛ In addition to checking the drug name and strength etc. it is a good practice to identify medications by their specific color, shape or size as well
4. **When new stock is received or unused drugs are returned** from patient care areas, drug name and strength must be carefully checked before placing back in the shelf/bin. Goal is to avoid placement of drugs in the wrong location (shelf or bin)
5. **Check patient parameters** (like allergy, contraindications, weight, age etc.) and **drug parameters** (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing
6. It is a good practice to use **auxiliary labels** as a reminder that the drug is a LASA drug.



7. **Double-check** before preparation and dispensing
8. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or

	prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	2. **Staff administering drugs must be aware and educated** about the risks involved with LASA drugs 3. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 4. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 5. Before administration always **check medicine in hand** against name and strength prescribed ☛ Once nursing staff receives LASA medication they should verify this with the original order to ensure they have received the correct medication. ☛ Remember: administration end is the last checkpoint to catch the error if any mistake is made at the prescribing or dispensing 6. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 7. Never use **one patient's medicines on other** patient 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 2. Any **medication error or near miss** related to LASA Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember LASA-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	1. All patients are encouraged to know the name, shape and color of the medications they are taking so that they become partners in ensuring that the correct medications are given to them 2. Nurses must not ignore patient or family's concern if raised, regarding the shape/color/appearance of medicines being administered to them. 3. If such a concern is raised, nurses must recheck the medicine, its dilution, strength, physician order (if needed) to ensure correct medicine is being administered and satisfy the patient/family accordingly 4. Same practice is to be ensured by pharmacy while dispensing medicines to patients directly

Ref:

1. List of confused drug names, February 2019, ISMP; https://www.ismp.org/recommendations/confused-drug-names-list?check_logged_in=1

2. Survey on LASA Drug Name Pairs: Who Knows What's on Your List and the Best Ways to Prevent Mix-Ups? May 2009, https://www.ismp.org/resources/survey-lasa-drug-name-pairs-who-knows-whats-your-list-and-best-ways-prevent-mix-ups

3. Look-Alike, Sound-Alike Medication Names, May 2007, WHO, https://www.who.int/docs/default-source/integrated-health-services-(ihs)/psf/patient-safety-solutions/ps-solution1-look-alike-sound-alike-medication-names.pdf?sfvrsn=d4fb860b_2&download=true

4. Guide on handling Look-Alike Sound-Alike medicines, Pharmaceutical Services Division Ministry of Health Malaysia, 2012, https://www.pharmacy.gov.my/v2/sites/default/files/document-upload/guide-handling-lasa.pdf

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.17. Liposomal forms of drugs / Lipid Based Drugs and their conventional counterparts:

Why are these high alert?

Lipid-based forms of the medication appear to have less severe toxicity, but the conventional form of the medication may be inadvertently substituted at an inappropriate dose, risking possible severe cardiotoxicity, including cardiorespiratory arrest.

How to Ensure Safe Use of Lipid Based Drugs:

Lipid Based Drugs: Pertains only to those drugs available in **both** lipid-based and conventional formulations, including Amphotericin B, Chemo drugs like DOXOrubicin **etc.***	
Storage	1. Primarily stored in the pharmacy 2. When in nurses' custody, these must be stored in medication trolley or medication fridge as appropriate depending on the storage requirements of these drugs 3. Availability of these drugs on floor stock of nursing or patient care units is **not allowed**. • **Only Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC)** of the hospital should authorize stocking of any of these drugs on patient care units (outside pharmacy) 4. When lipid based formulations are stored in healthcare setting, **storage bins should be labelled** with name of drug in **bold**, strength, warning: "High Alert medication". Brand names can be used for reference purpose after the generic name. See the example below: 5. Lipid based drugs are **sound-alike or read-alike** (or could be look-alike) with their conventional counterparts, use tall-man lettering, highlight its strength, brand name, color or shape etc. in order to correctly read/identify the drug name. See the example below: **DOXOrubicin** **10 mg** **Conventional Form** **LIPOsomal DOXOrubicin** **20 mg (DOXULIP)** **Lipid Based Form** 7. Store both conventional and lipid based drugs apart from each other and label the bins properly 8. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing lipid based drugs **CAUTION HIGH ALERT MEDICINE**

	11. **Medicines discontinued or hold by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock immediately (to avoid any accidental administration). 12. Never leave any **unlabeled syringe or infusion bag** in patient care area
Prescribing	1. Doctors who may prescribe lipid-based drugs and/or conventional counterparts have been educated about the differences between these formulations and the risk of patient harm if these products are confused with each other. 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. Check **appropriateness & clarity** of order esp. dose, rate, route of administration and duration of treatment because it differs for lipid based drugs and their conventional counterparts. 4. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Drug name, dose, rate, route, frequency, dilution, duration of therapy • Any special instructions • **Never use abbreviations**: E.g. i. Doxo 20mg in 10ml normal saline IV stat. It does not show if conventional doxorubicin was intended or liposomal doxorubicin? therefore, always write full name ii. Avoid naked decimals e.g. **.2mg** as it can be misread as **2mg** – always write **0.2 mg**. iii. Avoid trailing zero e.g. **250.0mcg** as it can be misread as **2500mcg** – always avoid trailing zero and write **250 mcg** 5. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Pharmacist and other pharmacy staff who may dispense, handle or prepare lipid-based drugs and/or conventional counterparts have been educated about the differences between these formulations and the risk of patient harm if these products are confused with each other. 2. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#). 3. It is a best practice that pharmacy dilutes the lipid based drugs in standard dilutions and dispense in **pre-mixed, ready to use form.** 4. The drug name, dose, rate, route, frequency, dilution, duration of therapy must be carefully checked and ensure that the right medicine is ordered 5. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 6. **Check necessary info**, patient parameters (like allergy, weight, contraindications, renal function etc.) and drug parameters (dose, rate, route, concentration for infusion, duration, duplications, interactions etc.) during order/prescription review while dispensing

	7. It is best practice to affix **caution stickers** / **auxiliary labels** while dispensing and storing these drugs (see storage section for detail) 8. **Double-check** the medication before dispensing 9. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. 6. is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary labs, patient parameters (like age, weight, allergy, contraindications etc.) and drug parameters (dose, rate, route, duration, duplications, interactions etc.) during order review and before administering 7. **Any unused** (or hold, discontinued) opiates must be immediately returned to original stock or pharmacy 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or hospital protocol 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Counsel and guide patient as applicable

1 ***Ref**:*

ISMP Medication Safety Self-Assessment ® for High-Alert Medications – 2017,
https://www.ismp.org/sites/default/files/attachments/2018-01/EntireAssessmentWorkbook.pdf

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.18. Moderate sedation agents, Moderate and minimal sedation agents for children

Why are these high alert?

Sedation carries some major risks that can lead to serious patient harm or even death. These include but not limited to are:

Errors in dose/route, over-sedation, failure to properly monitor the patient pre, intra and post-procedure, failure to properly assess and re-assess patient before sedation, failure to properly or timely initiate the rescue treatment including the use of reversal agents, lack of staff competency who administers and/or monitor sedation, inadequate patient education and lack of life support measures and necessary drugs and equipment in case of emergency.

How to Ensure Safe Use of Sedation (Moderate or Minimal):

Drugs use: **IV form** of DexMEDETOmidine, Midazolam, Ketamine etc.* **Oral form** of Chloral Hydrate, Midazolam etc.*	
Definition: **Minimal sedation:** A drug-induced state during which patients respond normally to verbal commands. Although cognitive function and physical coordination may be impaired, airway reflexes and ventilatory and cardiovascular functions are unaffected. **Moderate sedation**: A drug-induced depression of consciousness during which patients respond purposefully to verbal commands, either alone or accompanied by light tactile stimulation. No interventions are required to maintain a patent airway, and spontaneous ventilation is adequate. Cardiovascular function is usually maintained.	
Scope for Moderate Sedation: Unless otherwise stated, these items pertain to all moderate sedation agents (e.g., ketamine, propofol, midazolam, DexMEDETOmidine, etomidate, fentaNYL in combination with another agent(s) [e.g., midazolam, propofol], nitrous oxide in oxygen) administered to adults, neonates, and pediatric patients undergoing a procedure in any setting (e.g., hospital, surgery center, freestanding imaging facility, dental facility, private office). **Scope for Minimal Sedation:** Unless otherwise stated, these items pertain to all minimal sedation agents (e.g., midazolam, diazePAM, ketamine [using injection solution], chloral hydrate, nitrous oxide in oxygen) administered only to neonates or pediatric patients undergoing a procedure in any setting (e.g., hospital, surgery center, freestanding imaging facility, dental facility, private office). **Exclusions:** Sedation of patients undergoing mechanical ventilation in a critical care environment, or sedation used to provide analgesia to patients postoperatively or to patients with chronic painful conditions or receiving hospice/end-of-life care.	
Storage	1. Primarily stored in the pharmacy

2. When in nurses' or physician custody, these must be stored in medication trolley or medication fridge as appropriate depending on the storage requirements of these drugs
3. Availability of these drugs on floor stock of nursing or patient care units is **not recommended**.
    - Healthcare facility may allow the storage of selected drugs in patient care areas where moderate and/or minimal sedation is administered to perform certain type of procedures. This decision should be guided by the evidence, and need, as per the type and nature of the procedures performed.
    - **Only Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC)** of the hospital should authorize stocking of any of these drugs on patient care units (outside pharmacy)
4. When these drugs are stored in healthcare setting, **storage bins should be labelled** with name of drug in **bold**, strength, warning: "High Alert medication". Brand names can be used for reference purpose after the generic name. See the example below:
5. If any of these drugs are **sound-alike, read-alike or look-alike**, use tall-man lettering, highlight its strength, brand name, color or shape etc. in order to correctly read/identify the drug name. See the example below:

DexMEDETOmidine
200 mcg/2ml ***(Precidex)***
High Alert Medicine

ETOMIdate
2mg/ml ***(Etomidate Lipuro)***
High Alert Medicine

9. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing these drugs

CAUTION HIGH ALERT MEDICINE

13. **Drugs available in multiple strengths**: e.g. Ketamine (100mg and 500mg) must be carefully checked:
    - Decision must be taken to purchase only one strength for organization's use
    - Or to restrict higher strength for specific specialties or patient care areas only
    - If both strengths are purchased, actions must be taken to avoid mix-ups and wrong dose errors
14. **Medicines discontinued or hold by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock immediately (to avoid any accidental administration).
15. Never leave any **unlabeled syringe or infusion bag** in patient care area
16. **Appropriate resuscitation and reversal agents** are readily accessible and accompanied by a clear indication for when they should be used, their order of use,

	directions for administration near the point of use, and a protocol or coupled order set that permits emergency administration.
Prescribing	1. Only an **Anesthetist or practitioner trained in moderate-deep sedation** and advance life support, as determined by the organization, should prescribe these drugs ➔ It is a best practice that Practitioners involved in minimal or moderate sedation participate in at least annual reviews, simulation training of rare emergencies, and practice drills of the facility's emergency protocols to ensure proper functioning of the equipment and coordination of staff roles in such emergencies. 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. Check **appropriateness & clarity** of order esp. dose, rate, route of administration. 4. Order/prescription must be **complete and non-ambiguous**: a. i.e. proper indication, patient's drug allergy status, weight as needed b. Drug name, dose, rate, route, frequency, dilution, duration of therapy c. Any special instructions d. **Never use abbreviations**: E.g. i. Mida 10mg IV stat is not safe, always write full name "Midazolam" ii. Avoid naked decimals e.g. **.2mg** as it can be misread as **2mg** – always write **0.2 mg**. iii. Avoid trailing zero e.g. **250.0mcg** as it can be misread as **2500mcg** – always avoid trailing zero and write **250 mcg** iv. **Avoid using symbol for units** such as **50μg**, as it could be misread as **500**. Always write **50 mcg** or 50 microgram Some important considerations while prescribing: ➔ The physician planning sedation conducts a **pre-procedure assessment** of the patient that is based on predefined criteria for assessment approved by the healthcare facility ➔ During sedation and patient recovery, **supplemental oxygen and age-/size-appropriate equipment and medications that may be needed to RESCUE** or resuscitate a sedated patient are readily accessible, regardless of the location of the procedure or recovery ➔ **Protocols and order sets exist and are used to RESCUE** a patient who has entered a higher level of sedation than intended, taking into consideration factors that influence the necessity and urgency of reversal o Reversal agents are not administered electively to solely decrease patient recovery time o Patients who receive a reversal agent are monitored for signs of re-sedation for at least 90 minutes after administration of the reversal agent.

	5. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#). 2. It is a good practice that pharmacy dispenses drug in most ready to use form possible, especially for smaller doses esp. for pediatrics and neonates, 3. The drug name, dose, rate, route, frequency, dilution, duration of therapy must be carefully checked and ensure that the right medicine is ordered 4. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 5. **Check necessary info**, patient parameters (like allergy, weight, contraindications, renal function etc.) and drug parameters (dose, rate, route, concentration for infusion, duration, duplications or of other opioid analgesics and/or sedative agents, interactions etc.) during order/prescription review while dispensing 6. It is best practice to affix **caution stickers** / **auxiliary labels** while dispensing and storing these drugs (see storage section for detail) 7. **Double-check** the medication before dispensing 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **Verbal order:** During a procedure, drug names and doses communicated verbally by the prescriber are read back (or repeated back, if conditions do not allow immediate transcription of the verbal order) to the prescriber for verification before administration 6. **Drugs dilution** shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label if not to be administered immediately. ☛ **Never leave any unlabeled syringe or infusion bag** in patient care area or at patient bed side 7. It is best practice to **perform a 2nd check** for dose, dilution and rate of administration before administration 8. **Any unused** (or hold, discontinued) sedating agents must be immediately returned to original stock or pharmacy 9. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to

	medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or hospital protocol 2. **When sedation is 'Orally' administered**, it takes some time to exert the effect. Therefore, meanwhile, the patient must not be left alone and should be monitored at regular intervals as per the organization's protocol. If a family member accompanies the patient during this time period, they must be educated about warning signs and how to call for immediate help. 3. After the procedure, patients are **monitored in a recovery area** staffed with **practitioners who are trained** to monitor and recover sedated patients 4. **Predefined criteria** for adults (e.g., Aldrete Scoring System, Post-Anesthetic Discharge Scoring System), and for neonates and/or pediatric patients if applicable (e.g., ability to remain awake for at least 20 minutes in a quiet environment), exist to determine when a patient has approached a pre-sedation state and can be discharged from the facility or no longer requires post-procedure recovery monitoring. 5. A **longer period of monitoring** beyond meeting predefined criteria (as per point 3) is required for patients who have received a long-acting sedative and/or have an anatomical airway problem or underlying medical condition that might compromise blood pressure or ventilation (e.g., sleep-disordered breathing), or if the ability of the responsible adult to observe the patient after discharge is limited. 6. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 7. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	1. Patients must be briefed about the procedure, level of sedation, pain control and possible risks before the procedure (informed consent to be taken as per organizational protocol where needed) 2. Patients who are discharged post-procedure are accompanied by a responsible adult who agrees to drive the patient home; and staff reasonably confirm that a responsible adult will be available to observe the patient for the remainder of the day. 3. Patients and/or the responsible adult staying with the patient are instructed to observe for signs of rebound sedation, and when and how to seek immediate medical attention. 4. Special instructions are given to the adult responsible for neonates and/or younger pediatric patients who will be transported home, regarding the need to carefully observe the child's head position to avoid airway obstruction

1 ***Ref**:*
2 ISMP Medication Safety Self-Assessment ® for High-Alert Medications - 2017
3 *https://www.ismp.org/sites/default/files/attachments/2018-01/EntireAssessmentWorkbook.pdf*

Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan

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10.19. Neuromuscular blocking agents

Why are these high alert?

Neuromuscular blocking agents are high-alert medications because of their well-documented history of causing catastrophic injuries or death when used in error. These drugs are used during tracheal intubation, during surgery of intubated patients, and to facilitate mechanical ventilation of critically ill patients. However, neuromuscular blockers have been inadvertently administered to both adult and pediatric patients who were **not** receiving proper ventilatory assistance. Because neuromuscular blockers paralyze the muscles that are necessary for breathing, some patients have died or sustained serious, permanent injuries if the paralysis was not witnessed by a practitioner who could intervene. In short, NMBAs can only be given to already intubated patients or to assist the intubation process. (Intubation is done to put a patient on ventilator i.e. artificial breathing).

The most common type of error with neuromuscular blockers appears to be the administration of the wrong drug. Analysis of reported events showed that neuromuscular blockers were not the intended drug in approximately half of all wrong-drug errors.

How to Ensure Safe Use of NMBAs/Paralyzing Agents:

NMBAs/Paralyzing Agents: **Atracurium, CisAtracurium, Rocuronium, Succinylcholine (Suxamethonium) etc.***	
Storage	1. Primarily stored in the pharmacy in **cool temperature** (refrigeration) i.e. 2-8^{0}C. **Do not freeze** 2. When in nurses' custody, these must be stored in medication refrigerator and under **authorized access only** 3. Paralyzing agents must be **stored separate from other drugs** in the fridge (ideally in a separate lidded, labelled container), so that chances of mix-ups or accidental wrong drug picking can be avoided 4. Availability of these drugs on floor stock of nursing or patient care units is **strictly discouraged**. • **Keep only if absolutely necessary** (e.g. can consider keeping in floor stock if frequency of patient intubation is very high in certain units e.g. ER, ICUs or Operating Rooms (ORs). But should only be handled by practitioners authorized to intubate patients, e.g. anesthetists) • **Reversal agent** (Neostigmine) should also be available immediately when needed in specified patient care areas esp. ORs • **Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC)** of the hospital should authorize stocking of any NMBAs on patient care units (outside pharmacy)

➔Note: Limiting access to these products is a strong deterrent to inadvertent use.

5. When stored in healthcare setting, **storage bins should be labelled** with name of drug in **bold**, highlight warning: "Paralyzing Agents" and mention "High Alert medication". Brand names can be used for reference purpose after the generic name. See the example below:

Atracurium 50 mg/5 ml
Warning: Paralyzing Agent
High Alert Medicine

6. If any drug is **sound-alike or read-alike** with another, use tall-man lettering, highlight its strength, color or shape etc. in order to correctly read/identify the drug name. See the example below:
Suppose ***Atracurium and Cis-Atracurium*** are read-alike, so you can label the bin highlighting their different strengths and brand names for reference:

ATRAcurium
50mg/5ml
Brand: ACUron
Warning: Paralyzing Agent

CIS-ATRAcurium
10mg/5ml
Brand: CISCuron
Warning: Paralyzing Agent

Examples of Tallman lettering for read alike/sound-alike NMBAs e.g.,
ATRAcurium vs **CIS-ATRA**curium and **ACU**ron vs **CIS**curon

7. It is a best practice to label each ampule/vial of NMBAs with auxiliary colored sticker (see sample below), so that individual vial/ampule bears warning of being a Paralyzing Agent, and that wrong administration can be prevented.

Warning – Use in Intubated Patients Only
WARNING: PARALYZING AGENT
CAUSES RESPIRATORY ARREST
Isolate unused drug and send back to pharmacy immediately
High Risk Drug - High Risk Drug - High Risk Drug – High Risk Drug

➔The auxiliary label should be attached to the neck of vial/ampule so that the actual printing on the vial/ampule's body is not obscured esp. the drug name and strength (see the picture).

	 8. **NMBAs discontinued or hold by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock immediately (to avoid any accidental administration). This includes both intact vials/ampules, filled syringes and diluted infusions. 9. Never leave any **unlabeled syringe or infusion bag** containing NMBA in patient care area 10. If **pre-filled syringes** of NMBAs are needed in certain areas e.g. in Operating rooms (ORs), then the auxiliary label (as described above; point # 7), should also be used on the pre-filled syringe in addition to routine labeling of contents of the syringe.
Prescribing	1. Only an **Anesthetist or practitioner trained in intubation** and advanced life support, as determined by the organization, should prescribe NMBAs 2. Outside the OR or procedural areas, orders for NMBAs should only be part of an **intubation protocol**, or an order set to maintain a specific level of paralysis while the patient is on a ventilator only. 3. Order should include the **need for ventilation support** till NMBAs are stopped and patient is successfully extubated and ventilator is removed 4. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 5. Check **appropriateness** of paralyzing drug according to patient's condition, dose (as per patient age, weight and other physiological conditions). 6. It is a best practice to have a **pre-printed order form** for prescribing NMBAs with necessary safety checks as mentioned above (to be filled by the doctor) **7.** These should **never** be ordered on **PRN/ need basis** or **"As needed for agitation"** 8. Always **refer** to these drugs as "neuromuscular blockers" or "paralyzing agents." Never call them "muscle relaxants." 9. **Maintain adequate analgesia and sedation** during administration of neuromuscular blocking agents. Write orders for: • Eye lubrication when corneal protection is indicated • Deep vein thrombosis (DVT) prophylaxis as indicated 10. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Drug name, dose, route, frequency, duration of therapy • Any special instructions • Never use abbreviations or short forms, write full form

	11. While writing **transfer orders** for a patient who is extubated and moving out of ICU/OR/ER, never write "resume the same medications" upon patient transfer. As it can result in accidental continued administration of NMBAs even after extubation 12. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Always **question the order** if patient's location is not suggestive of likely intubation e.g. orders coming from clinics, daycare or general wards etc. should be carefully checked 3. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 4. **Check necessary info**, patient parameters (like allergy, contraindications, renal function, weight etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 5. It is a best practice that pharmacy dispenses NMBAs in **most ready to administer** form possible, and as **just-in-time** (dispense only when needed) 6. It is best practice to affix **caution stickers** / **auxiliary labels** while dispensing and storing the NMBAs (see storage section for detail) 7. **Double-check** the medication before dispensing 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. If a neuromuscular blocker has been administered, all of the drug should be **flushed** from the IV line or the line should be changed (and any source container removed) **prior to extubation**. Errors have occurred when residual drug in IV line was infused after extubation and patient was paralyzed and sustained harm 6. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. 7. Infusion must always be given with **rate controlled device** to avoid accidental free flow of infusion 8. It is a good practice to have a **2nd check** for dose, route, dilution by another staff 9. It is recommended that all **orders must be reviewed by pharmacist** first and then administered.

	• But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary labs, patient parameters (like intubation status, allergy, contraindications etc.) and drug parameters (dose, route, frequency, duplications, interactions etc.) during order review and before administering 10. **Any unused** (or hold, discontinued) NMBAs must be immediately returned to original stock or pharmacy (or discarded as appropriate) 11. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or hospital protocol 2. **Vital signs, Neuromuscular function and ventilator settings** etc. are monitored 3. Patients on prolonged paralysis with NMBAs (ventilator dependent patients) should be assessed for adequate pain relief, sedation, eye lubrication and deep vein thrombosis (DVT) prophylaxis 4. **Prevent from joint/limb injury**; Maintain careful alignment of joints and spine. Use spinal precautions during turning. Use pillows to maintain lateral neck alignment and hip abduction during repositioning. 5. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 6. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Not applicable – counsel family as and when indicated.

Ref:

1. Paralyzed by Mistakes – Reassess the Safety of Neuromuscular Blockers in Your Facility; P T. 2019 Mar; 44(3): 91-93, 107.https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6385733/;

2. STANDARD OF CARE FOR THE PATIENT ON A NEUROMUSCULAR BLOCKING AGENT https://www.lhsc.on.ca/critical-care-trauma-centre/standard-of-care-for-the-patient-on-a-neuromuscular-blocking-agent#;

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.20. Opioids

Why are these high alert?

Errors with opiates have led to serious adverse events, including severe allergic reactions, failure to control pain, over-sedation, respiratory depression, seizures, and death. Listed below are some of the error-related risks associated with opiates (IV, epidural, transdermal, oral liquid concentrates, immediate/sustained release) that have been reported:

Dosing errors (e.g. wrong infusion pump settings, giving high doses to opioid naïve patients, failure to remove previous transdermal patch when applying new, wrong IV to oral dose conversions, wrong dose errors with the use of patient Controlled Analgesia – PCA), use of **dangerous abbreviations or confusing orders**, **wrong route** (epidural vs IV), **mislabeled or unlabeled syringes** resulting in an accidental overdose, **monitoring problems** (i.e. Failure to notice respiratory depression due to insufficient, improper, or untimely monitoring of patients receiving opiates), **unsafe disposal** esp. of transdermal patches.

How to Ensure Safe Use of Opiates:

Opioids/Narcotic Drugs: **Commercially available:** Morphine Sulfate inj. and oral tablets/capsules, Fentanyl inj. and Transdermal (T/D) patches, Pethidine inj. etc.* **Compounded by pharmacy:** Morphine sulfate syrup, infusions or pre-filled syringes etc.*	
Storage	1. Primarily stored in the pharmacy strictly **under lock and key and under direct supervision of a pharmacist** 2. When in nurses' custody, these must be stored in narcotic cabinet strictly **under lock and key** and in **authorized access only** 3. Availability of these drugs on floor stock of nursing or patient care units is **strictly discouraged**. • **Keep injectable forms only if absolutely necessary** (e.g. in operating rooms (ORs), Emergency, Cath lab etc.) • **Only Drug (or Pharmacy) & Therapeutics Committee (D&TC/P&TC)** of the hospital should authorize stocking of any of these opiates on patient care units (outside pharmacy) ➔Note: Limiting access to these products is a strong deterrent to inadvertent use or misuse. 4. When stored in healthcare setting, **storage bins should be labelled** with name of drug in **bold**, strength, warning: "High Alert medication". Brand names can be used for reference purpose after the generic name. See the example below:

Fentanyl inj. 250 mcg/5 ml
High Alert Medicine

5. If any drug is **sound-alike or read-alike** with another, use tall-man lettering, highlight its strength, color or shape etc. in order to correctly read/identify the drug name. See the example below:
   Suppose ***Fentanyl T/D patch is available in 2 strengths*** as depicted below, and confusion or mix-ups can occur between the two, so label the bin highlighting their strengths and using different label colors to differentiate them further:

Fentanyl Transdermal Patch
25 mcg
High Alert Medicine

Fentanyl Transdermal Patch
50 mcg
High Alert Medicine

9. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing these drugs

CAUTION HIGH ALERT MEDICINE

6. All bags and syringes of **neuraxial opioids** (epidural/intrathecal use) and/or local anesthetics are labeled with a prominent **auxiliary warning** (e.g., For Epidural Use Only; For Intrathecal Use Only) in a large font size (e.g., greater than 20 point) on both sides of the bag or syringe

For Intrathecal use only

For Epidural Use only

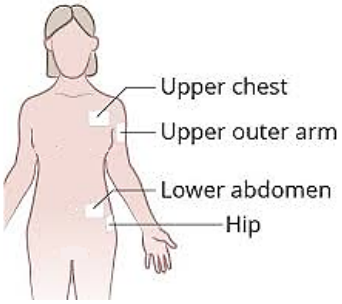
7. **Medicines discontinued or hold by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock immediately (to avoid any accidental administration). This includes both intact vials/ampules, filled syringes and diluted infusions.
8. All storage areas must keep a **complete record** of stock (i.e. quantity in hand, quantity used, wasted or returned), prescribed by, dispensed by, administered by, discarded/wasted by including witness in written form, as per the narcotic handling requirements laid down by the regulatory authority. The intent is to prevent pilferage, diversion and/or misuse.
9. Never leave any **unlabeled syringe or infusion bag** containing opiate in patient care area
10. To respond to emergencies caused by opiate overdoses, a standard protocol has been established by the healthcare facility that guides the administration of a **RESCUE agent** (i.e., naloxone) after prescriber notification; and the RESCUE

	agent is easily accessible, along with directions for use, in all clinical areas where opiates are administered. 11. Lipid (Fat) emulsion is readily accessible wherever neuraxial opioids and/or local anesthetics are administered together; and the lipid emulsion is accompanied by clear indications for when it should be used, directions for administration near the point of use, and a protocol or coupled order set that permits emergency administration
Prescribing	1. Only **authorized physicians** to prescribe narcotics can prescribe these drugs 2. Organizations should have written **opiate use protocols** in place and concerned staff (doctors, nurses and pharmacists) are trained to use it • Organization should establish protocols for pain management, including a standard pain scale for assessment, guidelines for the use of specific analgesics (indication and contraindications), standard order forms/screens, conditions requiring a dose reduction, and requirements for monitoring, use of rescue agents etc. 3. **Oral route** is a preferred and safer route of pain management and should be used if clinically indicated. IV route should be switched to oral route as soon as it is feasible to do so. 4. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 5. Check **appropriateness & clarity** of order esp. dose, rate, route of administration and duration of treatment Some important considerations while prescribing opiates are: ➔ Check if patient is **opiate naive or opioid-tolerant**. Also check if patient has a history of opioid dependency ➔ Check if patient is **already on any opioid analgesic** (e.g. Tramadol, Nalbuphine, Codeine, Buprenorphine etc.) or sedatives, that can increase the risk of sedation and/or respiratory depression ➔ Check the **equi-analgesic doses** when converting from one opioid to other or from one route to other e.g. IV / PO ➔ Ensure the **duration of use** of a single T/D patch (usually 1 patch is valid for 72hrs) ➔ Prescribe and dispense liquid medications with the **dose specified in milligrams** (not mls). ➔ Consider administration of adjuvant agents (e.g., nonsteroidal anti-inflammatory agents, gabapentin, dexMEDETOMidine) to reduce opioid use ➔ Effect of 1st patch will be evident after at least 24hrs. So during first 12 hrs period you may need to continue previous pain medicines. Assess patient accordingly ➔ Taper and discontinue opioids to avoid withdrawal symptoms 6. It is a best practice to have a **pre-printed order form** for prescribing opioids with necessary safety checks as mentioned above (to be filled by the doctor) • Especially preprinted orders for PCA. Include maximum bolus, demand, and lock-out doses and monitoring guidelines.

	• Standardize to a single type of drug (e.g., morphine) as the opiate of choice for PCA • Standardize the neuraxial opiates (epidural/intrathecal use) protocols; i.e. type of drug, type of anesthetic agent, concentration, max dose, need of preservative free product where applicable etc. 7. These should **never** be ordered on PRN/ need basis **without mentioning the frequency or ceiling dose per day.** 8. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Drug name, dose, rate, route, frequency, dilution, duration of therapy • Any special instructions • **Never use abbreviations**: E.g. i. MST 2mg in 10ml NS0.9% IV stat. MST was intended for morphine sulfate, but can be misunderstood as magnesium sulfate or any other drug. Therefore, always write full name ii. Avoid naked decimals e.g. **.2mg** as it can be misread as **2mg** – always write **0.2 mg**. iii. Avoid trailing zero e.g. **250.0mcg** as it can be misread as **2500mcg** – always avoid trailing zero and write **250 mcg** iv. **Avoid using symbol for units** such as **50μg**, as it could be misread as **500**. Always write 50 mcg or 50 microgram 9. The **dose/rate calculation and titration** shall be done based on individual patient's requirement and pain control 10. Establish protocols for **reversal agents that** can be administered without additional physician orders when warranted (use of standing orders) 11. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#). Check the prescription is valid and written by an authorized physician 2. It is a best practice that pharmacy dilutes the opioids in standard dilutions and dispense in **pre-mixed, ready to use form.** 3. When opiates are used in opioid naïve patients (esp. T/D patches), pharmacist to ensure that the dose is in safe range to avoid excessive sedation or respiratory depression 4. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 5. **Check necessary info**, patient parameters (like allergy, weight, contraindications, renal function etc.) and drug parameters (dose, rate, route, concentration for infusion, duration, duplications, interactions etc.) during order/prescription review while dispensing 6. **Never Cut the patch to dispense a certain/lower dose** as it will cause rapid leak of medicine in to the skin and may lead to overdose/death

	7. It is best practice to affix **caution stickers** / **auxiliary labels** while dispensing and storing these drugs (see storage section for detail) 8. **Double-check** the medication before dispensing 9. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare drug** in hand against drug name, strength and route mentioned in doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. If an opioid injection/infusion is prepared and diluted in patient care unit: • The **calculation** i.e. mg or mcg to be added in the given volume of diluent (e.g. NS0.9% or D5W) must be verified and ideally double checked. • Only **compatible diluent** must be used to avoid any precipitation etc. 6. **Drugs dilution** in wards shall be done by a trained nursing staff and concentration with date, time of preparation is mentioned on the label. 7. Use different infusion pumps for epidural and IV infusions 8. Label the distal ends of all access lines to **distinguish IV from epidural lines** such as: "Epidural use" or "IV use" at the point of drug administration. (this is to prevent accidental epidural administration of IV injection) 9. Infusion must always be given with **rate controlled device** to avoid accidental free flow of infusion 10. It is a best practice to have a **2nd check** by another staff of the patient, medication order, and appropriateness of the drug, dose, pump settings, and line placement for opiate infusions. 11. It is recommended that all **orders must be reviewed by pharmacist** first and then administered. • But if pharmacist's review is not possible (e.g. medicine is taken from patient care unit's floor stock) the drug must ideally be administered in presence of the prescriber • Otherwise, nursing staff to check necessary labs, patient parameters (like age, weight, allergy, contraindications etc.) and drug parameters (dose, rate, route, duration, duplications, interactions etc.) during order review and before administering 12. **For transdermal patch:**

- The **date, time, and anatomical location** of an opioid transdermal patch applied to a patient by a practitioner is documented on the patient's Medication Administration Record (MAR) and on the patch
- In inpatient settings, at **least once per shift**, staff verifies that the opioid patch is still in place on the patient's skin in the same anatomical location where it had been documented.
- Practitioners **remove any previously applied transdermal opioid** patches prior to the application of a new patch and document the patch removal on the patient's MAR
- An organizational policy on the **proper disposal of opioid patches** (e.g., use of designated waste bins, flushing down the toilet, incineration or not thrown in ordinary trash receptacles) exists and is followed
- Patch must be removed **before moving the patient for MRI scan**
  - Apply patch to **healthy skin** on a flat surface, such as chest, back, flank, or upper arm only
  - Hair at application site may be clipped (do not shave).
  - If application site must be cleaned prior to application, clean site with clear water and allow drying completely. Do not use soaps, oils, lotions, alcohol, or any other agents to cleanse skin.
  - Do not remove patch from pouch until you are very sure and ready to apply it (to avoid wastage)
  - Immediately after removal from sealed package, firmly press patch in place and hold for 30 seconds. Wash hands immediately with soap and water after applying patch
  - If there is difficulty with patch adhesion, the edges of the system may be taped in place with first-aid tape. If there is continued difficulty with adhesion, an adhesive film dressing that is see-through (e.g. Tegaderm) may be applied over patch.



- **One patch is for 72 hours (3 days).** Do not reuse patch if it falls off before 72 hrs. Use new patch and apply on different site
- Do not use **damaged or leaking patches**
- **Never Cut the patch** as it will cause rapid leak of medicine into the skin and may lead to overdose/death

13. **Any unused** (or hold, discontinued) opiates must be immediately returned to original stock or pharmacy (or discarded as appropriate with witness documentation)
14. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to

	medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out **as per physician orders or hospital protocol** • i.e. vital signs, pain score, respiratory rate, quality of respiration, sedation level etc. 2. Establish **guidelines for appropriate monitoring** of patients who are receiving opiates, including frequent assessment of the quality of respirations (not just a respiratory rate) and specific signs of over sedation. • Ensure resources (personnel and equipment) are available to monitor patients per established guidelines. • Use standardized formats for documenting pain control and monitoring values. • Ensure that oxygen and naloxone are available where opiates are administered • Do not rely on pulse oximetry readings alone to detect opiate toxicity. Use capnography to detect respiratory changes caused by opiates, especially for patients who are at high risk (e.g., patients with sleep apnea, obese patients). 3. **Predefined discharge/transfer criteria** for adults, neonates, and/or pediatric patients exist to make clear the minimum amount of time that a patient must be monitored after receiving opioids, and the level of alertness and respiratory adequacy required to be discharged from the facility or transferred from the procedural/operative area 4. **Fetal heart rate patterns** are monitored at facility-defined frequencies by a qualified practitioner immediately before, during, and after administration of neuraxial analgesia during labor and delivery 5. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 6. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	1. Administer opiates to reach a pain score mutually agreed upon by patient and clinicians prior to procedures to avoid unrealistic expectations of no pain and reduce the risk of over-sedation. 2. Instruct patients who use fentanyl patches to apply them properly, avoid heat exposure, avoid secondary exposures to other family members through their in contact clothes or by laying close together, and to store and dispose of the patches in a secure manner to avoid unintended access by children, pets, or drug-seeking individuals. 3. Dispose of used patches by folding sticky sides together and then discard.

	4. Educate patients and families about PCA preoperatively, preferably before admission when patients are alert, not after they have received anesthesia. Teach patients how to use PCA, and warn against dosing by proxy. 5. Patients receive verbal and written information at an appropriate reading level and in their preferred language about the signs and symptoms of an epidural abscess or post-dural puncture headache and what to do if it occurs since patients may be discharged before the onset of symptoms

***Ref**:*

1. HIGH ALERT Medication Feature: Reducing Patient Harm from Opiates – ISMP, 2007, https://www.ismp.org/resources/high-alert-medication-feature-reducing-patient-harm-opiates
2. ISMP Medication Safety Self-Assessment ® for High-Alert Medications – 2017, *https://www.ismp.org/sites/default/files/attachments/2018-01/EntireAssessmentWorkbook.pdf:*

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.21. Parenteral nutrition / Total Parenteral Nutrition (TPN):

Why are these high alert?

Includes: TPN (Total Parenteral Nutrition) or PPNs (Partial Parenteral Nutrition); collectively termed as Parenteral Nutrition (PN) in this document;

PN is a complex product comprising of usually multiple ingredients and components (many of which are high alert itself such as concentrated electrolytes, Dextrose 25% and above, Insulin and/or heparin etc.); these can have dosing implications or interaction potentials, moreover any error in prescription, preparation or compounding of PN, administration and proper patient monitoring can lead to serious harm to the patients.

Further anticipated adverse effects of PN include complications associated with intravenous access (e.g., thrombosis, bloodstream infection) and metabolic homeostasis (e.g., hyper- or hypoglycemia, fluid and electrolyte disorders) etc.

Some errors reported in the literature regarding PN related errors include:

- Calcium/phosphorus precipitation (wrong sequence of compounding)
- Wrong dextrose concentration; leading to severe hypo/hyper-glycemia
- Confusion of 5% dextrose with concentrated potassium chloride;
- Catheter misconnections; Infusion of PN via an epidural catheter or peripheral vs central line administration
- Hyperkalemia
- Hypermagnesemia
- Iron overload
- Zinc overdose
- Insulin/heparin additives (due to confusion with units and dosage designations)

Three organizations American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.), the American Society of Health-System Pharmacists (ASHP), and the National Advisory Group have published guidelines for ordering, transcribing, compounding and administering PN that should be referred while developing local TPN guidelines.

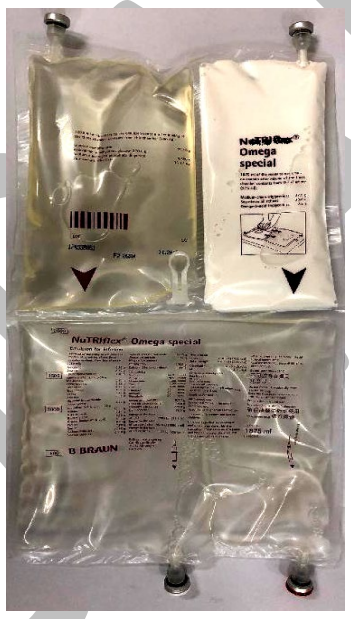
How to Ensure Safe Use of TPN/PN:

TPN/PPN (PN) includes:

Commercially available in standard formulation or can be compounded by pharmacy as per individual patient need.

Storage

1. Commercially available PN bags must be stored as per manufacturer's recommended optimum temperature and humidity limits within pharmacy
2. **Central line** PN bags must be stored separately from **Peripheral line** PN bags
3. **Lipid containing** bags must be stored away from **Lipid free** PN bags
4. When prepared against physician order, the compounded bag should be dispensed as soon as possible due to **limited stability** (24-48hrs; refer to specific product for details).
    - However, if any delay is anticipated, it should ideally be stored in cool temperature (2-8^{0}C) until dispensed.
    - Also, these must be hanged for infusion as soon as possible due to limited stability (24 hrs). If any delay is expected in administration, store in medication fridge meanwhile.
5. Availability of PN bags on floor stock of nursing or patient care units is **not allowed**.
6. Brand names of commercially available PN bags can be confusing and risk of wrong dispensing remains. So in addition to their brand names boldly label them as per their **number of chambers** (2 or 3) and **presence of lipids** (or not) in the bag. See the example below:

	
3 chambered bag	**2 chambered bag**
Lipid containing	**Lipid Free**

9. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing PN bags

CAUTION HIGH ALERT MEDICINE

	17. **If PN orders discontinued or hold by doctor,** bags must be stored away from active medicines due for administration, and discarded as per hospital policy (to avoid any accidental administration).
Prescribing	1. Doctors who may prescribe PN, have been **educated** about the proper prescribing protocols and are **trained** to monitor and manage complications of PN therapy. 1. Remember, **oral and/or enteral nutrition are the preferred options**. As parenteral nutrition (PN) is an invasive, expensive and high risk, thereby it must be used for specific clinical indications when it is not possible to meet nutritional requirements via the GI tract or when there is bowel dysfunction resulting in inability to tolerate enteral nutrition for a prolonged time 2. **Ordering Pre-requisites:** Ordering physician is responsible to ensure that: • Patient is a **right candidate** for parenteral nutrition • PN is **used with caution** in patients with electrolyte imbalance, renal or hepatic compromise, and metabolic acidosis, or alkalosis. Major Acid-base and electrolyte abnormalities should be corrected prior to starting PN, or corrected by infusions through a separate intravenous line. • PN should not be used to correct metabolic imbalances • Hospitalized patients especially children are at high **risk for malnutrition**. Physician is responsible to perform basic nutritional assessment before the start of PN (clinical dietician consult can be called where required) and repeating nutritional assessment at regular intervals or as the clinical situation changes. • A complete **nutritional assessment** includes underlying disease, a dietary history, anthropometrics, metabolic status, and an estimate of the nutritional & fluid requirements for the individual patient. 3. **Route of administration of PN:** • A **central venous access** is required if: Nutrients osmolality > 900 mOsm/L is required to be infused –and- If patient is likely to need parenteral nutritional support for more than two weeks • **Peripheral catheters** are only appropriate for infusions of PN with osmolarity up to 900 mOsm/L, and lines need to be replaced frequently. These limitations mean that they can be used for PN in conjunction with partial enteral feeds, and only for a short time (few days to one week). 4. PN must be ordered on **pre-printed order form** specific to adult and pediatric (and neonatal) PN 5. Must **verify correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 6. Check baseline **lab reports** before starting PN, including renal and hepatic functions, lipid profile and serum electrolytes as indicated, and repeat periodically thereafter (see monitoring section for details) 7. Check **appropriateness & clarity** of order esp.: • PN's **micro** (Electrolytes, mineral, vitamins) and **macro** (Carbohydrate, Amino acid, Fat/Lipid) **contents** • Any **additives**: e.g. insulin, heparin or albumin etc.

	• **Clearly specify dose** of each ingredient in total 24hrs volume, with special focus on units of doses (mcg vs mg vs gm) mentioned, and their max limits per day, and as per weight and age of the patient. • Use only **standard unit of measure** as allowed by the organization for ordering electrolytes (mEq vs mMol for example) • Total **Calories** per 24hrs PN, • Total **volume** (mls) per 24hrs PN, • **Route** of administration (central/peripheral) and, • Expected **duration** of treatment with PN etc. 8. Order/prescription must be **complete and non-ambiguous**: • i.e. proper indication, patient's drug allergy status, weight as needed • Any special instructions • **Never use abbreviations/short forms e.g.**: i. Potassium 20mEq. It does not specify if potassium phosphate was intended or potassium chloride? therefore, always write full name ii. Never use chemical name e.g. KCl, always write full name: Potassium Chloride iii. Avoid naked decimals e.g. **.2mg** as it can be misread as **2mg** – always write **0.2 mg**. iv. Avoid trailing zero e.g. **250.0mcg** as it can be misread as **2500mcg** – always avoid trailing zero and write **250 mcg** 9. **If the PN is hold** due to any reason, review other drugs (especially Insulin) that can effect blood glucose levels and lead to hypoglycemia in absence of carbohydrate source (PN). 10. If insulin is ordered to be added in PN, check the possible duplication of insulin orders other than PN as well. 11. **Promote Culture of Safety**: Given the high risk associated with PN if any staff (doctor, pharmacist or nurse) or patient shows concern related to it or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. All PN orders should preferably be received in Compounding pharmacy by the **cut-off time limit** defined on daily basis. This will ensure safe PN preparation by a trained team and saving wastage of ingredients used in compounding of PN. 2. Must **verify correct patient** before preparation and dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#). 3. All PN preparation will be done under **strict aseptic measures** in laminar flow hood 4. **No additive** shall be added in PN bag outside laminar flow hoods or on nursing floor/wards/patient home 5. PN orders will be **reviewed for appropriateness** and completeness by the designated PN pharmacist. In case of incorrect, ambiguous or incomplete order, hold preparation and clarify the order with the prescriber. Always confirm – never assume. • **Amended/corrected PN form's** copy is to be sent along with PN bag to the ward, in order for nurses to be aware of the necessary changes

	6. Check necessary patient parameters (like allergy, weight, contraindications, renal function, lab test etc.) and PN parameters (dose, rate, route, volume, calories, osmolarity, duration, duplications, interactions etc.) during order/prescription review before preparation 7. Pharmacy will do the **calculations** for 'ml' of each ingredient to be added in PN bag as per dose mentioned in PN request form and strength available. • These calculations should be double-checked to avoid any calculation errors • PN recipe / Calculation sheet is given to pharmacy staff for preparation • Ingredients will be verified through calculation sheet or verification checklist. 8. **After preparation** PN bags are clamped securely inside hood, checked for any precipitates, discoloration or leakage etc. 9. Pharmacist will check **final weight** of PN bag and match it with the total 'ml' of PN required/ordered 10. Label is prepared and pasted on the PN bag while ensuring minimum of following information on the label: • Correct patient identity (name + MR#) • Ingredients name and quantity added • Total Volume (ml) • Highlight Route (Central vs Peripheral) • Addition of lipid (yes/no) • Correct date and time of preparation and expiry date • Correct rate of administration (ml/hour) 11. All PN prepared bags solutions are to be individually and appropriately **transported** to respective wards (or handed over to OPD patients with handling, storage and transport instructions) 12. It is best practice to affix **caution stickers** / auxiliary labels while dispensing (see storage section for detail) 13. **Promote Culture of Safety**: Given the high risk associated with PN if any staff (doctor, pharmacist or nurse) or patient shows concern related to prescription or preparation, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Always **compare PN** in hand against actual doctor's order before administration 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. **No additive** shall be added in PN bag outside pharmacy, on a nursing floor/ward or patient home 6. **Amended/corrected PN form's copy** shall be dispensed along with prepared PN bag to the ward. Nurse will ensure that this copy is attached in the patients' file 7. PN should be administered via a **volumetric infusion pump**, NOT by gravity.

	• PN should ideally be administered via a dedicated lumen • Route (central vs peripheral line) is confirmed before PN administration • Catheter patency can be confirmed by a manual saline flush. The catheter should be gently aspirated to obtain flashback of blood prior to the administration of hypertonic solutions 8. **Standard Cannula site care** should be provided and regularly checked for any cannula site reaction 9. PN is typically administered as a **continuous infusion over 24 hours** unless otherwise ordered. If rate is altered by physician (change from actual order), nurses will mention the new rate on a separate sticker, with date, time and sign and will paste on PN bag • The PN solution bag must be changed after 24 hours (or as recommended by manufacturer), irrespective of the amount of residual PN solution left in the bag, and the bag is discarded • PN administration sets must be changed every 24 hours, with each bag change. Sterile technique, utilising dressing pack and sterile gloves when changing administration sets and bags, must be maintained. Chlorhexidine 2% must be used with any manipulation of administration sets/connections. • Catheter patency should always be confirmed during a line change. Label and date administration sets 10. **Any unused** (or hold, discontinued) PN must be immediately stopped and discarded as per hospital policy 11. **Promote Culture of Safety**: Given the high risk associated with PN if any staff (doctor, pharmacist or nurse) or patient shows concern related to prescription or preparation, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is to be carried out as per physician orders or hospital protocol; but generally includes: • Electrolytes (Na, K, Mg, Cl **daily** – Phosphorus **alternate days**) • Liver function test (ALP, AST, ALT, Bilirubin **weekly**) • **Baseline** Triglycerides level (then **weekly or until stable** or whenever changes in lipid dose is made) • Creatinine (**weekly**) • Blood glucose level (**daily**) • Albumin level as needed • Fluid intake and output (esp. with signs of fluid overload) • Patient Weight monitoring • Infusion site reactions • Fever and signs of infection 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization.

	3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Counsel and guide patient as applicable and especially if PN is being administered in home setting. General patient education points should include: 1. How PN is ordered and what important labs test are to be done regularly 2. How PN can be safely administered 3. Complications related to PN 4. How to monitor patient while on PN therapy 5. How to transport and store the PN bag 6. Warning signs and common administration issues for which help should be sought etc.

Ref:

1. Total Parenteral Nutrition, Multifarious Errors; 2013, https://psnet.ahrq.gov/web-mm/total-parenteral-nutrition-multifarious-errors

2. Patient Safety Tip of the Week April 21, 2020 - Parenteral Nutrition Safety Issues https://www.patientsafetysolutions.com/docs/April_21_2020_Parenteral_Nutrition_Safety_Issues.htm

3. Parenteral Nutrition Safety, April 15, 2020; https://www.pharmacypracticenews.com/Review-Articles/Article/04-20/Parenteral-Nutrition-Safety/57830

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10.22. Oxytocin injection

Intravenous (IV) oxytocin used antepartum is indicated: to induce labor in patients with a medical indication, to stimulate or reinforce labor in selected cases of uterine inertia, and as an adjunct in the management of incomplete or inevitable abortion. Used postpartum, IV oxytocin is indicated: to produce uterine contractions during expulsion of the placenta and to control postpartum bleeding or hemorrhage. However, improper administration of oxytocin can cause hyperstimulation of the uterus, which in turn can result in fetal distress, the need for an emergency cesarean section, or uterine rupture.

In February 2020, ISMP analyzed 52 voluntary reports associated with oxytocin submitted to the ISMP National Medication Errors Reporting Program (ISMP MERP) between 1999 and 2019. About 10% of the reports described more than one oxytocin error that had occurred. About 44% of the reported events originated during dispensing, with many relating to mix-ups between oxytocin and look-alike product vials. About a quarter (23%) originated during administration, and 13% during prescribing. Overall, about 8% of the reports were hazards that did not result in errors. A quarter (25%) of all events resulted in maternal, fetal, or neonatal harm.

How to Ensure Safe Use of Oxytocin:

It includes*: Oxytocin 5 International Unit (IU) per ml injection	
Storage	1. Primarily stored in the pharmacy as per manufacturer's storage instructions (mainly in refrigerator at 2-8^{0}C) 2. When in patient care unit, must be stored in **authorized access only** 3. Availability of oxytocin on floor stock of nursing or patient care units is generally **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance. Or in Labor & Delivery units only) • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of oxytocin on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with brand and generic name and strength in **bold** to avoid mix-ups. 5. To avoid errors with **Look-Alike**, **sound-alike or read-alike** appearance against any other drug available in the inventory, use recommended techniques for proper differentiation e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc. • Each facility should **identify possible Look-Alike and Sound-Alike drugs** with Oxytocin (both brand name or generic name wise) and preventive

	actions must be taken to avoid mix-ups and accidental wrong drug administration 6. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration)
Prescribing	1. To be **prescribed only by** physicians with Obstetric/Gyne training 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. It is recommended that oxytocin is prescribed as per **standard protocol or guidelines** defined by the organization for managing labor and listed indications ☛ Best practice requires the use of standard order sets for prescribing oxytocin antepartum and/or postpartum that reflect a standardized clinical approach to labor induction/augmentation and control of postpartum bleeding. Include administration requirements, patient monitoring, standard treatment of oxytocin-induced uterine tachysystole and other safety measures. ☛ Use of standard order sets will also reduce drug selection errors during prescribing 4. Ensure **appropriateness of order** as per patient age, weight and other physiological conditions. 5. Order/prescription must be **complete and non-ambiguous** i.e.: ☛ Proper indication, patient's drug allergy status, weight, age as needed ☛ Any special instructions ☛ **Prescribe safely e.g.**: o **Clearly write name, dose, route and rate of administration** o **Never use abbreviations or short forms.** E.g. **"Oxy or OXT**": write full form i.e. 'Oxytocin' o **Avoid naked decimals** e.g. **.5 units** as it can be misread as **5 units** – always write **0.5 unit** o **Avoid trailing zero** e.g. **10.0 units** as it can be misread as **100 units** – always avoid trailing zero and write **10 units** o **Avoid using symbol for units** such as **5U or 5IU**, as it could be misread as **50 or 510**. Always write **5 UNITs** o When selecting drugs from **computerized order entry system**, type full name (Oxytocin) or at least first 4 letters: OXYT, in order to avoid selection of wrong drug with similar first letters e.g. Oxycodone or brand names of other drugs starting with OXY etc. o **Standardize how oxytocin doses, concentrations, and rates are expressed**. Always communicate orders for oxytocin infusions in terms of the dose rate (e.g., milliunits/minute) to lessen the opportunity for misinterpretation. 6. **Standing orders**: specific orders to be written: ☛ To monitor patient's response to these drugs (see monitoring section); including when and how frequently to be done. ☛ When to hold infusion and when to notify physician etc.

	7. **Incomplete hand-offs at transitions of care.** The lack of clear communication and/or documentation during transitions of care are also a key contributor to oxytocin incidents. 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check patient parameters** (like allergy, contraindications, weight, age etc.) and **drug parameters** (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. **If a prescription is generated from a non-labor & delivery unit, or for a patient who is not apparently pregnant, always verify with physician before dispensing.** Possibility is there that Oxytocin was not the intended drug in that prescription (either name is misread or mistakenly written/ordered) 5. Where possible pharmacy should prepare, dilute and dispense Oxytocin in **ready-to-use form.** o Standardize to a single concentration/bag size for both antepartum and postpartum oxytocin infusions (e.g., 30 units of oxytocin in 500 mL of Lactated Ringer's) o Before dispensing of the bags to patient care units, boldly label both sides of the bags to differentiate them from plain hydrating solutions and magnesium infusions. 6. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing Oxytocin **CAUTION HIGH ALERT MEDICINE** 7. **Double-check** before dispensing 8. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Before administration always **check medicine in hand** against name and strength prescribed 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. If oxytocin infusions must be prepared on patient care units (instead of pharmacy), an **independent double check** of the preparation is recommended

	6. **Dilution and preparation** of infusion must be done by a trained nursing staff and infusion must be **immediately labeled** with Oxytocin concentration on the bag ☛ Unlabeled infusion bags containing Oxytocin can lead to serious patient or fetal harm ☛ Standardize to a single concentration/bag size for both antepartum and postpartum oxytocin infusions (e.g., 30 units of oxytocin in 500 mL of Lactated Ringer's) 7. Administer by IV infusion using **infusion/rate control device** ☛ Mix-ups of IV lines (e.g. between Oxytocin infusion and that of IV fluid bag like Ringer's Lactate or other infusions in progress during labor like Magnesium Sulphate etc.) and misconnections to the wrong infusion pump have resulted in drug or dose errors and omissions. ☛ Use smart infusion pump drug library to prevent dosing and rate related errors where possible 8. **Incomplete hand-offs at transitions of care.** The lack of clear communication and/or documentation during transitions of care are also a key contributor to oxytocin incidents. 9. Never use **one patient's medicines on other** patient 10. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. It is essential to monitor patient fluids (both intake and outtake) while administering oxytocin and the frequency of uterine contractions, patient blood pressure, and heart rate of the unborn fetus. 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Educate and guide the patient generally about labor induction and related procedures for a successful and safe outcome.

Ref:

1. Errors Associated with Oxytocin Use: A Multi-Organization Analysis by ISMP and ISMP Canada, February 13, 2020, https://www.ismp.org/resources/errors-associated-oxytocin-use-multi-organization-analysis-ismp-and-ismp-canada

2. Oxytocin, Eva V. Osilla, July 2021, NCBI Bookshelf, https://www.ncbi.nlm.nih.gov/books/NBK507848/

3. Induction of labor with Oxytocin, William Grobman, Feb 2022, https://www.uptodate.com/contents/induction-of-labor-with-oxytocin#H81827198

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.23. Vasopressin

Vasopressin is an antidiuretic hormone released from the posterior pituitary gland. Commercial injections of vasopressin are used in conditions like Vasodilatory Shock refractory to the application of fluids and catecholamines and certain other off-label indications. Vasopressin is high alert medicine because of reported serious patient harm as a result of dosing errors, wrong rate of infusion and mix-ups between Look-Alike or Sound-Alike products.

In large doses, it may cause increased blood pressure (BP), bradycardia, arrhythmias, heart block, peripheral vascular constriction or collapse, coronary insufficiency, decreased cardiac output, myocardial ischemia, or myocardial infarction (MI).

How to Ensure Safe Use of Vasopressin:

It includes*: Vasopressin 20 Units per ml injection	
Storage	1. Primarily stored in the pharmacy 2. When in patient care unit, must be stored in **authorized access only** 3. Availability of Vasopressin on floor stock of nursing or patient care units is generally **discouraged**. • **Keep only if absolutely necessary** (e.g. in case pharmacy is closed or at distance. Or in critical care, resuscitation units only) • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of vasopressin on patient care units (outside pharmacy) 4. When stored in healthcare facility, **bins should be labelled** with brand and generic name and strength in **bold** to avoid mix-ups. 5. To avoid errors with **Look-Alike**, **sound-alike or read-alike** appearance against any other drug available in the inventory, use recommended techniques for proper differentiation e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc. • Each facility should **identify possible Look-Alike and Sound-Alike drugs** with Vasopressin (both brand name or generic name wise) and preventive actions must be taken to avoid mix-ups and accidental wrong drug administration 6. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration)
Prescribing	1. To be **prescribed by** physicians with critical care training 2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. It is recommended that vasopressin is prescribed as per **standard protocol or guidelines** defined by the organization for managing refractory vasodilatory shock

	☛ Best practice requires the use of standard order sets for prescribing vasopressin and dose titration and monitoring of patient's response ☛ Use of standard order sets will also reduce drug selection errors during prescribing 4. Ensure **appropriateness of order** as per patient age, weight and other physiological conditions. 5. Order/prescription must be **complete and non-ambiguous** i.e.: ☛ Proper indication, patient's drug allergy status, weight, age as needed ☛ Any special instructions ☛ **Prescribe safely e.g.**: o **Clearly write name, dose, route and rate of administration** o **Never use abbreviations or short forms.** E.g. **"Vaso or VSP"**: write full form i.e. 'Vasopressin' o **Avoid naked decimals** e.g. **.03 units** as it can be misread as **3 or 0.3 units** – always write **0.03 unit** o **Avoid using symbol for units.** Don't write 'u', write full form as 'units' o **Standardize how vasopressin doses, concentrations, and rates are expressed**. Always communicate orders for vasopressin infusions in terms of the dose rate (e.g. units/minute) to lessen the opportunity for misinterpretation. o Titrate to **lowest dose compatible** with clinically acceptable response o The **vasopressin doses are usually minute** like 0.03units/min or 0.005units/min. If not clearly written or ordered, it can result in several fold high dose e.g. 0.03 unit can be misunderstood as 0.3 units (a 10-folds high dose). - To avoid such mishaps, it is a best practice to verify correct dose / rate administered on daily basis while rounding on patient bedside - Verbal orders must be avoided 6. **Standing orders**: specific orders to be written: ☛ To monitor patient's response to these drugs (see monitoring section); including when and how frequently to be done. ☛ When to taper or hold infusion and when to notify physician etc. 7. **Incomplete hand-offs at transitions of care.** The lack of clear communication and/or documentation during transitions of care are also a key contributor to vasopressin incidents. 8. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check patient parameters** (like allergy, contraindications, weight, age etc.) and **drug parameters** (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing

	4. **If a prescription is generated from a non-intensive care unit, or for a patient without the related indications/diagnosis, always verify with physician before dispensing.** Possibility is there that Vasopressin was not the intended drug in that prescription (either name is misread or mistakenly written/ordered) 5. Where possible pharmacy should prepare, dilute and dispense Vasopressin in **ready-to-use form.** 6. The **Vasopressin doses are usually small** like 0.03units/min or 0.005units/min. If not properly calculated and prepared, it can result in several fold high dose e.g. 0.03 unit can be misunderstood as 0.3 units (a 10-folds high dose). o To avoid such mishaps, verify correct dose from physician order o Verbal orders must be avoided 7. It is a good practice to paste **caution stickers** (High Alert Medicine) while dispensing vasopressin **CAUTION HIGH ALERT MEDICINE** 8. **Double-check** before dispensing 9. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts 3. Before administration always **check medicine in hand** against name and strength prescribed 4. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 5. If Vasopressin infusions must be prepared on patient care units (instead of pharmacy), an **independent double check** of the preparation is recommended 6. **Dilution and preparation** of infusion must be done by a trained nursing staff and infusion must be **immediately labeled** with Vasopressin concentration on the bag 7. The **Vasopressin doses are usually minute** like 0.03units/min or 0.005units/min. If not properly calculated and prepared, it can result in several fold high dose e.g. 0.03 unit can be misunderstood as 0.3 units (a 10-folds high dose). ☛ To avoid such mishaps, it is a best practice to verify correct dose / rate administered on daily basis esp. at the time of shift change ☛ Verbal orders must be avoided 8. Administer by IV infusion using **infusion/rate control device** ☛ Use smart infusion pump drug library to prevent dosing and rate related errors where possible 9. **Incomplete hand-offs at transitions of care.** The lack of clear communication and/or documentation during transitions of care are also a key contributor to vasopressin incidents. 10. Never use **one patient's medicines on other** patient

	11. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. Monitor fluid intake and output closely, especially in comatose or semicomatose patients. 2. Monitor electrolyte balance periodically. 3. Perform ECGs periodically during therapy. 4. Observe for early signs of water intoxication (e.g., drowsiness, listlessness, headache, confusion, anuria, weight gain). 5. Monitor serum electrolytes, fluid status, and urine output after vasopressin discontinuation. 6. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 7. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Not applicable

Ref:

1. Getting to the Root of the Matter, Scott A. Flanders, June 2005, PSNet, https://psnet.ahrq.gov/web-mm/getting-root-matter
2. Vasopressin, DrugBank online; https://go.drugbank.com/drugs/DB00067
3. Vasopressin, Drugs.com, https://www.drugs.com/monograph/vasopressin.html

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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10.24. Promethazine inj:

Promethazine injection is a commonly used injectable product that possesses antihistamine, sedative, anti-motion sickness, and anti-emetic effects. The drug is also a known vesicant that is highly caustic to the intima of blood vessels and surrounding tissue. Although deep intramuscular (IM) injection into a large muscle is the preferred parenteral route of administration, the product may be given by slow IV push, the method typically used in most hospitals. Internationally, several serious, tragic, local injuries after infiltration or inadvertent intra-arterial injection of promethazine inj. have been reported.

Severe tissue damage can occur regardless of the route of parenteral administration, although IV and inadvertent intra-arterial or subcutaneous (SC) administration results in more significant complications, including burning, erythema, pain, swelling, severe spasm of vessels, thrombophlebitis, venous thrombosis, phlebitis, nerve damage, paralysis, abscess, tissue necrosis, and gangrene. Sometimes a surgical intervention, such as fasciotomy, skin graft, and even amputation, has been required.

How to Ensure Safe Use of inj. Promethazine:

It includes*: Promethazine inj. 25mg/ml	
Storage & Procurement	1. Primarily stored in the pharmacy 2. When in patient care unit, must be stored in **authorized access only** 3. Availability of promethazine on floor stock of nursing or patient care units is generally **discouraged**. • **Drug (or Pharmacy) & Therapeutic Committee (D&TC/P&TC)** of the hospital should authorize stocking of promethazine on patient care units (outside pharmacy) 4. **Limiting the concentration**. Because 25 mg/mL is the highest strength of promethazine that can be given intravenously, only this concentration (not 50 mg/mL) should be stocked in inventory. 5. When stored in healthcare facility, **bins should be labelled** with brand and generic name and strength in **bold** to avoid mix-ups. 6. To avoid errors with **Look-Alike**, **sound-alike or read-alike** appearance against any other drug available in the inventory, use recommended techniques for proper differentiation e.g. tall-man lettering, bold labeling of bins/shelves, storing apart, use of brand names as a reference and use of auxiliary/colored labels etc. 7. **Drugs discontinued or changed by doctor** must be stored away from active medicines due for administration, and sent back to pharmacy or returned to stock without any delays (to avoid any accidental administration)

Prescribing	1. **Prescribers must be aware and educated** about the risks involved with inj. Promethazine
	  ○ **Use oral route or alternate safer drugs** where possible to avert the dangers of injection promethazine
	2. Must verify **correct patient** before ordering (use two identifiers i.e.: patient name & Medical Record # (MR#)
	3. Ensure **appropriateness of order** as per patient age, weight and other physiological conditions.
	4. Order/prescription must be **complete and non-ambiguous** i.e.:
	  ☛ Proper indication, patient's drug allergy status, weight, age as needed
	  ☛ Any special instructions
	  ☛ **Prescribe safely e.g.**:
	  ○ **Clearly write name, dose, route and rate of administration**
	  ○ **Never use abbreviations or short forms.** Always write full form
	  ○ **Limiting the dose**. Promethazine 6.25 to 12.5 mg should be considered the starting IV dose, especially for elderly patients.
	  ○ **Give instructions to dilute and administer slowly** via IV route
	5. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.

Dispensing	1. Must verify **correct patient** before dispensing (use two identifiers i.e.: patient name & Medical Record # (MR#) 2. In case of incorrect, ambiguous or incomplete order, hold dispensing and **clarify the order** with the prescriber. Always confirm – never assume. 3. **Check patient parameters** (like allergy, contraindications, weight, age etc.) and **drug parameters** (dose, route, frequency, duplications, interactions etc.) during order/prescription review while dispensing 4. Use **auxiliary labels** as a reminder that the drug is a vesicant and that it should be diluted and should be administered slowly through a running IV tube.  5. **Double-check** before dispensing 6. **Promote Culture of Safety**: Given the high risk associated with this medicine if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Administration	1. **Staff administering inj. promethazine must be aware and educated** about the risks involved 2. Must **verify correct patient** before administration (use two identifiers i.e.: patient name & Medical Record # (MR#) 3. Follow the **6 rights of safe drug administration**: Right patient, Right medication, Right dose, Right time, Right route, Right documentation in charts

	4. Before administration always **check medicine in hand** against name and strength prescribed 5. In case of incorrect, ambiguous or incomplete order, **clarify the order** with the prescriber (or pharmacy) first. Always confirm – never assume. 6. **Diluting the drug**. Further dilution of the 25-mg/mL strength is required to reduce vesicant effects and to enable slow administration. For example, the drug can be diluted in 10 to 20 mL of normal saline if it is to be given via a running IV line. Alternatively, it can be prepared in mini-bags containing normal saline if the pharmacist has time to dispense them as needed for individual patients. Extravasation is also recognized more quickly when promethazine is diluted than when it is given in a smaller volume. 7. **Using large patent veins**. Promethazine should be administered only via a large-bore vein, preferably via a central venous access site, not by veins in the hand or wrist. The patency of the access site should be checked before administration. According to the package insert, aspiration of dark blood does not preclude intra-arterial placement of the needle because blood can become discolored upon contact with promethazine. The use of syringes with rigid plungers or small-bore needles might obscure typical arterial backflow if practitioners rely on this method alone. The medication should be injected through a running IV line at the port that is farthest from the patient's vein. 8. **Administering the drug slowly**. IV promethazine can be administered over 10 to 15 minutes. 9. Never use **one patient's medicines on another** patient 10. **Promote Culture of Safety**: Given the high risk associated with these medicines if any staff (doctor, pharmacist or nurse) or patient shows concern related to medication or prescription, carefully review it along with them and resolve the confusion in timely, professional and courteous manner.
Monitoring	1. Monitor for any **signs of extravasation** or **patient's complaint** of burning or pain at injection site. 2. Any adverse drug reaction (**ADR**) noticed shall be communicated to the physician (or pharmacy) immediately and is reported as per ADR reporting policy of the organization. 3. Any **medication error or near miss** related to High Alert Medications must be reported without the fear of punitive/disciplinary action. Once errors are reported actions must be taken to prevent similar errors in future (Remember high alert medicine-related errors can be fatal so harm can only be minimized if these are reported and concrete preventive steps are implemented so that other patients remain safe)
Patient Education	Before administration, patients should be advised to let the practitioner know immediately whether burning or pain occurs during or after the injection.

Ref:

1. Preventing Serious Tissue Injury with Intravenous Promethazine (Phenergan), Matthew Grissinger, April 2005, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2697094/

2. ISMP 2018-19 Targeted Medication Safety Best Practices for Hospitals Webinar – January 18, 2018 Questions and Answers, https://www.ismp.org/sites/default/files/attachments/2018-03/TMSBP%20webinar%202018%20Q%26A%20.pdf

3. Promethazine Conundrum: IV Can Hurt More Than IM Injection!, November 2, 2006, https://www.ismp.org/resources/promethazine-conundrum-iv-can-hurt-more-im-injection

**Medicines' availability status changes from time to time in market, hence refer to the current registered and available products of this class in Pakistan*

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11. SAMPLE HIGH ALERT MEDICINE LISTS:

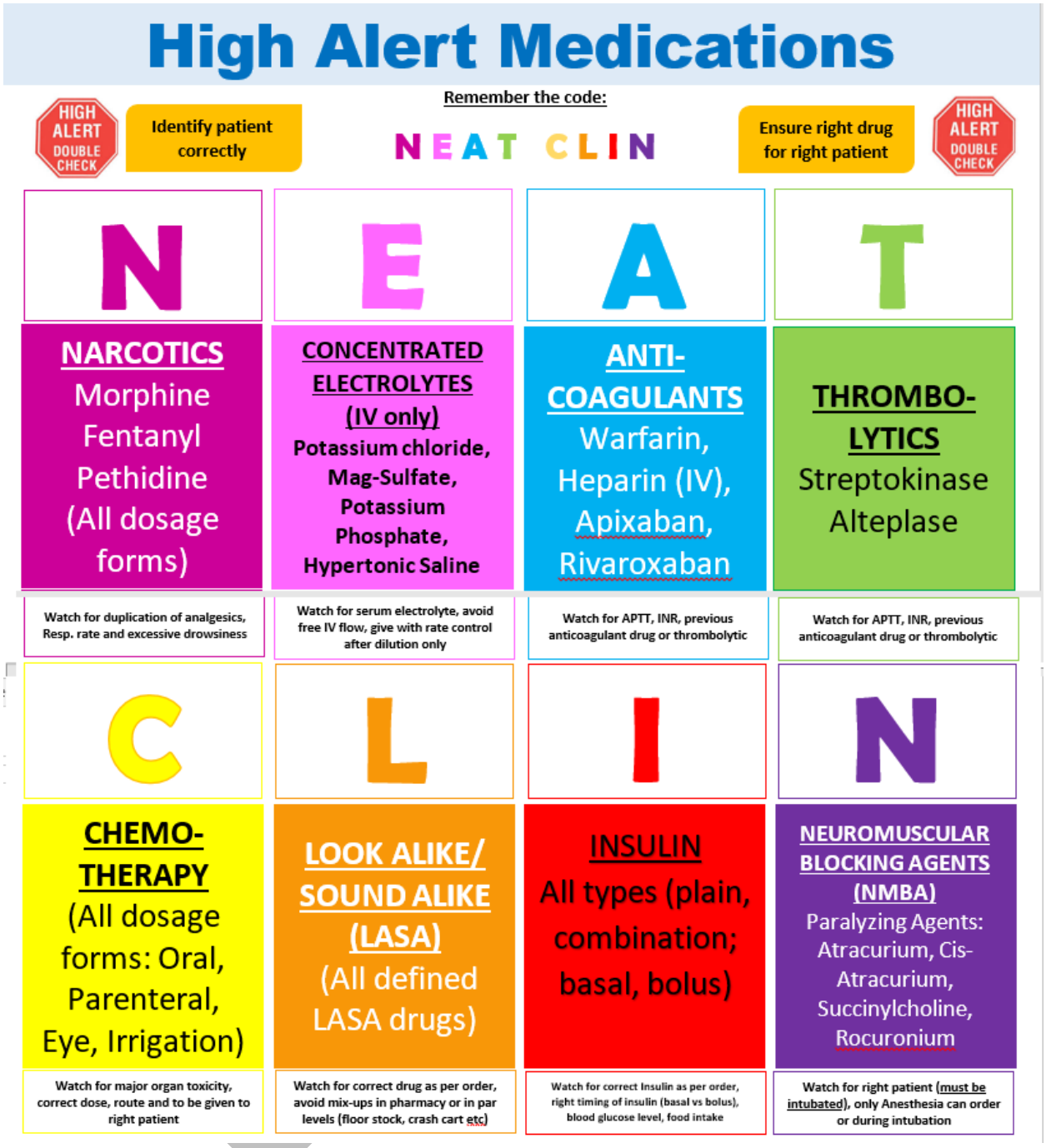
Once the organization approves the list of high alert medicines for its internal use, the next important step is the dissemination of this information to all concerned staff (including doctors, nurses and pharmacists). Remembering multiple drugs as 'High Alert' can be difficult during the patient care activities, therefore, it is important that organizations use creative means for making it easy to remember and recall by the healthcare staff. Such methods may include but not limited to are:

1. Pocket HAMs/LASA cards
2. HAMs/LASA Cards attached to neck straps along with staff ID cards
3. Colored flyers and posters on prominent places (staff café, nursing stations, doctors' room and pharmacies etc.)
4. Computer based reminders, screen savers, alerts, facility's webpage display etc.
5. Use of acronyms to remember see example below: SPACE-LANDID, NEAT-CLIN etc.

Remember the acronym SPACE LANDID for High Alert Medicines, and be extra careful in their handling, prescription, dispensing, preparation, administration and monitoring:

S	P	A	C	E
Sedating Agents	**Parenteral Nutrition (TPN/PPN)**	**Anticoagulants**	**Chemotherapeutic Agents**	**Concentrated Electrolytes**
IV form of: Dexmedetomidine, Midazolam, Ketamine etc.* Oral form of Chloral Hydrate, Midazolam etc.* **if used in indications other than palliative or end-of-life care*	**Both commercial products and those compounded by pharmacy**	Anticoagulants: **Warfarin, low molecular weight heparin (Enoxaparin), Unfractionated heparin** Direct oral anticoagulants and factor Xa inhibitors: **Rivaroxaban, Fondaparinux, Apixaban etc.**	**All parenteral and oral chemo and liposomal chemo formulations**	**Potassium Chloride for inj. concentrate and injections of Magnesium Sulphate, Potassium Phosphate, IV Hypertonic saline (and their infusions)**

L	A	N	D	I	D
LASA drugs	**Anti-Infectives**	**Narcotics**	**Dextrose 25%**	**Insulins**	**Dialysis (HD, PD) solutions**
As per hospital's LASA medication list	**IV form of Amphotericin, Vancomycin, Aminoglycosides**	**Pethidine, Morphine, Fentanyl** All routes including oral, Parenteral and transdermal form	**Dextrose water 20% and above for parenteral use**	**All types of Insulin All routes of administration (IV, SC)**	**Both Hemodialysis and peritoneal dialysis solutions**


High Alert Medications
HIGH ALERT DOUBLE CHECK
Identify patient correctly
Remember the code:
NEAT CLIN
Ensure right drug for right patient
HIGH ALERT DOUBLE CHECK
N
E
A
T
NARCOTICS
Morphine
Fentanyl
Pethidine
(All dosage forms)
CONCENTRATED ELECTROLYTES (IV only)
Potassium chloride, Mag-Sulfate, Potassium Phosphate, Hypertonic Saline
ANTI-COAGULANTS
Warfarin, Heparin (IV), Apixaban, Rivaroxaban
THROMBO-LYTICS
Streptokinase
Alteplase
Watch for duplication of analgesics, Resp. rate and excessive drowsiness
Watch for serum electrolyte, avoid free IV flow, give with rate control after dilution only
Watch for APTT, INR, previous anticoagulant drug or thrombolytic
Watch for APTT, INR, previous anticoagulant drug or thrombolytic
C
L
I
N
CHEMO-THERAPY
(All dosage forms: Oral, Parenteral, Eye, Irrigation)
LOOK ALIKE/ SOUND ALIKE (LASA)
(All defined LASA drugs)
INSULIN
All types (plain, combination; basal, bolus)
NEUROMUSCULAR BLOCKING AGENTS (NMBA)
Paralyzing Agents: Atracurium, Cis-Atracurium, Succinylcholine, Rocuronium
Watch for major organ toxicity, correct dose, route and to be given to right patient
Watch for correct drug as per order, avoid mix-ups in pharmacy or in par levels (floor stock, crash cart etc)
Watch for correct Insulin as per order, right timing of insulin (basal vs bolus), blood glucose level, food intake
Watch for right patient (must be intubated), only Anesthesia can order or during intubation

ANNEX A

ENDORSEMENT

The Hospital Pharmacy Section (HPS) of the International Pharmaceutical Federation (FIP) has reviewed these Guidelines on the safe prescribing, dispensing, administration, and monitoring of HAMs. Prepared by member experts from the Pakistan Society of Health-System Pharmacists (PSHP) in collaboration with the Division of Pharmacy Services, Drug Regulatory Authority of Pakistan (DRAP). This comprehensive document is aligned with global priorities set by the World Health Organization (WHO) and the FIP. The third WHO Global Patient Safety Challenge: Medication Without Harm seeks to find ambitious solutions to ensure the safety of medication practices.

The FIP Development Goals (DGs), launched in September 2020, are a key resource for transforming the pharmacy profession over the next decade. This document supports multiple DGs, but in particular is aligned with DG 19: Patient Safety. The document is also aligned with the FIP HPS Basel Statements which consider medication safety a foundation of hospital pharmacy practice. The FIP HPS is supportive of the approach, methods, and commitment to patient safety displayed by the authors, reviewers, and other individuals involved in the development of these HAMs Guidelines.

Although each individual organization and jurisdiction will need to adopt specific HAMs policies and guidelines to care for their unique patient populations outside of Pakistan, this work can serve as a useful resource as we all seek to eliminate medication-related harm worldwide.

Robert Moss

President FIP Hospital Pharmacy Section

Supported by

fip International Pharmaceutical Federation

Hospital Pharmacy Section

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