THE NATIONAL GUIDELINES ON HIGH ALERT MEDICATIONS

11 August 2021

ACKNOWLEDGEMENTS

The *National Guidelines on High Alert Medications 2021* has been developed by the High Alert Medication (HAM) Workgroup (see Table A-1 for composition) under the National Medication Safety Committee (NMSC) 2017-2021 term (see Table A-2 for composition). The HAM workgroup would like to thank the nominated contributors who participated in the guideline drafting (listed in Table A-3), resource persons (listed in Table A-4) for their assistance in providing medication error data and institutions' HAM policies as well as nursing representatives from various public healthcare institutions (PHIs) for their inputs to the guidelines.

Table A-1. Composition of High Alert Medication Workgroup, July 2017 – June 2021

Name	Institution	Designation
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Mr Wu Tuck Seng (Co-lead)	NUH	Director, Pharmacy Department
Prof Ding Zee Pin	NHC	Senior Consultant, Department of Cardiology; Chairperson, Pharmacy & Therapeutics Committee
Dr Kurumbian Chandran	NTFGH	Director of Endocrinology; Co-chair of the Medication Safety Committee

Table A-2. Composition of the National Medication Safety Committee, July 2017 – June 2021

Name	Institution	Designation
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Dr Liew Mei Fong	AH	Director, Intensive Care Unit
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Name	Institution	Designation
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Table A-3. List of guideline contributors

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Table A-4. List of Resource Persons for the High Alert Medication Workgroup

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INTRODUCTION

In March 2017, the World Health Organisation (WHO) launched ‘Medication without Harm: the third global patient safety challenge’ with the goal to reduce severe, avoidable medication related harm by 50% over the next 5 years. One key focus of this was to promulgate guidance on safe use of High Alert Medications (HAMs).

In line with the WHO’s goal, the National Medication Safety Committee (NMSC), which was reconvened in July 2017, has developed the National Medication Safety Strategy and identified HAM risk mitigation as one of its key initiatives to reduce avoidable medication related harm. To provide reference for best recommendations in managing the risk associated with HAMs, the HAM workgroup has come up with a set of guidelines for HAM usage based on findings from current practices in institutions and actual medication safety events.

The HAM workgroup looked at HAM related medication events (2015-2018) and reviewed the failed processes for incidents in each HAM category to identify gaps within the mitigation strategies to be addressed in the guidelines. In 2019, the Institute for Safe Medication Practices (ISMP) Medication Safety Self-Assessment® for HAM was also conducted in 22 PHIs and the Workgroup reviewed the aggregate reports to distil relevant recommendations to be included in the guidelines.

Built upon the “*National Medication Safety Guidelines Manual”* published by the Ministry of Health in June 2013, the updated guidelines contain recommendations which were developed with the aim of promoting safe use of HAMs in the local and current context, to set the minimum safety standard to close identified gaps.

CONTENT

1. HAM REFERENCE LIST AND GENERAL HAM RECOMMENDATIONS

1.1 Overview and the 5 Core HAM Categories

HAMs are medications that bear a heightened risk of causing significant patient harm when used wrongly. Although errors with these drugs may not be common, the consequences of such errors can be devastating to patients.

In 2016, at the Serious Reportable Events (SRE) forum which discussed medication error related SREs, MOH shared that the HAM list cited in the National Medication Safety Guidelines 2013 could be used as a base on which institutions' HAM lists could be built upon. After the forum, all institutions were requested to share their institutional HAM lists and accompanying precautionary measures via a questionnaire. Replies from institutions suggested inconsistent HAM lists and non-compliance with the 2013 guidelines on the adoption of the Standardized HAMs Reference List. As MOH continues to receive incident reports related to HAM medications, there is an urgent need to push for safety recommendations in this area.

Based on local medication error data, the National Medication Safety Committee (NMSC) identified 5 core HAMs with the highest numbers of locally reported errors, and issued an advisory to inform PHIs of the core HAM categories on 3 February 2021:

1) Insulin
2) Anticoagulants
3) Opioids[1]
4) Concentrated electrolytes
5) Cytotoxics, chemotherapeutic agents

[1] Opioids include opiates and synthetic opioids e.g. Fentanyl, Hydrocodone, Oxycodone and Methadone, but may exclude tramadol based on each institution's own risk assessment. The previous MOH HAM list only contained opiates, instead of the larger drug class of "opioids" listed within the Institute for Safe Medication Practices (ISMP) HAM list, however, NMSC noted that the largest number of medication errors were related to Fentanyl (opioid) overdose. Given the high incidence of medication errors, NMSC recommends aligning with ISMP HAM listing and classify "Opioids" instead of "Opiates" as HAM.

1.2 Standardized HAM Reference List

The updated HAM Reference List reflects the core HAMs (see Table 1.1), which are highlighted due to their higher propensity for error as reflected in local medication error incidents, and thus are deemed to pose greater risk as compared to the non-core HAMs. The core HAMs encompass all oral and parenteral formulations for Insulin, Anticoagulants, Opioids, Cytotoxics and Chemotherapeutic Agents. For concentrated electrolytes, please refer to the reference list in Table 1.2.

Table 1.1 High Alert Medications Reference List

S/N	MOH HAM Reference Categories
Core HAM Categories	
1	Insulin
2	Anticoagulants
3	Opioids
4	Concentrated Electrolytes
5	Cytotoxics, chemotherapeutic agents
Non-core HAM Categories	
6	Neuromuscular agents
7	Anaesthetic agents
8	Inotropes
9	Sedatives
10	Hypoglycaemic agents
11	Vasopressors
12	Radio-contrast agents

Table 1.2 Reference List for Concentrated Electrolytes

S/N	Description	Concentration (Volume)
1	Calcium chloride injection	10% (10ml)
2	Calcium gluconate injection	10% (10ml)
3	Magnesium Sulphate 49.3% injection	2 mmol/ml
4	Potassium Chloride 7.45% injection	1 mmol/ml

S/N	Description	Concentration (Volume)
5	Potassium Dihydrogen Phosphate 13.6% injection	1 mmol/ml
6	Sodium Chloride Infusion	Equal to or greater than 3% (500ml)
7	Sodium Bicarbonate Injection	8.4% (250ml)
8	Sodium Phosphate Injection	1 mmol/ml

Operational challenges can be associated with including every oral and parenteral formulation for each of the 5 core HAMs in institutional HAM lists. Institutions should be guided by a risk-based approach to include specific drugs or formulations of drugs listed in the core HAM list.[2] A risk assessment and stratification exercise for each drug in the 5 core HAM classes is encouraged, taking into consideration usage patterns and operational workflows in each institution. Depending on the risk stratification for each drug, different mitigation measures can be devised to balance medication safety and operational feasibility. Existing protocols for HAM mitigation measures should be followed, unless the medication is not available in the institution. The risk-based approach for inclusion of drugs into the HAM list also encompasses alternative dosage forms such as transdermal opioid medications. Discussions and key decision points in the risk assessment and stratification process should be documented and endorsed by institutions' CMBs (or as designated by CMB).

Institutions are also expected to develop their own action plans to systematically review, implement and evaluate their efforts to build a safer environment to manage all high risk medications in their own context. Institutions should also take into consideration their medication safety data to further build upon the HAM reference list by addressing the issues and practices relevant to them.

[2] This direction supersedes Advisory 01/2021 dated 3 February 2021, which stipulates that all oral and parenteral formulations of drugs in the 5 core HAM classes are to be included in institutions' HAM lists.

1.3 General Recommendations for HAM Management

There are three primary principles that healthcare organizations can use to safeguard against medication errors that might result from HAM:

a) Eliminate or reduce the possibility of error

- Ward stocks should be kept in automatic dispensing cabinets that limit access to specific drugs whenever possible, otherwise, storage areas for HAM should be clearly demarcated
- Limiting the available concentrations and volumes, either for the whole institution or for specific sites
- Use of auxiliary warning labels or HAM stickers to differentiate and highlight HAM from other drugs
- To employ closed loop medication management e.g. barcode scanning verification upon administration, whenever possible
- To use assistive technologies (e.g. barcode technology) in drug-related logistics when topping up, or returning unused drug to storage areas

b) Make errors visible through detection

- Conduct independent double-checking prior to administration of HAM to catch errors before they reach the patient.
- Information technology systems used in the hospital (e.g., pharmacy computer system, computerized prescriber order entry system, smart pump technology, automated compounding devices) are routinely tested to assure that maximum and minimum dose alerts are present and functional for high-alert drugs, and alerts are built for those that do not have them.

c) Minimize the harm consequences of errors

- Change practices to reduce the adverse effects of errors that do occur (e.g. close monitoring to improve early detection of errors and institute prompt remedial action)

In addition, to prevent recurrence of harm due to identified failed processes, PHIs are highly encouraged to develop robust recommendations and explore utilizing human

factor analysis as part of Root Cause Analysis for HAM related errors as much as possible. Incorporating a human factor perspective can help with identifying failed processes that are due to human error, and devising appropriate mitigating strategies to guard against future recurrences.

2. INSULIN

2.1 Overview

Insulin is a high alert medication commonly associated with adverse events in patients. The intent of these guidelines is to summarise safe insulin practices to reduce the risk of preventable harm when used. Each institution should carefully review the guidelines and adopt and implement safe practices in a manner that is appropriate for their institution.

2.2 Gaps identified from local incidents

Most insulin-related medication events were due to failed processes as detailed in Table 2.1 below:

Table 2.1 Common gaps identified from local incidents

S/N	Stage	Common gaps identified
1	Prescribing	• Omission of insulin due to a lack of communication or incomplete handover by staff • Wrong frequency ordered leading to delay in administration • Omission of basal insulin in patients with Type 1 Diabetes Mellitus with risk of developing iatrogenic hyperglycaemia and Diabetic Ketoacidosis (DKA) • Failure to adjust insulin prescription for a fasting patient • Ordering the wrong type of insulin due to lack of knowledge of various insulin types • Mix-ups of Look-Alike, Sound-Alike (LASA) insulins
2	Dispensing	• Packing and supply of wrong disposable insulin pens that look-alike
3	Administration	• Timeliness and compliance with prescribed diet (e.g. conflicts with off-site procedures and treatments) • Scheduled insulins not withheld when patient is fasting

S/N	Stage	Common gaps identified
		• Miscommunication of insulin doses served when adjusting insulin orders are prescribed, resulting in higher doses of insulin administered than intended • Non-insulin syringe used to administer insulin in the management of hyperkalaemia resulting in insulin overdose and hypoglycaemia • Knowledge gaps amongst staff with respect to new technologies in insulin administration that may have resulted in errors • Wrong route of insulin administration (e.g. intravenous instead of subcutaneous administration)

2.3 Recommended precautionary measures

Institutions are strongly encouraged to adopt both the general and specific recommendations below.

2.3.1 General recommendations

<u>Evidence-based insulin protocols</u>

Institutions to develop and utilize evidence-based insulin protocols for the following:

a) Transitions from intravenous to subcutaneous insulin
b) Management of insulin (or insulin secretagogues) during planned and unplanned interruptions of oral, enteral, and parenteral nutrition (e.g. patients being fasted for procedure or surgery)
c) Management of concentrated insulin
d) Management of patients with clinically significant episodes of hyper- and hypoglycaemia
e) Management of severe electrolyte imbalances, e.g. hyperkalemia
f) Management of pregnant and postpartum patients with pre-existing Type 1 or Type 2 diabetes
g) Management of patients receiving glucocorticoid therapy

h) Post-discharge insulin management

Considerations prior to transitions of care

Prior to transitions of care, a process is in place to ensure that patients will have

a) Sufficient supply of prescribed insulin and consumables
b) Clear instructions for all prescribed insulin and blood glucose monitoring and
c) Clear follow-up care plan
d) Timely medication reconciliation conducted (refer to The National Guidelines on Medication Reconciliation (2018)).

2.3.2 Specific recommendations

Recommendations specific for insulin management at different stages of the patient journey are listed in Table 2.2 below.

Table 2.2 Recommendations for insulin at different stages of the patient journey

S/N	Stage	Recommendations
1	Storage	Institutions are to have: a) Clear policies and procedures for the uniform storage of insulin products throughout the institution. b) Processes to allow storage of insulin products in secured areas, and for clear differentiation of various types and strengths of insulin products. c) Guidelines or policies for safe and secure storage of patient-specific insulin during inpatient stay. d) Processes for storage of different types of syringes (e.g. similar-looking syringes, such as tuberculin and insulin syringes).
2	Prescribing	Prescriber to: a) Check with patient or carer on the type, dose, frequency and device through which insulin is administered where possible, and not rely solely on electronic health records.

S/N	Stage	Recommendations
		b) Ascertain the timing of administration of the last insulin dose prior to making a new order of insulin. c) Exercise caution when ordering insulin with LASA names, e.g. NovoMix or NovoRapid. d) Ensure the type, strength, form, brand, and dose of insulin is prescribed in full. e) Spell out 'Units' in full when prescribing insulin. f) State the strength when prescribing concentrated insulin *(e.g. U-300 insulin glargine 10 units).* g) Refer to standard charts for insulin dose conversions and titrations when using concentrated insulin. h) Ensure that basal insulin is prescribed for patients who have insulin-requiring diabetes, including but not limited to those with Type 1 diabetes, pancreatic diabetes. Where appropriate, consult an endocrinologist or practitioner trained in insulin management for the care of patients with Type 1 Diabetes or Latent-Autoimmune Diabetes in Adults (LADA). i) Use sliding scale subcutaneous insulin regimen appropriately. Sliding scale subcutaneous insulin regimen may be clinically indicated in the inpatient setting in patients with diabetes for the following reasons: i. <u>In fasting patients while waiting for a procedure, or in patients with erratic food intake</u>. In this setting, we recommend it to be used only temporarily. Patients should be returned to a regular diabetes treatment regimen as soon as possible, once it is deemed safe. ii. <u>As supplemental insulin alongside other strategies to manage their hyperglycaemia.</u> Sliding Scale Subcutaneous Insulin Regimen use as the only strategy for managing hyperglycaemia is strongly discouraged.

S/N	Stage	Recommendations
3	Labelling and dispensing (not applicable for insulins dispensed to patients for home use)	When labelling and dispensing insulin pens or vials, institutions are to: a) Provide guidance on safe labelling techniques , like affixing patient's label on the barrel of the insulin pen instead of the cap or the box, to avoid risk of insulin mix-up. b) Have all information on pharmacy label, and pertinent product information from the manufacturer readily visible. c) Ideally have a tamper-evident seal affixed over the cap and barrel of unused insulin pens, to allow easy differentiation of used and unused pens returned to pharmacy. d) Where possible, dispense insulin pens to the clinical units with a patient-specific barcode label.
4	Administration	a) Institutions to have standard protocols that consider the following: i. Steps to prepare and administer insulin. ii. Need to label pre-drawn syringes of insulin if not to be immediately administered to patient (refer to The National Standards for Labelling of Injectables in Healthcare Facilities (2018)). iii. Processes should avoid use of verbal communication of point-of-care blood glucose values to determine insulin doses where possible. iv. Steps for staff to follow prior to subcutaneous insulin administration, which should include the following: • Confirm that there is an appropriate indication. • Assess the patient's most current blood glucose value, time and dosage of insulin during the last round of administration, and if the patient has symptoms of hypoglycaemia. • Inform the patient, where possible of their most current blood glucose level, their dose, the full

S/N	Stage	Recommendations
		name of the insulin and the insulin's intended action. v. Use of appropriate delivery device for the right insulin concentration, especially concentrated insulin. b) Syringes are never used to draw insulin from a prefilled pen or refill cartridge. c) Individual insulin pen is not to be used on more than one patient. d) Where possible, barcode scanning is used to verify that the correct insulin is administered to the correct patient.
5	Patient education	Patients on insulin (and caregivers, where applicable) are to be educated on knowledge and skills required for self- care management, including: a) Type, dose and frequency of insulin that they are prescribed with and device used for administration. b) Injection technique. c) Recommended storage method based on pharmaceutical company guidelines. d) Self blood glucose monitoring technique, interpretation of blood glucose readings and glucose targets. e) Timing insulin doses with mealtimes. f) Recognition, treatment and prevention of hyper- and hypoglycaemia, and consult with care providers where needed. g) Common types of errors possible with their insulin therapy and how to prevent or detect these errors, where feasible.

3 ANTICOAGULANTS

3.1 Overview

Recommendations in this chapter are focused on oral vitamin K antagonist – warfarin, Direct Oral Anticoagulants (DOACs) – rivaroxaban, dabigratan, apixaban and edoxaban; and parenteral unfractionated heparin as well as low molecular weight heparin.

Anticoagulants like warfarin, DOACs and heparins have a narrow therapeutic index. Both subtherapeutic and supratherapeutic doses can lead to serious complications. Various food, herbs and medications can interfere with anticoagulants. The increasing popularity of DOACs, which has fewer drug interactions but require dosing adjustments according to their indications, renal function and age, mandates safety measures to be in place to ensure appropriate use.

3.2 Gaps identified from local incidents

The majority of current mitigation strategies in place are focused on monitoring for bleeding or minimising thromboembolic risks of patients. However, most commonly identified failed processes gathered from recent medications events and the ISMP Medication Safety Self-Assessment® for HAM involve failed processes in administration, non-adherence to available protocols and knowledge deficits in dosage adjustments (e.g. lack of timely renal dose adjustments for DOACs), details in Table 3.1 below.

Table 3.1 Common gaps identified from local incidents

S/N	Stage	Common gaps identified
1	Prescribing	• Lack of awareness of interactions (warfarin / DOACs) • Dosage adjustments not done in renal impairment (DOACs) • Poor accessibility to calculated creatinine clearance (CrCl) values in electronic prescribing systems; lack of

S/N	Stage	Common gaps identified
		awareness of discrepancies in CrCl due to the differences between absolute and adjusted body weight
2	Dispensing	• Majority of dispensing errors involve wrong strength errors
3	Administration	• Duplicate doses or missed doses
4	Patient education	• Inadequate patient education on potential drug interactions (warfarin can interact with many common drugs (e.g. aspirin-containing medications, antacids or laxatives, antibiotics, paracetemol-containing medications) and food/drinks (e.g. Vitamin K rich foods (kale, spinach), alcohol, grapefruit/cranberry juice) • Lack of means for ad-hoc INR checks

3.3 Recommended precautionary measures

Errors that have occurred are mostly preventable through the implementation of precautionary measures, improved communication, close monitoring and education of both patients and healthcare professionals.

Table 3.2 Recommended risk mitigation measures for anticoagulants

S/N	Stage	Recommendations
1	Procurement	a) Only commercially prepared, premixed IV solutions of unfractionated heparin to be used in the facility (where available).
2	Storage	a) Number of strengths available for each HAM anticoagulant to be minimised if possible, otherwise, to limit the number of strengths kept as ward stock with corresponding mitigation measures if more than one strength is kept.
3	Prescribing	a) Prescribing and dosing protocols for each anticoagulant should be available. b) Institutions may wish to restrict prescribing of specific drugs to selected specialties only.

S/N	Stage	Recommendations
		c) Institutions to develop protocols to guide the rounding of doses for certain anticoagulants (e.g., enoxaparin 83 mg could be rounded to 80 mg, a weight-based heparin bolus dose of 2,485 units could be rounded to 2,500 units). d) If handling a substantial pool of patients on long-term anticoagulants, to establish an anticoagulation service. e) Electronic prompts for HAM anticoagulants may be built into the electronic prescribing system e.g. interaction checker for duplicate anticoagulants, renal dosing adjustment requirements. f) Order only in units. Do not use “U” for ordering. Write out “units” in full. g) Standardised ordering doses (including dilution strengths) should be available for selection in the electronic prescribing system.
4	Administration	a) Smart pumps should be used for the parenteral administration of HAM anticoagulants, whenever possible (refer to The National Guidelines on the Safe Use of Infusion Pumps in Healthcare Facilities (2019) for recommendations on safe usage of infusion pumps and smart pumps).
5	Patient education	a) Patient to be provided with detailed patient counselling for initiation or switching of anticoagulants. b) Patient to be provided with patient information (including potential drug / food / supplement interactions, drug indication, dosage and timing for consumption; contact information for enquiries on anticoagulation (where feasible) medication and monitoring; and a recommended means for ad-hoc INR checking). c) It is highly encouraged to make medication alert identification (e.g. card available for patients on long term anticoagulation).

4 OPIOIDS

4.1 Overview

Opioid medications confer significant risks of harm including overdose, death and abuse. In recent years, we have seen increasingly frequent reports of harm involving opioids.

4.2 Gaps identified from local incidents

Majority of failed processes identified are related to erroneous route of administration and erroneous dose, details in Table 4.1 below.

Table 4.1 Common gaps identified from local incidents

S/N	Stage	Common gaps identified
1	Storage	• Lack of identification/ clear labelling of different controlled drugs kept in controlled drug cabinet
2	Prescribing	• Use of verbal orders in prescribing which led to incorrect doses administered • Knowledge deficit on opioid prescribing and dose titration
3	Preparation	• Lack of independent double-checking for verification of drug
4	Administration	• Lack of training in use of smart pump, syringe/ infusion pump and unfamiliarity with use of drug library in syringe/ infusion pump • Lack of standardisation of verbal medication order and read-back in unit of measure (UOM) upon administration • Lack of patient assessment and physical check for duplicate opioid patches on patient's body, especially at points of handover • Knowledge deficit on the application of half-dose opioid patches, resulting in staff cutting or folding patches in half for use on patients.

S/N	Stage	Common gaps identified
		• Lack of independent double checking of medication order prior to administration
5	Dispensing & Patient Education	• Lack of proper counselling to patient and caregiver on prescribed opioid doses • Lack of standardisation in dispensing measuring cup vs spoon vs oral syringe for oral liquid medications

4.3 Recommended precautionary measures

Errors that have occurred are mostly preventable through the implementation of precautionary measures, including patient education, please see Table 4.2 for details.

Table 4.2 Recommended risk mitigation measures for opioids

S/N	Stage	Recommendations
1	Storage	a) Use of auxiliary warning labels in controlled drug cabinets in all areas. b) To store drugs in designated locked and controlled drug cupboards/ automated dispensing cabinet locked bins at all times.
2	Prescribing	a) Institutions may consider limiting prescribing of IV and infusion opioids to trained personnel (as defined by institutions). b) To be aware that there may be more than one dosage formulation (e.g. oral morphine solution) available as well as interaction with other drugs that may lead to respiratory depression. c) Dilution information and common doses should be available for selection in the electronic prescribing system. d) Avoid verbal orders of opioid prescriptions whenever possible, unless there are exceptional circumstances (e.g. medical emergencies).

S/N	Stage	Recommendations
		e) Drug names, doses, dosage forms and administration route communicated verbally by the prescriber are read back (or repeated back, if conditions do not allow immediate transcription of verbal order) to prescriber for verification before administration. f) Standardised ordering doses should be available in prescribing systems and synced with infusion pumps/ smart pumps for administration if electronic ordering systems allow. g) Equianalgesic dosing charts for oral, parenteral, and transdermal (e.g., fentaNYL patches) opioids have been established and are available and easily accessible to all practitioners when prescribing, dispensing, and administering opioids.
3	Preparation & Dispensing	a) Promulgate a medication dilution guide for drug library. b) Implement independent double checking or bar code verification for drug preparation and labelling.
4	Administration	a) Independent double checking must be done prior to administration. Both checking and counterchecking personnel should be competent in double-checking (including pump setting where applicable), and must witness the whole process from preparation to the start of administration or its completion based on institutional guidelines. b) To employ closed loop medication management e.g. drug barcode scanning verification before medication administration i.e. barcode medication administration (BCMA), whenever possible. c) Administration of opioids using smart pumps should be restricted to staff trained in the use of smart pumps only. d) Limit different types of dilutions that can be prescribed by standardising the dilutions in ordering doses. e) Ensure patient assessment and physical checks are done (including checks on when the last opioid patch

S/N	Stage	Recommendations
		was applied) when new opioid patch medications are administered to patient. f) Enhanced monitoring beyond pulse oximetry (e.g., capnography, apnea alarms) can be done where feasible, for patients who receive Patient Controlled Analgesics (PCA) or other IV opioid infusions to treat pain. This is relevant whenever risk factors (such as obesity or low body weight, sleep apnea, the use of basal infusions or concomitant medications that potentiate the effects of opioids, or conditions such as asthma) exist, and/or when Nurse Controlled Analgesia is employed.
5	Patient education	a) Where feasible, patient education and detailed patient counselling should be done for all patients with opioid prescriptions, with teach-back to ensure patient's/lay caregiver's understanding. b) Rationalise use of dosing devices (medication cups, spoons, oral syringes) by standardising these with prescribed doses when dispensing to patients to minimise risk of overdose. c) Educate patients (and lay caregivers, where applicable) to monitor for signs and symptoms of opioid toxicities e.g. excessive sedation, somnolence and disorientation and what to do when they encounter such adverse effects and who to call.

5 CONCENTRATED ELECTROLYTES

5.1 Overview

Amongst HAM categories, concentrated electrolytes are ranked fifth in terms of number of errors reaching the patient in Singapore. Concentrated electrolytes covered in this scope include but are not limited to the reference list in Table 1.2 (see page 8), and according to the availability in the institutions.

Errors involving concentrated electrolytes can lead to serious complications. It is critical that the availability, access, prescribing, ordering, preparation, distribution, labelling, verification, administration and monitoring of these agents be organised in such a way that possible adverse events can be avoided and eliminated.

Standardizing the dosing, units of measure and terminology are cardinal for the safe use of concentrated electrolyte solutions. Moreover, mix-ups of specific concentrated electrolyte solutions must be avoided (e.g., confusing sodium chloride with potassium chloride). These efforts require special attention, appropriate expertise, inter-professional collaboration, verification processes and several forcing functions that would ensure safe use. Institutional and cultural changes are essential to ensure fail-safe systems are in place to avoid harm associated with the inappropriate use of concentrated electrolyte solutions.

5.2 Gaps identified from local incidents

Most commonly identified failed processes gathered from recent medications events and the ISMP Medication Safety Self-Assessment® for HAM involve slips and lapses and knowledge gaps. Details of common gaps identified from local incidents are listed in Table 5.1 below.

Table 5.1 Gaps identified from local incidents

S/N	Stage	Gaps identified
1	Prescribing	• Wrong dose ordered due to slip and lapses • Poor team communication

S/N	Stage	Gaps identified
		• Lack of knowledge
2	Dispensing/issuing to ward	• Violation of protocol in drug labelling
3	Administration	• Erroneous dilution • IT issue with maximum dose alerts • Violation of protocol in drug administration

5.3 Recommended precautionary measures

While slips and lapses are hard to eliminate, the use of Information Technology and smart pumps (by trained personnel) could help reduce human errors. To adequately address knowledge gaps, compulsory institutional guidelines for all concentrated electrolytes classified as HAM are required and these guidelines (with information on indications, dosages, mode of dilution/administration/ contraindications/ renal correction dosage, monitoring) should be available and easily accessible.

Table 5.2 Recommended risk mitigation measures for concentrated electrolytes

S/N	Stage	Recommendations
1	Storage	a) Concentrated electrolytes should be stored in patient care units where clinically essential, within locked/limited access areas (access to authorised personnel as defined based on institutional policies). b) Concentrated electrolytes must be individually labelled with HAM stickers on ward stock, pharmacy bins and buffer shelves. c) Recommend to use premix of concentrated electrolytes where possible. d) Institutions must have guidelines and polices for storage of concentrated electrolytes. e) Where operationally feasible, it is recommended to limit the availability of vials of concentrated forms of electrolytes that require dilution before IV administration as unit/ward stock (including in automated dispensing cabinets) on any patient care

S/N	Stage	Recommendations
		units (including in operating room/anesthesia stock) and dispensing of such vials to patient care units for individual patients.
3	Prescribing	a) Institutions must have prescribing guidelines with indications and dosing protocols, readily available for staff reference. b) Appropriate clinical decision support mechanism (e.g. alert prompts, links to guidelines, institution protocol order sets) should be in place for ordering of drug in the system. c) When order is placed in system, it is good to have system functionality to show the latest relevant lab result (for example, if potassium chloride is ordered, patient's latest lab result for potassium level is shown). d) Standard guidelines and order sets exist and are adhered to for each indication for which IV hypertonic sodium chloride is used (e.g., hyponatremia, elevated intracranial pressure, other off-label use). e) Standard protocols for adult, pediatric, and/or neonatal electrolyte replacement therapy include the following: Type and frequency of patient monitoring required (e.g. continuous ECG monitoring, patient assessment, serum electrolyte level and other laboratory monitoring) during IV administration and following therapy to evaluate the patient's response.
4	Administration	a) Institutions must have dosing protocols for IV hypertonic saline which includes directions for administration (e.g. maximum concentration, rate of administration, the concentration at which administration through a central IV access line is required) and the type and frequency of patient monitoring required during IV administration (e.g., patient assessment parameters, laboratory monitoring). b) Institutions must have "not for IV bolus" stickers or other stickers which convey similar meaning for Potassium Chloride, Potassium dihydrophosphate, hypertonic saline and sodium Phosphate

S/N	Stage	Recommendations
		c) Where available, it is recommended to use smart infusion pumps for all concentrated electrolytes, as these are equipped with dose error reduction software and a “loading dose” (sometimes called a “bolus dose”) feature that automatically starts/resumes the maintenance infusion at the prescribed rate of infusion once the loading dose has infused. Loading doses are never administered via a basic infusion mode. d) Where infusion pumps are used, independent double checking of pump settings should also be carried out by trained personnel prior to administration. e) Where available, it is recommended to perform barcode verification upon administration for concentrated electrolytes.
5	Monitoring	a) Institutions must have guidelines in place on the monitoring required for each type of concentrated electrolyte (e.g. ECG for Potassium Chloride, checking Potassium levels after administration, extravasation protocol). b) Institutions must have set triggers to team doctor if laboratory value is too high or too low (e.g. Potassium level > 6 or < 2.5 mmol/L). If not operationally feasible to do so, to have guidelines and workflows to ensure timely communication of critical lab results.

6 CYTOTOXICS, CHEMOTHERAPEUTIC AGENTS

6.1 Overview

Most cytotoxics have a narrow therapeutic index and are often used in complex, multi-drug regimens. Errors involving cytotoxics can result in serious toxicities in patients. The cytotoxics covered in this scope includes chemotherapy agents used for the treatment of cancer as well as those used for non-malignant diseases.

6.2 Gaps and common issues identified from local incidents

Slips and lapses, lack of knowledge and inadequate protocol are some of the failed processes identified, as listed in Table 6.1 below.

Table 6.1: Gaps and Issues identified from local incidents

S/N	Stage	Gaps/Issues identified
1	Preparation	• Inadequate protocol for checking medication prepared in clean room/diagnostic imaging room • Wrong drug retrieved by staff
2	Dispensing	• Patient instructed to continue drug despite intended discontinuation due to lack of communication/knowledge
3	Administration	• Extravasation of IV cytotoxic drugs

6.3 Recommended precautionary measures

The following recommended precautionary measures in Table 6.2 are not exhaustive. Institutions should consider implementing additional measures for error prevention where appropriate. Patient education was included as well-informed patients and caregivers are better able to detect a wrong medication order and question conflicting information. They are the critical last link in the medication safety chain to prevent errors related to cytotoxics.

Table 6.2 Recommended risk mitigation measures for cytotoxics

S/N	Stage	Recommendations
1	Storage	a) LASA cytotoxic agents should not be stored in close proximity whenever possible to minimize mix-ups. Efforts should be made to distinguish between these LASA cytotoxic agents if they are to be stored in the same area (e.g. using Tall-man lettering for similar drug names or different colored labels for bin containers). b) The use of barcode technology for topping up and return of cytotoxics at storage areas is recommended where available. c) Proper storage to prevent breakage , use of warning labels to indicate presence of hazardous drugs on-site and the availability of spill kits may be considered. Staff should be trained on how to manage spillage and use the spill kits.
2	Prescribing	a) 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. b) Drug doses should be expressed clearly in terms of amount to be taken per dose/per day to prevent misinterpretation. (E.g oral chemotherapy doses to be described as amount of medication to be taken per dose and not total daily dose in divided doses, chemotherapy drugs for specific days are written explicitly, prescribing total chemotherapy doses for whole entire cycle to be avoided). c) Prescribing of cytotoxics should be restricted to practitioners who are deemed qualified by the institution (e.g. through credentialing and privileging framework). d) Electronic prescribing systems i.e. computerized prescriber order entry (CPOE) should be implemented where possible to further enhance the

S/N	Stage	Recommendations
		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 (e.g. hard stops when dose ordered exceeds maximum defined dosage of a drug or when a wrong route is chosen).
3	Dispensing, Preparing and Administration	a) Independent double-checks must be done when processing, preparing, dispensing and administering orders involving cytotoxics. The use of barcode technology (e.g. bar code medication administration (BCMA)) or other similar assistive technologies is highly recommended to provide an extra safety check, where available. b) Standardized guidelines for reconstituting, diluting, admixing, packaging and labeling of cytotoxics should be established within each institution. c) Preparation of sterile cytotoxics should only be performed by trained personnel in accordance with prevailing regulations and healthcare institutions' policies. d) Near misses involving medication errors related to the medication use process of prescribing, preparing, dispensing and drug administration should be reported and analysed with root cause analysis done if possible to improve medication safety. e) Standardized guidelines with strategies to prevent or minimize the occurrence of vesicant cytotoxic extravasation should be instituted, which should include identification of patients who are at risk of experiencing such adverse events and a system to identify drugs with vesicant properties. Guidelines for the management of cytotoxics extravasation should also be readily available should these events occur. Institutions should have policies in place to

S/N	Stage	Recommendations
		train staff in the handling and administration of cytotoxic drugs.
4	Patient education	a) Patient and caregiver education is pertinent in ensuring proper self-administration of cytotoxics. The educational activities should be performed taking into consideration the patient's and/or caregiver's learning needs, abilities, preferences and readiness to learn. b) Patients (and/or caregivers) must be provided detailed counselling when cytotoxics are initiated, switched or discontinued. c) Patients (and/or caregivers) must also be counselled on the storage and safe handling procedures, and safe management and disposal of unused drugs. d) Patient educational materials should be provided where appropriate. e) Drug dosing calendars or diaries may also be provided to help track the self-administration of cytotoxics.
5	Others	a) Sharing of reported cytotoxic drug adverse drug reactions, published black box warnings and precautions from manufacturers, drug regulatory authorities and medication safety bodies e.g. ISMP for learning purposes is encouraged and is good safety practice. b) Staff should be equipped with knowledge on the safe handling of cytotoxic drugs, including safe disposal of such drugs and handling of patients' soiled items.

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