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Pharmaceutical Services Programme

# HAZARDOUS DRUGS SAFE HANDLING GUIDE FOR MOH FACILITIES



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# PREFACE




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Hazardous drugs pose significant health risks to healthcare personnel, patients, and the environment if not handled properly. Exposure may lead to both acute and long-term adverse effects, including irritation, reproductive toxicity, and cancer. To support safe practices, the National Institute for Occupational Safety and Health (NIOSH) under the U.S. Centers for Disease Control and Prevention (CDC) provides an updated list of hazardous drugs, categorising them based on their toxicity and handling requirements.

Exposure can occur at any stage of the medication-use process, with risk levels influenced by the drug's properties, formulation, route of exposure, and work activities involved. Effective risk management through proper assessment and control measures is therefore essential.

This guideline aims to assist pharmacy and clinical units within Ministry of Health (MOH) hospitals in identifying hazardous drugs, assessing exposure risks, and implementing appropriate safety measures. Emphasis is placed on drugs listed in the NIOSH List of Hazardous Drugs in Healthcare Settings 2024, while also providing general principles applicable to other hazardous drugs.

It is hoped that this guideline will serve as a practical and reliable resource to strengthen institutional safety programmes, promote a culture of safety, and ensure the responsible management of hazardous drugs in healthcare facilities.

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# ACRONYMS AND ABBREVIATIONS

| | |
|---|---|
| **ASHP** | American Society of Health-System Pharmacists® |
| **ATRA** | Tretinoin |
| **BCG** | Bacillus Calmette-Guerin vaccine |
| **BSC** | Biosafety Cabinet |
| **CDC** | U.S. Centers for Disease Control and Prevention |
| **CDR** | Cytotoxic Drug Reconstitution |
| **CP2** | Pharmacotherapy Review Form |
| **CVAD** | Central Venous Access Device |
| **FDA** | Food and Drug Administration |
| **FDA-CDER** | Food and Drug Administration- Center for Drug Evaluation and Research |
| **IARC** | International Agency for Research on Cancer |
| **ISOPP** | International Society of Oncology Pharmacy Practitioners |
| **IVC** | Intravenous Cannula |
| **MABs** | Monoclonal Antibodies |
| **MOH** | Ministry of Health |
| **MSHI** | Manufacturer's Special Handling Information |
| **NGO** | Non-Governmental Organisation |
| **NIOSH** | National Institute for Occupational Safety and Health |
| **NTP** | National Toxicology Program |
| **ONS** | Oncology Nursing Society |
| **PhIS** | Pharmacy Information System |
| **PPE** | Personal Protective Equipment |
| **PUR** | Polyurethane |
| **PVC** | Polyvinylchloride |

# 1.0 INTRODUCTION

Hazardous drugs are pharmaceuticals that could pose health hazards to humans, animals and the environment if not handled properly. Studies have shown that workplace exposure to these drugs may lead to adverse health effects such as ocular irritation, headache, cough, dizziness, nausea and vomiting, skin rashes, adverse reproductive outcomes (infertility, spontaneous abortion), and possibly leukaemia and other cancers.

In 2004, the National Institute for Occupational Safety and Health (NIOSH) of the U.S. Centre for Disease Control and Prevention (CDC) started to publish and maintain a list of hazardous drugs to help healthcare workers and employers in recognizing which drugs are considered hazardous. All drugs carrying Manufacturer's Special Handling Information (MSHI) in their package inserts, or those that could potentially or known to cause carcinogenicity, developmental toxicity (including teratogenicity), reproductive toxicity, genotoxicity, or organ toxicity at low doses, are defined as "hazardous" by NIOSH. These drugs are then further categorised into two groups which are being tabulated in Table 1 and Table 2 of the list:

**a) Table 1. NIOSH List of Hazardous Drugs in Healthcare Settings 2024**

Drugs that have manufacturer's special handling information (MSHI) in the package insert and/ or meet the NIOSH definition of a hazardous drug and one or more of these criteria:

- Are classified by the National Toxicology Program (NTP) as "known to be a human carcinogen";
- Are classified by the International Agency for Research on Cancer (IARC) as Group 1 "carcinogenic to humans" or Group 2A "probably carcinogenic to humans";

Majority of drugs tabulated are cytotoxic anti-cancer agents with a few antivirals, hormonal agents and immunosuppressants.

**b) Table 2. NIOSH List of Hazardous Drugs in Healthcare Settings 2024**

Drugs that meet the NIOSH definition of a hazardous drug, and

- Do not have MSHI;
- Are not classified by the NTP as "known to be a human carcinogen";
- Are not classified by the IARC as Group 1 "carcinogenic to humans" or Group 2A "probably carcinogenic to humans";

These groups of drugs are not carcinogenic but may exhibit developmental toxicity, reproductive toxicity and/ or other types of toxicities as described in the NIOSH definition of a hazardous drug.

Exposure to hazardous drugs can occur at any stage of handling from the receipt of shipment from supplier to the disposal of waste. The potential for hazardous drugs to cause harm in healthcare workers and the severity of that harm vary depending on factors that include:

**a) The drug inherent toxicity**

Cytotoxic anti-cancer agents may damage healthy cells in the handler's body and cause unwanted effects. Some were associated with the occurrence of leukaemia and other cancers.

**b) Drug formulation/ dosage form**

Hazardous drugs are commercially available in a variety of formulations/ dosage forms - capsules, tablets, powders, liquids (injectables, eye/ ear drops, oral solutions/ syrups), creams and others. Modifying the formulation/ dosage form before use elevates the degree of exposure.

**c) Route of exposure**

The potential routes of occupational exposure include inhalation, skin or mucous membrane absorption, ingestion, and accidental injection (e.g. needle-prick injury).

**d) Type of work/ activity performed**

Level of risk differs depending on work process and actions involved, for example, personnel who manage drug inventory are at lower risk of exposure than those compounding the drugs.

It is a necessity to have an institutional safety program in place to protect healthcare personnel who handle hazardous drugs and prevent environmental pollution. Risk management for the handling of these drugs requires risk assessment and implementation of control measures. This document provides guidance to pharmacy and clinical units in MOH hospitals on identifying hazardous drugs, assessing exposure risks, and implementing measures to protect healthcare personnel, patients, and caregivers. Information and advice provided within this guide focused on hazardous drugs listed in Table 1 of the NIOSH List of Hazardous Drugs in Healthcare Settings 2024 as well as drugs that are not listed but fulfilled the criteria described. Meanwhile, drugs listed in Table 2, or those that fulfil the specified criteria, should be handled in accordance with institutional protocols, standard occupational safety guidelines, or the manufacturer's recommendations, as applicable.

## References:


1. NIOSH [2024]. NIOSH list of hazardous drugs in healthcare settings, 2024. By Ovesen JL, Sam-mons D, Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP, Whittaker C. Cin-cinnati, OH: U.S. Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2025-103 (Supersedes 2016-161).
2. Managing hazardous drug exposures: information for healthcare settings, Hodson L, et al, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2023-130, https://doi.org/10.26616/NIOSHPUB2023130

# 2.0 HANDLING OF HAZARDOUS DRUGS AT MANUFACTURING PHARMACY

The Manufacturing Pharmacy of MOH hospitals commonly compounds both sterile and non-sterile preparations that are not commercially available for patient use. The Cytotoxic Drug Reconstitution (CDR) unit handles large volumes of sterile injectable hazardous drugs which are listed in the NIOSH List of Hazardous Drugs on routine basis whilst the other units may be compounding non-sterile preparations such as oral solutions/ syrups, topical creams and other preparations containing hazardous drugs, when necessary. The work process involved in producing these preparations would expose all personnel to hazardous drugs in the absence of safe work practices and exposure controls such as engineering controls, administrative controls, and PPE. All operations within CDR unit are governed by local standards set by Pharmaceutical Services Program of MOH (refer the latest edition of Manual for Sterile Preparations, MOH) as well as international standards such as the Pharmaceutical Inspection Co-operation Scheme (PIC/S), United States Pharmacopeia (USP) and other relevant references.

## 2.1 DEVELOPING FACILITY-SPECIFIC CDR SERVICE DRUG LIST

The primary aim of Cytotoxic Drug Reconstitution (CDR) Service is to safely provide ready-to-use sterile hazardous drug doses as prescribed by the doctors. The number and type of drugs kept vary widely across MOH facilities. Hence, there is a need to develop a facility-specific CDR service drug list for the reference of all hospital personnel. This list should be revised periodically and whenever new hazardous drugs or new toxicological data or safety recommendations on existing drugs become available.

Assessment on whether a hazardous drug should enter the facility-specific CDR service drug list should not be based solely on the NIOSH List of Hazardous Drugs as it does not include new drugs marketed after its last review and it does not cover non-FDA approved drugs (used outside U.S). In addition, this list does not take into account specific risk factors related to the use of the individual drugs which include the dosage form, the potential routes and magnitude of exposure, work practices, and the presence or absence of any exposure controls such as PPE. Not all hazardous drugs in the NIOSH list require handling by CDR service and shall be based on facility-specific risk assessment.

CDR unit usually manages the injectable cytotoxic anti-cancer preparations and a few other agents in Table 1 of NIOSH Hazardous Drug List 2024. New drugs or others that do not meet the criteria described warrant further evaluation before placing them on the CDR service drug list. Factors to be evaluated should include:

**a) Toxicity profile of the drug**

Determine if the drug is potentially or known to be cytotoxic or carcinogenic or genotoxic based on credible drug references, databases or registries. If it carries safe handling information in its package insert, it should be handled according to manufacturer recommendations.

**b) Formulation and dosage form**

The drug may be presented as powder requires reconstitution, injectable liquid requires dilution, ready-to-use prefilled syringe, etc. It may or may not need alteration on its initial pharmaceutical form via sterile reconstitution/ dilution before medication administration.

**c) Route of exposure**

Determine the possibility of exposure through inhalation, skin or mucous membranes absorption, ingestion, or accidental injection when handling the drug.

Sterile drug products that are potentially or known to be cytotoxic/ carcinogenic/ genotoxic, which requires aseptic manipulation/ alteration on its initial pharmaceutical form before use, and may cause significant exposure if not handled within the controlled environment of CDR unit should be listed (**refer Appendix 1**).

Clinical trial drugs are medications under investigation, with no or incomplete toxicological data to be managed in accordance with study protocols. Infectious agents such as the Bacillus Calmette-Guerin vaccine (BCG) are not classified as drugs by the FDA and have different hazard profiles that do not fulfil the evaluation criteria under NIOSH. These agents should not be prepared by the CDR unit to avoid contamination on other drug preparations. On the other hand, the non-hazardous monoclonal antibodies and other high-cost drugs which are parts of patients' chemotherapy regime may be included in the list if deemed necessary (e.g. enable vial sharing to reduce wastage, etc). However, the finished products prepared by CDR would be considered hazardous due to cross contamination during production. For common supportive treatment medications such as Folinic Acid, Mesna (unless admixed with Ifosfamide or Cyclophosphamide) and others are best not to be listed for CDR service to preserve limited resources (e.g. manpower, consumables, etc) allocated for the purpose of cytotoxic drug reconstitution.

Compounding of oral or other non-injectable hazardous drugs using sterile starting materials and drug products inside a CDR biosafety cabinet is acceptable, if a validated formulation is available. However, compounding activities using non-sterile materials e.g. tablet and capsule should be avoided due to risk of microbial contamination to sterile equipment and

cleanroom environment. If deemed absolutely unavoidable, the BSC used for both parenteral and non-sterile preparation must be decontaminated after non-sterile preparation and then purged for a minimum of 30 minutes prior to use for preparation of parenteral drugs. Alternatively, compound the non-sterile preparations last of the production session to avoid disruption of CDR service. Decontaminate and purge BSC accordingly before the next session. All other equipment used needed to be decontaminated thoroughly as well. Compounding of such non-sterile preparations is on a case-by-case basis only and should not be listed on the CDR service drug list. Commercially available ready-to-use products should be sourced whenever feasible.

**Notes:**

a) NIOSH defines hazardous drug as a drug that is:

i. Approved for use in humans by the FDA-CDER;

*AND*

ii. Not otherwise regulated by the U.S. Nuclear Regulatory Commission;

*AND*

iii. *either;*

- Is accompanied by prescribing information in the "package insert" that specifies special handling information (Manufacturer Special Handling Information-MSHI) to protect workers handling the drug;

*OR*

- Is identified as a carcinogenic hazard, developmental hazard, reproductive hazard, genotoxic hazard, or other health hazard by exhibiting one or more of the following

toxicity criteria in humans, animal models, or in vitro systems:

- carcinogenicity;
- developmental toxicity (including teratogenicity);
- reproductive toxicity;
- genotoxicity;
- organ toxicity at low doses;

*OR*

- structure and toxicity profile that mimics existing drugs determined hazardous by exhibiting any one of the previous five toxicity types

unless the drug also exhibits a molecular property that may limit the potential for adverse health effects in healthcare workers from exposure to the drug.

b) National Toxicology Program (NTP)

i. An agency within the U.S. Department of Health and Human Services (DHHS) that manages a cancer classification system for human carcinogens.

ii. NTP publishes the Report on Carcinogens, a congressionally mandated listing of chemicals that are known to be human carcinogens or reasonably anticipated to be human carcinogens.

iii. Reports are open for access on-line

c) International Agency for Research on Cancer (IARC)

i. The IARC is a unit within the World Health Organisation (WHO) that serves as an international research agency on cancer.

ii. IARC produces well respected "Monographs on the Evaluation of Carcinogenic Risks to Humans." And classified the agents to:

- Group 1 (carcinogenic to humans)
- Group 2A (probably carcinogenic to humans)
- Group 2B (possibly carcinogenic to humans)
- Group 3 (Not classifiable as to its carcinogenicity to humans
- Group 4 (Probably not carcinogenic to humans)

iii. Monographs are open for access on-line

d) Manufacturer's special handling information (MSHI)

i. MSHI is not highly scrutinised by the U.S. FDA but most manufacturers do choose to identify genotoxic/ cytotoxic hazardous drugs for special handling to protect the workers who must handle them.

ii. Information found in package inserts may differ by country due to differences in regulation and product registration requirement.

iii. Specific labeling for cytotoxic agents (only) is compulsory for product registration in Malaysia.

e) Besides the above-mentioned, most current recommendations from other credible sources of reference should be taken into account as well for decision making: (not exhaustive)

- Safety Data Sheets or Material Safety Data Sheets
- Product labeling approved by the U.S. FDA
- Established drug references such as:
  - US Pharmacopeia,
  - Micromedex,
  - LEXIComp,
  - DrugBank (http://www.drugbank.ca/),
  - DailyMed (http://dailymed.nlm.nih.gov/dailymed/), etc.
- Special health warnings from drug manufacturers, FDA, and other professional groups and organisations (e.g. ASHP, ONS, ISOPP, etc)
- Reports and case studies published in medical and other healthcare profession journals
- Evidence-based recommendations from other facilities that meet the criteria defining hazardous drugs (e.g. BC Cancer Agency, eviQ, etc)

f) Toxicological profile of all drugs is subject to change as there may be new findings from time to time. Ensure all references used including NIOSH Hazardous Drug List, package insert, reports from NTP and IARC monographs, etc are as current as available.

## References


1. NIOSH [2024]. NIOSH list of hazardous drugs in healthcare settings, 2024. By Ovesen JL, Sam-mons D, Connor TH, MacKenzie BA, DeBord DG, Trout DB, O'Callaghan JP, Whittaker C. Cin-cinnati, OH: U.S. Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2025-103 (Supersedes 2016-161).

2. NIOSH [2023]. Managing hazardous drug exposures: information for healthcare settings. By Hodson L, Ovesen J, Couch J, Hirst D, Lawson C, Lentz TJ, MacKenzie B, Mead K. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2023-130, https://doi.org/10.26616/NIOSHPUB2023130.

3. Cancer Classification Systems May 14, 2020 V2. Agency for Toxic Substances and Disease Registry. https://www.atsdr.cdc.gov/pha-guidance/resources/ATSDR-Cancer-Classification-Systems-508.pdf.

4. ASHP Midyear 2020 Clinical Meeting and Exhibition. NIOSH, USP <800>, and EPA: Update on All Things Hazardous Session 285- Post Session Question Review. https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/compounding/docs/NIOSH-session-285-QA.pdf.

5. Drug Registration Guidance Document (DRGD) Third Edition, Seventh Revision January 2024. National Pharmaceutical Agency, Ministry of Health, Malaysia. https://www.npra.gov.my/easyarticles/images/users/1153/DRGD%20January%202024/MAIN-BODY-Drug-Registration-Guidance-Document-DRGD-3rd-Edition-7th-Revision-January-2024.pdf.

6. Hazardous Medication List: Reducing Occupational Exposure to Hazardous Medication for All Staff, Feb 2023 (ver 2.3). Alberta Health Services (Pharmacy Services, Health Professions Strategy and Practice and Workplace Health and Safety) and Covenant Health (Pharmacy Services), Canada.

7. BCCA Pharmacy Practice Standards for Hazardous Drugs: Module 1 Safe Handling of Hazardous Drugs. BC Cancer Agency, British Columbia, Canada: July 2008.

# 3.0 HANDLING OF HAZARDOUS DRUGS AT THE LOGISTICS PHARMACY AND SUBSTORES

The logistics pharmacy and substores play a critical role in the safe distribution of hazardous drugs. There are multiple studies reporting detection of cytotoxic residue from the manufacturing process on the outer surfaces of the vials of many commercial drugs received in pharmacies. The possibility that such contamination may extend to the inside of packing cartons or onto the package inserts cannot be excluded. All personnel who handle unopened vials including those who receive shipping cartons, unpack and arrange stock are at risk of exposure. Hence, effective safety protocols and training are pivotal to protect all handlers, as well as to prevent contamination of the surrounding environment and cross-contamination with non-hazardous materials. Spill kit (**refer Appendix 2**) and appropriate Personal Protective Equipment (PPE) for all activities involving hazardous drugs (**refer Appendix 1**) must be readily available.

All logistics pharmacy personnel should be well informed about the toxic nature of hazardous drugs and safe handling procedures in accordance with institutional protocols/ policies. In general, the safety recommendations for tasks performed at the logistics pharmacy are as followed:

**a) Receive and unpack shipment from supplier**

i) Wear disposable gloves and examine shipment for outward signs of damage or breakage.

ii) If there are (suspected) broken cartons/ containers/ vials, examine these items within a controlled environment.

iii) Policies and procedures must be in place for handling damaged shipment of hazardous drugs (e.g. quarantine and return to suppliers, dispose immediately as cytotoxic waste, etc).

iv) All personnel must be trained to handle leakage/ spill caused by broken cartons/ containers/ vials (**refer Appendix 2, 3 and 4**)

v) Some shipments from suppliers may not carry cytotoxic warning labels. Hence, all personnel must be made aware of which drugs that they are receiving are hazardous.

**b) Storage of hazardous drug**

i) Designate an area for hazardous drugs storage to separate them from other inventory in a manner that prevents cross contamination and accidental personnel exposure.

ii) Restrict access to authorised personnel only (e.g. logistics pharmacy personnel only, CDR unit personnel only).

iii) All hazardous drugs must be made easily identifiable with cytotoxic warning labels (**refer Appendix 5**).

iv) Store hazardous drugs in properly sized bins or on shelves that have guards to prevent accidental falling and breakage.

v) Hazardous drugs in the cold room/ refrigerator must be stored in individual leak and break-proof bins separately from non-hazardous drugs (if possible have designated refrigerator(s) for hazardous drug storage only).

vi) Spill kits must be kept in close proximity to the location of hazardous drugs stock.

vii) Wear disposable gloves when stocking, conducting inventory and arranging drug packages for further distribution.

**c) Distribution and Transportation to other units within facility**

i) Trolleys or other vehicles used to transport stock must be equipped with guards to prevent falling and breakage.

ii) Wear disposable gloves when handling distribution and transportation of hazardous drugs to other units.

iii) Hazardous drugs must be delivered directly (without detours) to the end-user's unit within the facility.

iv) Spill kit must be readily available to personnel involved in the transport of cytotoxic drug preparations.

v) All personnel involved in the transport of the drugs must receive training on dealing with breakages and spills.

**d) Spill management and cytotoxic waste disposal**

i) All personnel must be trained and retrained annually in hazardous drug safe handling and spill management.

ii) All cytotoxic waste which includes the items listed below should be disposed of in accordance with institutional cytotoxic waste management protocols:

- Disposable PPE (including gloves) worn when managing hazardous drug cartons/ containers/ vials in inventory
- All worn disposable PPE, contaminated single-use equipment and waste generated from spill management
- Items contaminated by leakage/ spill episodes (if applicable)
- Unused expired hazardous drugs (if any) of all types of dosage form should be disposed as cytotoxic waste (not regular pharmaceutical waste)

**Note(s):**

❖ The use of gloves does not substitute the need for hand-washing after completion of each task.

- ❖ Risk of exposure is low with intact boxes/ bottles/ blister packs of tablets and capsules.
- ❖ Oral cytotoxic drugs in the form of powder or liquid needed to be handled as carefully as the injectable drugs. Handle as spill if bottles/ containers are broken or leaked.

## References:


1. International Society of Oncology Pharmacy Practitioners. *Standards for the Safe Handling of Cytotoxics*. International Society of Oncology Pharmacy Practitioners, 2022.
2. Managing hazardous drug exposures: information for healthcare settings, Hodson L, et al, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2023-130, https://doi.org/10.26616/NIOSHPUB2023130
3. Power LA, Coyne JW. ASHP Guidelines on Handling Hazardous Drugs. Am J Health Syst Pharm. 2018 Dec 15;75(24):1996-2031. doi: 10.2146/ajhp180564. Epub 2018 Oct 16.

# 4.0 HANDLING OF HAZARDOUS DRUGS AT THE IN-PATIENT PHARMACY AND CLINICAL AREA (WARD AND DAY CARE UNIT)

## 4.1 INTRODUCTION

There is no one universal approach that can protect healthcare workers against exposure to hazardous drugs in all tasks. Multiple precautionary measures have to be taken concurrently to reduce the risk of workplace exposure and environmental contamination which include but not limiting to the following:

a) Ensure hazardous drugs are handled as per accepted safe handling standards at all stages:

   i) Receipt, storage, and transport

   ii) Drug compounding or preparation

   iii) Administration

   iv) Handling body fluids following administration

   v) Deactivation and/ or decontamination

   vi) Cleaning and disinfecting

   vii) Spill management

   viii) Waste disposal

b) Label, tag, or mark all containers of cytotoxic drugs and waste with the hazard warnings.

c) Wear PPE and use exposure controls as appropriate for each task (**refer Appendix 1**).

d) Always practice “non touch technique’ when handling hazardous drugs.

e) Provide proper home care and safe handling education to patient and caregiver when required.

f) An institutional list of hazardous drug kept/ use should be created and updated in a timely manner for the reference of all personnel.

## 4.2 HANDLING OF HAZARDOUS DRUGS AT THE IN-PATIENT PHARMACY

Controls and safe handling procedures should be in place for the storage, supply/ dispensing and disposal of hazardous drug/ waste within In-Patient Pharmacy:

**a) Storage**

i) Designated storage areas/ containers are recommended and separated from the non-hazardous agents.

ii) These areas must be clearly defined and labelled as hazardous drugs storage locations.

iii) Easily recognisable warning labels should be attached to shelving to alert all pharmacy personnel.

**b) Supply/ Dispensing**

i) Drugs should be supplied in Unit-of-Use packages or in quantity enough for one particular cycle/ block of treatment only.

ii) Wear a single layer of gloves when handling hazardous drugs and wash hands thoroughly after handling the drugs. Use a surgical mask if handling loose tablets/ capsules (not blister-packed).

iii) All equipment (e.g tray, forcep, etc) used in the dispensing of cytotoxic tablets and capsules must be designated to this purpose only and clearly labelled as such.

iv) Cytotoxic tablets and capsules should not be counted using an automated counting machine to prevent generation of powdered hazardous contaminants at the work space.

v) Tablets and capsules should not be crushed or broken. If required, please refer to Chapter 4.3 Handling of Hazardous Drugs at Clinical Area (Ward and Day Care Unit).

vi) Avoid pouring liquid hazardous drugs whenever possible. When unavoidable, perform the procedure with caution and thoroughly clean all equipment accordingly afterward.

vii) All non-disposable materials exposed to hazardous agents including counting trays, tools, etc should be washed thoroughly with soap and water after use. Rinse the sink and dry with a paper towel after washing. Dispose of towel as cytotoxic waste.

viii) Labelling requirement for cytotoxic drugs supplied to wards:

- Zip-lock envelopes/ containers of the cytotoxic drugs should be clearly labelled to inform those handling them of their hazardous nature and the precautions to be taken.
- Stick the “Cytotoxic” hazard symbol (**refer Appendix 5 for example**) on drug envelopes or containers or alternatively, use an envelope with warning printed on it.
- The back of the drug envelope should be transparent to ease identification of its content without having to remove or open the envelope.

**c) Disposal**

i) Decision to reuse returned drugs for other patients (if it is allowed) should be based on criteria set by institutional policy.

ii) The causes for drug return should be identified and documented on the patient's pharmacotherapy review record (e.g. on CP2 form, case note, medication return (PhIS), etc) whenever possible.

iii) Disposal of non-injectable hazardous drugs should be performed in the same manner as for cytotoxic injectables and waste, with additional precautionary steps, to reduce risk of environmental contamination:

- Loose tablets/ capsules: Pack in sealed plastic bag before putting them into sharps bin/ cytotoxic waste bag/ bin
- Oral liquids: Close the medicine bottle tightly, put into a sealed plastic bag before discarding it into sharps bin/ cytotoxic waste bag/ bin

iv) Cytotoxic waste bags/ bins must be clearly labelled and properly sealed/ tied/ closed

v) Do not throw hazardous drugs in the trash or down the drain, and don't flush them down the toilet

vi) If cytotoxic waste is mixed with other pharmaceutical waste, it should be handled in the same manner as cytotoxic waste.

vii) Waste should be handled and disposed as per institutional cytotoxic waste management protocol.

## 4.3 HANDLING OF HAZARDOUS DRUGS AT THE CLINICAL AREA (WARD and DAY CARE UNIT)

Nursing personnel caring for cancer patients in the ward and daycare unit are constantly at risk of exposing themselves to the health hazard effects of hazardous drugs handled by them on a routine basis. It is crucial to ensure that they are well trained to practice safely, be provided with all the necessary PPE and equipment, and safeguarded by stringent hazardous drug/ waste management protocols and policies. Precautionary measures should be spelled out clearly in written protocols/ policies covering all activities of handling cytotoxic drug/ waste from storage and administration till waste disposal.

**a) Personal Protective Equipment (PPE) Safety**

i) Appropriate Personal Protective Equipment (PPE) should be worn in all activities of handling hazardous drug/ waste (**refer Appendix 1**):

- Receipt, storage, and transport from the pharmacy
- Preparing drug doses
- Administration of the medications
- Handling patients' body fluids and waste following administration
- Cleaning and disinfecting
- Spill management
- Waste disposal

ii) Evaluate criteria/ characteristics of PPE required for each activity before purchase/ use. (**refer Appendix 6**)

iii) Measures to reduce risk of personnel exposure and cross-contamination include:

- Do not wear contaminated gloves to use the phone, type on a computer keyboard, program IV pumps, open doors and cabinets, or touch body parts (e.g., face, adjusting a mask).
- Inspect PPE for defects or tears before use.
- Do not reuse gloves, gowns, shoe covers, or any other disposable PPE.
- Change gloves after 30 minutes of wear, or earlier if damaged, or contaminated.
- Change gowns when leaving the handling area, after a spill or splash, or after two to three hours of continuous use.
- Remove shoe covers when leaving the compounding area or after cleaning a spill.
- Do not use eyeglasses as the sole means of eye protection; wear goggles with side shields or a face shield when risk splashing is possible.
- Dispose of all disposable PPE as cytotoxic waste after use.
- For non-disposable PPE (i.e., respirators, eyes, and face protection), decontaminate and clean after each use and properly dispose of all cleaning materials used to decontaminate this equipment.

**b) Storage in Clinical Area (Wards/ Daycare Unit)**

i) Hazardous drugs must be delivered to qualified/ trained personnel in the wards/ day care units who take responsibility for the appropriate storage of the drugs as stated on the labels.

ii) The drugs should be stored separately from other non-hazardous drugs at a designated area with access limited to staff only.

iii) Storage should have features that prevent containers of cytotoxic drugs from falling and clearly labelled with cytotoxic warning signs.

iv) Parenteral doses of cytotoxic drugs should be stored in a designated refrigerator or cupboard.

v) Oral cytotoxic drugs can be stored in the patient's own medication bin within the drug trolley as long as it is clearly labelled or inside a container/ bin/ box designated for cytotoxic drugs placed inside the cupboard/ refrigerator.

vi) Do not re-use bottles which have contained cytotoxic medication for other purposes.

vii) Spill kit must be readily accessible. All staff shall be trained in safe handling of hazardous drugs and spill management.

## 4.4 ADMINISTRATION OF HAZARDOUS DRUGS VIA PARENTERAL ROUTE

The standard precautions of administering hazardous drugs via the parenteral route:

a) Ensure patient consent for chemotherapy is obtained. Education provided by nursing staff before the start of treatment.

b) Practice ***aseptic non-touch technique*** throughout the parenteral administration process.

c) Ensure appropriate PPE are worn (**refer Appendix 1**).

d) Use syringes and IV infusion sets with luer-lock fittings/ connections to maintain an appropriate needle-less and closed system.

e) Always check the connections on the infusion set for leakage or cracking.

f) Inspect the sealed chemotherapy bag before opening to ensure no spillage has occurred within the bag.

g) Open cytotoxic doses directly onto designated trays or dressing pack.

h) Place a sterile gauze swab under the injection port during administration. Administration should be performed over a plastic-backed absorbent sheet/ pad.

i) Do not expel air from syringes. If air is in the syringe, hold it in such a way that the air is up near the plunger until the entire volume of drug is administered.

j) Ensure that the infusion set is primed with compatible fluid.

k) Always insert/ spike the infusion set into a cytotoxic infusion bag/ bottle at waist height.

l) Ensure patients are hydrated and premedicated as per treatment protocol before start of administration.

m) Ensure the rate of administration is correct.

n) Flush well between drugs using a compatible fluid.

o) If a drug is prone to photo-degradation, ensure that the infusion solution is covered with an opaque sheet/ bag.

p) Monitor regularly IV catheter sites for signs and symptoms of swelling and extravasation.

q) Monitor regularly for the signs and symptoms of allergy, infusion related reactions and other adverse effects.

r) If a special infusion set is required (DHEP-free, with or without filters, etc), use only those recommended.

s) DO NOT recap needles.

t) Ensure sharps disposal containers are readily accessible and additional disposal containers are available for cytotoxic waste.

u) DO NOT transport patients while hazardous drug administration is in progress.

v) Document medication administered completely and accurately including patient's response. In the event of incomplete or interruption of administration due to any reason, it should be clearly recorded.

### 4.4.1 PROCEDURE - PRE-ADMINISTRATION OF PARENTERAL CYTOTOXIC DRUGS (IM, SC, IV BOLUS, IV INFUSION)

Verification and preparation before chemotherapy administration should include:

1. Verify appropriate pre-hydration and premedication (anti-emetics, steroids, etc) given. Timing is crucial.
2. Determine the sequence of drugs to be given as per protocol: chemotherapy and non-chemotherapy drugs (Folinic acid, monoclonal antibodies, etc)
3. Check medication rights: (5Rs)
    a) Right Patient- Use at least two identifiers to verify the patient.
    b) Right Medication- Check drug label against prescription/ chemotherapy order/ form, date of administration and expiry date.
    c) Right Dose- Check the drug dose with the prescription/ chemotherapy order/ form to ensure it is correct.
    d) Right Route - Check that the route is appropriate for the medication to be administered.
    e) Right Time- Check the appropriate time to administer medication as per prescription/ chemotherapy protocol/ order.
4. Verify that patient consent has been obtained.
5. Explain to the patient/ caregiver about the procedure and possible unwanted effects of chemotherapy to be watched out for e.g. allergy reactions, discoloration of bodily fluid etc.

### 4.4.2 PROCEDURE - INTRAMUSCULAR (IM) AND SUBCUTANEOUS (SC) DRUG ADMINISTRATION

1. Position the patient comfortably.
2. Select an appropriate site for administration. If frequent injections are given, rotate the injection site.
3. Place a plastic-backed absorbent sheet under the injection site.
4. Perform hand hygiene.
5. Don appropriate PPE and gloves (**refer Appendix 1**).
6. Perform medication safety check (5Rs).
7. Inspect syringes containing cytotoxic drugs prepared by Pharmacy for any leakage, cloudiness or signs of precipitation/ contamination. Contact Pharmacy for further instructions if occurred.
8. Attach appropriately sized needles (if not using a pre-filled syringe). Do not expel air from the syringe.
9. Administer pre-medications (if any) as per protocol.
10. If the skin at the injection site is visibly soiled it should be cleaned first with soap and water.
11. Disinfect injection site with 60-70% alcohol-based solution on a single-use swab or cotton-wool ball or as per institutional protocol.
12. Administer the subcutaneous or intramuscular injection using the appropriate technique.
13. Apply gentle pressure over the injection site with a sterile cotton/ gauze and plaster. Avoid rubbing the site.
14. Dispose of all equipment used as cytotoxic waste.
15. Remove PPE and dispose of it as cytotoxic waste.
16. Perform hand hygiene.

### 4.4.3 CANNULA PLACEMENT AND LINE PREPARATION FOR IV DRUG ADMINISTRATION (BOLUS, INTERMITTENT and CONTINUOUS INFUSION)

Intravenous cytotoxic drugs may be administered as bolus injection, intermittent or continuous infusion as determined by the treatment protocol through a central venous access device (CVAD) or peripheral intravenous cannula (IVC). Cannula placement and IV-line preparation should be done accordingly:

**a) Intravenous Cannula (IVC)**

i) Vesicant drugs should be administered through a newly sited cannula.

ii) Choose an appropriate IVC type and size for the type of treatment and patient's veins - where possible, use a large vein in the middle of the forearm.

iii) Avoid cannulating-

- the back of hand, joints, points of flexion and the antecubital fossa.
- the arm on the side of an axillary lymph node dissection/ side of breast cancer/ lymphoedematous arm.
- the same vein repetitively due to risk of extravasation from the old site. If unavoidable, it MUST be proximal to the previous puncture site.

iv) Verify vein patency and integrity by checking if there is resistance when injecting fluid into the cannula, blood return and free flow access.

**b) Central venous access device (CVAD)**

i) Access CVAD as per institutional policy and guidelines.

ii) Use an appropriate needle size for implanted venous ports.

iii) Verify patency by withdrawing blood and flushing with 5 to 10 mL sodium chloride 0.9% or other compatible fluid.

iv) Do not use if resistance, pain or discomfort is felt during the flow of fluid.

The IVC and CVAD can be stabilised and secured with a transparent dressing/ tape to allow the site to be constantly seen. DO NOT cover the site of the injection.

**c) Extra precaution for vesicant drugs:**

i) If several drugs have to be given, administer a vesicant agent first followed by the other agents.

ii) If there is more than one vesicant drug, administer DNA binding drugs first, followed by non-DNA binding drugs, e.g. anthracyclines followed by vinca alkaloids.

iii) All vesicant drugs should be diluted and administered via a side port of a free-flowing IV infusion.

iv) Do not inject against resistance.

v) Check line patency and blood return regularly throughout the drug administration.

vi) Educate the patient and carers to immediately report symptoms such as pain, burning, stinging, swelling, or erythema during and after administration.

vii) Monitor the site for signs of extravasation or leakage e.g. blebbing (the formation of a raised, fluid-filled bubble under the skin) at the injection site.

viii) If extravasation is suspected or there is any doubt about vein integrity, STOP the infusion and remove the needle.

ix) Extravasation must be managed immediately to minimise tissue damages.

x) Avoid administration of vesicant drugs using infusion pumps whenever possible.

### 4.4.4 PROCEDURE - ADMINISTRATION OF CYTOTOXIC DRUGS VIA INTRAVENOUS CANNULA (IVC)

1. Position the patient comfortably.
2. Perform hand hygiene.
3. Don appropriate PPE and gloves (**refer Appendix 1**).
4. Prepare flush/ lock/ intravenous lines using non-touch technique. Prime IV tubing with non-cytotoxic compatible fluids below eye level (if required).
5. Insert IVC into the appropriate site using the appropriate size cannula.
6. Check the IVC for blood return and flush with 5 to 10 mL sodium chloride 0.9% to confirm patency.
7. Stabilised and secured IVC with a transparent dressing/ tape.
8. Connect IV administration line(s) and check that the IV infusion flows freely.
9. Place a plastic-backed absorbent sheet under the injection site (arm).

10. Inspect syringes/ drug containers for any leakage, cloudiness or signs of precipitation/ contamination. Contact Pharmacy for further instructions if occurred.

11. Perform medication safety check (5Rs).

12. Administer drugs in sequence as per treatment protocol and assess patency of IVC regularly throughout administration. Use a closed system transfer device (CSTD) where available.

13. If drug is to be given as bolus injection:

    a) Do not expel air from the syringe.

    b) Connect syringe, ensuring luer lock connections are secure.

    c) Administer via a side port of a free-flowing IV infusion.

    d) Use gauze to hold beneath the side port and syringe connection.

14. If drug is to be given as IV infusion:

    a) Clamp IV line.

    b) When spiking the IV bag/ bottle, place the bag/ bottle on a clean flat surface at waist height.

    c) Use gauze to hold beneath the bag/ bottle connection site and connect IV bag/ bottle appropriately (where a closed system is not used).

    d) On completion of infusion, do not disconnect the IV bag/ bottle.

15. Monitor patients for signs and symptoms of extravasation and hypersensitivity and/ or infusion-related reactions.

16. Flush the line on completion with a compatible fluid via a separate/ side line, do not disconnect the IV bag/ bottle from the line.

17. Disconnect line from IVC and dispose IV bag/ bottle with the infusion set still attached as cytotoxic waste.
18. Dispose of all equipment used as cytotoxic waste.
19. Remove PPE and dispose of it as cytotoxic waste.
20. Perform hand hygiene.

### 4.4.5 PROCEDURE - ADMINISTRATION OF CYTOTOXIC DRUGS VIA CENTRAL VENOUS ACCESS DEVICE (CVAD)

1. Position the patient comfortably
2. Perform hand hygiene
3. Don appropriate PPE and gloves (**refer Appendix 1**)
4. Prepare flush/ lock/ intravenous lines using non-touch technique. Prime IV tubing with non-cytotoxic compatible fluids below eye level (if required).
5. Access CVAD using aseptic non-touch technique and as per institutional protocol (if any)
6. Ensure patency of CVAD observing by aspiration (blood return) and injection (free flow of IV infusion)
7. Ensure insertion site can be visualised
8. Connect IV administration line(s) and check that the IV infusion flows freely
9. Inspect syringes/ drug containers for any leakage, cloudiness or signs of precipitation/ contamination. Contact Pharmacy for further instructions if occurred.
10. Perform medication safety check (5Rs)

11. Administer drugs in sequence as per treatment protocol and assess patency of IVC regularly throughout administration. Use a closed system transfer device (CSTD) where available.
12. If drug is to be given as bolus injection:
    a) Do not expel air from syringe
    b) Connect syringe, ensuring luer lock connections are secure
    c) Administer via a side port of a free-flowing IV infusion
    d) Use gauze to hold beneath the side port and syringe connection
13. If drug is to be given as IV infusion:
    a) Clamp IV line
    b) When spiking IV bag/ bottle, place bag/ bottle on clean flat surface at waist height
    c) Use gauze to hold beneath the bag/ bottle connection site and connect IV bag/ bottle appropriately (where a closed system is not used)
    d) On completion of infusion, do not disconnect IV bag/ bottle
14. Monitor patient for signs and symptoms of extravasation and hypersensitivity and/ or infusion-related reactions
15. Flush the line on completion with a compatible fluid via a separate/ side line, do not disconnect the IV bag/ bottle from the line
16. Disconnect line from CVAD and dispose IV bag/ bottle with the infusion set still attached as cytotoxic waste
17. De-access CVAD as per institutional protocol
18. Dispose of all equipment used as cytotoxic waste
19. Remove PPE and dispose of it as cytotoxic waste.
20. Perform hand hygiene

## 4.5 ADMINISTRATION OF HAZARDOUS DRUGS VIA ORAL ROUTE

Oral anticancer medicines can be potentially hazardous if handled carelessly. Accidental exposure may arise from handling loose tablets, capsules or oral liquids. Standard safe handling measures for oral cytotoxic medication should include:

a) Equipment/ tools such as re-useable medicine cups, tweezer and tablet cutter used for preparation and administration should be reserved for use in handling hazardous drugs only. Keep all equipment/ tools in designated container(s) with cytotoxic warning labels.

b) Patients should be advised to swallow tablets or capsules whole and not to chew them. Patients and carers should wash their hands thoroughly after taking/ administering oral anticancer medicines.

c) Do not use any tablets or capsules if it is evident that loose powder or liquid is present in the container, where this would not be expected (for example tablets are damaged or liquid filled capsules have leaked). Return the affected medications and request a replacement from the Pharmacy.

### 4.5.1 PROCEDURE- ADMINISTRATION OF A WHOLE CYTOTOXIC TABLET/ CAPSULE

1. Identify a designated and clean area/ workbench/ worksurface to prepare drugs.
2. Clean work surfaces with alcohol wipe, allow to dry.
3. Place an absorbent pad/ sheet on the work bench/ surface.
4. Prepare equipment/ tools at waist height.
5. Perform hand hygiene

6. Don appropriate PPE (**refer Appendix 1**)
7. Perform medication safety checks (5Rs).
8. Transfer the required number of tablets/ capsules from their container(s)/ envelopes using tweezers directly into the patient's medicine cup.
9. If not preparing the drug at the bedside, gloves must be changed before performing other work.
10. Instruct and ensure patients take the tablet/ capsule directly from the medicine cup without touching the tablet/ capsule. If a patient/ caregiver has touched the tablets/ capsules ensure that they wash their hands.
11. Discard the used disposable medicine cup as cytotoxic waste (if applicable).
12. While wearing PPE wash tweezers (and re-usable medicine cup) with soap and water. The same tweezer (and re-usable medicine cup) should be reserved for use for handling cytotoxic drugs only
13. After washing tweezers (and re-usable medicine cup), remove contaminated gloves and replace them with clean gloves.
14. Return tweezers (and re-usable medicine cup) to the cytotoxic container.
15. Rinse the sink and dry with a paper towel. Dispose of towel as cytotoxic waste
16. Remove PPE and dispose of as cytotoxic waste
17. Perform hand hygiene.

18. If a patient vomits after ingestion of tablets/ capsules, refer to a treating physician for further management. Clean the vomitus as per cytotoxic waste management.

**Note(s):**

- ❖ Unit-of-Dose/ Blister/ foil packed oral medicines should be dispensed into a medicine cup with their packaging intact. Push the tablets/ capsules out of their blister/ foil pack into the medicine cups at bedside.
- ❖ Use of single-use disposable medicine cups is preferred. For re-usable medicine cups, it must be washed and dried properly after each use.

### 4.5.2 PROCEDURE- CUTTING CYTOTOXIC TABLETS

1. Identify a designated and clean area/ workbench/ worksurface to prepare drugs.
2. Clean work surfaces with alcohol wipe, allow to dry.
3. Place an absorbent pad/ sheet on the work bench/ surface.
4. Prepare equipment/ tools at waist height.
5. Perform hand hygiene.
6. Don appropriate PPE (**refer Appendix 1**).
7. Perform medication safety checks (5Rs).
8. Put the tablet into the pill cutter in a zip-lock bag using designated tweezers.
9. Seal the bag.
10. Break the tablet cleanly using the tablet cutter.

11. Open the bag and transfer the required tablet portion(s) into a medicine cup with the tweezers.
12. Return the unused portion(s) of the tablet back into its container.
13. Discard the used disposable medicine cup as cytotoxic waste (if applicable).
14. Gloves must be changed before performing other work.
15. Instruct and ensure patients take the tablet/ capsule directly from the medicine cup without touching the tablet/ capsule. If a patient/ caregiver has touched the tablets/ capsules ensure that they wash their hands.
16. Place contaminated single-use medicine cup in zip lock bag and disposed of as cytotoxic waste (if applicable).
17. While wearing PPE wash tweezers, tablet cutter (and re-usable medicine cup) with soap and water. The same tweezer, tablet cutter (and re-usable medicine cup) should be reserved for use for handling cytotoxic drugs only.
18. After washing all the equipment, remove contaminated gloves and replace them with clean gloves.
19. Return tweezers, tablet cutter (and re-usable medicine cup) to the cytotoxic container.
20. Rinse the sink and dry with a paper towel. Dispose of towel as cytotoxic waste.
21. Remove PPE and dispose of it as cytotoxic waste.
22. Perform hand hygiene.

23. If a patient vomits after ingestion of medicine, refer to a treating physician for further management. Clean the vomitus as per cytotoxic waste management.

**Note(s):**

- ❖ Use of single-use disposable medicine cups is preferred. For re-usable medicine cups, it must be washed and dried properly after each use.

### 4.5.3 PROCEDURE- PREPARING LIQUID CYTOTOXIC DRUGS FROM TABLETS/ HARD CAPSULES

1. Identify a designated and clean area/ workbench/ worksurface to prepare drugs.
2. Clean work surfaces with alcohol wipe, allow to dry.
3. Place an absorbent pad/ sheet on the work bench/ surface.
4. Prepare equipment/ tools at waist height.
5. Perform hand hygiene.
6. Don appropriate PPE (**refer Appendix 1**)
7. Take an appropriate size (5ml and above) and type of syringe (oral syringe, enteral syringe or etc), remove the plunger.
8. IF WHOLE TABLET IS REQUIRED:
    a) Use tweezers to transfer tablets/ capsules from their original container(s) directly into the syringe chamber and restore the plunger.
    b) Expel air into sterile gauze moistened with sterile water (not soaking wet).
9. IF PART OF A TABLET IS REQUIRED:

a) Using tweezers place the tablet into the pill cutter in a zip-lock bag.

b) Seal the bag.

c) Break the tablet to obtain the required dose using a tablet cutter.

d) Open the bag and use the tweezers to collect the required tablet portion, place directly into the syringe chamber and restore the plunger.

e) Return the unused portion of the tablet back in the tablet container.

f) Expel air into sterile gauze moistened with sterile water (not soaking wet).

10. Dispose the sterile gauze immediately as cytotoxic waste.
11. Draw up a minimum of 2mL Water for Injection and 0.5mL air into the syringe.
12. Cap the syringe with a stopper.
13. Check the connections are secure.
14. Shake the syringe carefully until the tablet is fully dissolved. Label the syringe clearly.
15. Gloves must be changed before performing other work.
16. At bedside, perform medication safety checks (5Rs) before administration.
17. Administer directly into the patient's mouth, if prescribed to be given orally (if to be given via enteral feeding tube, please refer **Chapter 4.6 Administration of Cytotoxic Drugs via Enteral Route**).
18. Rinse the syringe by drawing equal volume of water and administer it directly into the patient's mouth to ensure full dose is given
19. Dispose oral syringe/ syringe and stopper as cytotoxic waste.

20. While wearing PPE wash pill cutter and tweezers used with soap and water.
21. After washing equipment, remove contaminated gloves and replace them with clean gloves.
22. Return tablet cutter and tweezers to the cytotoxic container.
23. Rinse the sink and dry with a paper towel. Dispose of towel as cytotoxic waste
24. Remove PPE and dispose of it as cytotoxic waste.
25. Perform hand hygiene.
26. If a patient vomits after ingestion of medicine, refer to a treating physician for further management. Clean the vomitus as per cytotoxic waste management.

**Note(s):**

- Hard capsules can be dissolved with the same method. The shell of the capsule should dissolve (may take some time) but the granules from inside the capsule might still be seen.
- Do not cut or open the hard capsules
- Use of oral syringe and mixing cannula would help to prevent accidental IV administration and needle prick injury.

### 4.5.4 PROCEDURE- ADMINISTRATION OF LIQUID CYTOTOXIC DRUGS

1. Identify a designated and clean area/ workbench/ worksurface to prepare drugs.
2. Clean work surfaces with alcohol wipe, allow to dry.
3. Place an absorbent pad/ sheet on the work bench/surface.
4. Prepare equipment/ tools at waist height.

5. Perform hand hygiene
6. Don appropriate PPE (**refer Appendix 1**)
7. Open the drug bottle.
8. Attach the oral syringe/ syringe to a mixing cannula/ needle and draw up the required volume of cytotoxic drug from the bottle.
9. Disconnect the oral syringe/ syringe from the mixing cannula/ needle and discard the mixing cannula/ needle immediately as cytotoxic waste.
10. If there is air in the oral syringe/ syringe that must be removed, expel air into sterile gauze moistened with sterile water (not soaking wet)
11. Dispose of the sterile gauze immediately as cytotoxic waste.
12. Disconnect and dispose of the mixing cannula/ needle and cap the oral syringe/ syringe with a stopper. Label the syringe clearly.
13. Gloves must be changed before performing other work.
14. At bedside, perform medication safety checks (5Rs) before administration.
15. Administer directly into the patient's mouth, if prescribed to be given orally (if to be given via enteral feeding tube, please **refer Chapter 4.6 Administration of Cytotoxic Drugs via Enteral Route**)
16. Rinse the syringe by drawing equal volume of water and administer it directly into the patient's mouth to ensure full dose is given.
17. Dispose oral syringe/ syringe and stopper as cytotoxic waste.
18. Dispose of all equipment used as cytotoxic waste.
19. Remove PPE and dispose it as cytotoxic waste.
20. Perform hand hygiene.

21. If a patient vomits after ingestion of medicine, refer to a treating physician for further management. Clean the vomitus as per cytotoxic waste management.

**Note(s):**

- ❖ Use of oral syringe and mixing cannula would help to prevent accidental IV administration and needle prick injury.

### 4.5.5 PROCEDURE- ADMINISTRATION OF SOFT CAPSULES (TRETINOIN [ATRA], ISOTRETINOIN)

1. **For patients with no swallowing difficulty,** handle as per administration of a whole cytotoxic tablet/ capsule.
2. **For patients with swallowing difficulty,** don appropriate PPE and may use either method below to administer medication:

   **a) <u>Method 1</u>**

   i) Puncture the capsule using a needle to make a small hole.

   ii) Squeeze the contents into soft fatty food e.g. oatmeal, lukewarm milk, ice-cream or yoghurt. The contents of the capsule have a slightly bitter taste.

   **b) <u>Method 2</u>**

   i) Puncture a small hole into the capsule.

   ii) Let the patient chew the capsule and ensure the contents are fully sucked

3. **For patients with enteral feeding tube,**

   a) Identify a designated and clean area/ workbench/ worksurface to prepare drugs.

   b) Clean work surfaces with alcohol wipe, allow to dry.

c) Place an absorbent pad/ sheet on the work bench/ surface.

d) Prepare equipment/ tools at waist height.

e) Perform hand hygiene.

f) Don appropriate PPE (**refer Appendix 1**).

g) Prepare each dose at the time of administration.

h) Transfer the required number of capsules from the bottle with a tweezer/ push the capsules from its blister pack into a medication cup.

i) Draw up 10ml olive oil/ soybean oil/ glycerol/ milk and place in another medicine cup.

j) Use a syringe and needle to carefully puncture the capsule and draw the fluid out from the capsule.

k) Squeeze the capsule to ease withdrawal of its content.

l) Put the fluid into the olive oil/ soybean oil/ glycerol/ milk.

m) Repeat the same for remaining capsules.

n) Mix the content in the medicine cup with a disposable spatula.

o) Discard empty capsules and other contaminated items e.g wipes, gauze, spatula, etc as cytotoxic waste.

p) Change and discard gloves as cytotoxic waste.

q) Draw the mixture into an oral syringe/ enteral syringe.

r) At bedside, perform medication safety checks (5Rs) before administration.

s) Refer Chapter 4.6 Administration of Cytotoxic Drugs via Enteral Route. After administration, rinse the oral/ enteral syringe with

equal volume of olive oil/ soybean oil/ glycerol/ milk but DO NOT rinse with water.

**Note(s):**

- There is a large inter and intra-patient variation in plasma tretinoin levels reported and doses may need to be adjusted to compensate. Dose adjustment is required when the patient is able to swallow the whole capsule.
- Administer immediately after preparation as tretinoin & Isotretinoin are light and moisture sensitive.
- Choice of vehicle used (olive oil/ soybean oil/ glycerol/ milk) to suspend Tretinoin & Isotretinoin for enteral feeding depends on availability. One vehicle may work better than the other.
- Medication safety precautions should be taken when handling sound-alike medications for both Tretinoin (ATRA) and Isotretinoin.

## 4.6 ADMINISTRATION OF CYTOTOXIC DRUGS VIA ENTERAL ROUTE

Handling patients with swallowing difficulty who require enteral administration of medication is a challenging task. It was estimated that

only 46% of oral cancer drugs had instructions for extemporaneous preparation of liquid formulations and only 38% of them had information related to enteral tube administration (**refer Appendix 7**). If data is not available in any published literature, the drug manufacturer should be contacted for further information if possible. Administer the freshly prepared drug with limited stability data immediately (within 1 hour of compounding) to minimise risk of compromised stability. Clinical decision making should always be subjected to critical assessment of risk versus benefit on case-by-case basis when there is no information related to the particular drug is available and/ or there is need to modify published compounding formula and administration procedures due to logistics and/ or technical constraints (e.g. nonavailability of equipment, devices and materials, etc).

The other technical aspects to be looked into are similar to those of non-cytotoxic drugs:

a) Ensure the type (polyvinylchloride (PVC), polyurethane (PUR), silicone or latex), size and position of the enteral feeding tube are appropriate. Interaction between the drug and the tubing material may occur.

b) Tube blockage may be caused by inappropriate drug formulations (inadequately crushed tablets), poor flushing and precipitation from drug-feed/ drug-drug interactions.

c) Drug-feed and drug-drug interactions can potentially reduce treatment effects or worsen the side-effects of drugs given. Therefore, it is important to design a feeding regimen and workflow that separate the cancer drug administration from others to limit drug-feed and drug-drug interaction.

d) Choose the appropriate size of syringe and avoid using syringes that are incompatible with parenteral devices. Syringe types that can be

used for enteral drug administration include oral syringe and female/ reverse luer syringe. Enteral syringes are available commercially.

e) Handle patients' enteral feeding in accordance with institutional protocol (if available).

### 4.6.1 PROCEDURE- ADMINISTRATION OF CYTOTOXIC DRUGS VIA NASOGASTRIC TUBE and PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) TUBE

1. Don appropriate PPE (**refer Appendix 1**), prepare the prescribed medicine and clean up accordingly (**refer Appendix 7 and the relevant chapters, Chapter 4.5.3 *Preparing Liquid Cytotoxic Drugs from Tablets/ Capsules,* Chapter 4.5.4 *Administration of Liquid Cytotoxic Drugs or* Chapter 4.5.5 *Administration of Soft Capsules (Tretinoin [ATRA], Isotretinoin*)

2. At bedside, perform medication safety checks (5Rs) before administration.

3. Place a plastic backed absorbent sheet/ pad under the connection site.

4. Place sterile gauze around the connection between the syringe and the gastric tube with adaptor connected.

5. If administered via naso-gastric tube, assess and confirm the position of the tube.

6. If administered via gastrostomy a separate extension tube must be designated for administering cytotoxic drugs.

7. Flush the tube with appropriate volume of water before medicine administration.

8. Administer the liquid medicine through the adaptor into the tube.

9. Draw an equal volume of water into the syringe and flush this via the tube to ensure that the total dose is administered.
10. Finally, flush the tube again with the appropriate volume of water.
11. Label the used naso-gastric or gastrostomy tube with a cytotoxic warning.
12. When no longer in use, the tubes should be disposed of as cytotoxic waste when removed.
13. Dispose oral syringe/ syringe and stopper as cytotoxic waste.
14. Dispose of all equipment used as cytotoxic waste
15. Remove PPE and dispose of it as cytotoxic waste.
16. Perform hand hygiene.

**Note(s):**

- The volume of water flushes prior and after drug administration may range from 5 - 30mls depending on patient's fluid requirement/ status. It may go as minimal as 5 ml for paediatrics or fluid-restricted patients.
- The extension tube used for drug administration via gastronomy should always be stored separate to other gastrostomy tubes and labelled as cytotoxic. Use an oral syringe adaptor on the tube if required.

## 4.7 ADMINISTRATION OF HAZARDOUS DRUGS - ALTERNATIVE ROUTES

Topical cytotoxic drug preparations are available in the forms of eye and ear drops, cream, ointment and gels. These preparations may need to be safely handled as much as the other dosage forms.

### 4.7.1 PROCEDURE- ADMINISTRATION OF CYTOTOXIC EAR/ EYE DROPS COMPOUNDED BY CDR UNIT (MITOMYCIN EYE DROPS, CICLOSPORIN EYE DROPS, GANCICLOVIR EYE DROPS, 5-FLUOROURACIL EYE DROPS, ETC)

1. Wash hands and prepare the required equipment.
2. Perform hand hygiene.
3. Don appropriate PPE (**refer Appendix 1**).
4. Perform medication safety check (5Rs) before application.
5. When applying ear drop:
    a) Clean the external ear of debris.
    b) Place a plastic-backed sheet underneath the patient's head.
    c) Tilt the patient's head so the affected ear is uppermost.
    d) Remove the cap of the eardrop bottle. Do not touch the dropper/ tip of the bottle.
    e) Straighten the auditory canal properly for the age of the:
        - Adult: Pinna pulled up and back.
        - Child: Pinna pulled straight back.
        - Infant and child under three: Pinna pulled back and down.
6. Squeeze the bulb of dropper/ bottle and allow drop(s) to fall on the side of the auditory canal.
7. Release the pinna and massage the tragus to help with movement of the drop into the canal.
8. Recap the bottle immediately after use.

9. Keep the patient in a lying position with the affected ear up for 5 minutes.

10. Drops that flow onto the neck may cause redness and irritation. Wipe off the excess liquid with a towel/ tissue/ gauze. Wash the area with soap and water. Then dry off with a towel/ tissue/ gauze. Discard it as cytotoxic waste.

11. When applying eye drops:

    a) Apply the white soft paraffin/ petroleum jelly (e.g. Vaseline) to the area immediately around the eye and on the cheek below the eye being treated to protect the skin from cytotoxic eyedrop

    b) Remove the cap of the eyedrop bottle. Do not touch the dropper/ tip of the bottle.

    c) Ask the patient to look up and away from the tip of the dropper/ bottle.

    d) Gently pull down the lower eye lid to create a pocket and deliver one drop into this pocket and then gently release the eye lid

    e) Do not let the tip of the dropper/ bottle touch the eye and lashes

    f) Recap the bottle immediately after use.

    g) Drops that flow onto the patient's cheek may cause redness and irritation. Wipe off the excess liquid with a towel/ tissue/ gauze. Wash the area with soap and water. Then dry off with a towel/ tissue/ gauze. Discard it as cytotoxic waste.

    h) If the patient has more than one eye drops being prescribed with, wait for about 5 minutes before using the next eye drops, and to use the cytotoxic eye drops as the last.

12. If the ear/ eye drops come into contact with a non-treatment/ affected area, wipe the area with gauze/ tissue and clean with warm soapy water.
13. Dispose all equipment used as cytotoxic waste.
14. Remove PPE and dispose of it as cytotoxic waste.
15. Perform hand hygiene.

**Note(s):**

- ❖ Minimise contact of the ear/ eye drops with patient's clothing
- ❖ Remove contact lenses before application of eyedrop
- ❖ Commercially available ready-to-use products containing drugs such as the Ciclosporin 0.05% eye drop, Chloramphenicol eye/ ear drop, etc can be handled as per manufacturer recommendations

### 4.7.2 PROCEDURE- TOPICAL APPLICATION OF CYTOTOXIC CREAMS, OINTMENTS OR GELS

1. Wash hands and prepare the required equipment.
2. Wash treatment/ affected area on the patient's skin with mild soap and dry thoroughly.
3. Perform hand hygiene.
4. Don appropriate PPE **(refer Appendix 1**).
5. Perform medication safety check (5Rs) before application.
6. Apply cream/ ointment/ gels using cotton-tipped applicator or disposable spatula.
7. Avoid contact with the patient's eyes, nose, mouth or areas close to the mucous membrane.

8. If cream/ ointment/ gels come into contact with non-treatment/ affected area, wipe the area with gauze and clean with soap and water.
9. Do not cover treatment/ affected areas with dressing unless otherwise instructed.
10. If necessary, after the required contact time, the area can be rinsed off carefully. Advise patients to have a shower rather than bath to ensure that they do not sit in bath water containing drug residue.
11. Dispose all equipment used as cytotoxic waste.
12. Remove PPE and dispose of it as cytotoxic waste.
13. Perform hand hygiene.

**Note(s):**

- Minimise contact of the cream/ ointment/ gels with patient's clothing

## 4.8 HANDLING OF BODY WASTE AFTER HAZARDOUS DRUG ADMINISTRATION

Cytotoxic drugs are primarily eliminated from the patient's body via renal and hepatic excretion. Therefore, all body substances may be contaminated with either the unchanged drug or active drug metabolites. The duration of the patient's body waste remaining "cytotoxic" depends on the type of drug received and rate of excretion (**refer Appendix 8**). It is acceptable to set a standardised timeframe of maximum 7 days for all

commonly used drugs. However, care should be taken to identify drug or new agents with extended duration of excretion.

Exposure to cytotoxic substances may occur in the ward/ daycare unit when:

a) handling vomitus, saliva, blood, excreta and fluid drained from body cavities

b) handling bedpans, urinals, soiled incontinence aids, emptying urinary catheter bags, colostomy/ urostomy bags and vomit bowls

c) handling bed linen or clothing soiled with patient waste, or potentially contaminated with the hazardous drug

d) touching or handling contaminated surfaces or equipment

e) cleaning body fluids from the floor (to handle as cytotoxic spill)

Safe handling measures to be taken by ward/ daycare unit personnel while handling patient's waste should include:

a) Appropriate PPE is worn when handling patient bodily fluids who completed chemotherapy in less than 7 days (**refer Appendix 1**)

b) Date and duration of drug administration should be clearly documented

c) Careful to avoid spills and splashes

d) Use indwelling catheter or appropriate incontinence aids for incontinent patients

e) Do not decant urine into a jug for measurement due to the risk of aerosol contamination; when urine is required to be measured, it should be weighed or measured using a leak-proof graduated urine measurement collector (disposable toilet and pan liners)

f) Appliances such as colostomy, ileostomy or urostomy bags, urinary catheters or incontinence aids, and heavily exuding dressing materials are double bagged prior to weighing and placed into the appropriate cytotoxic/ hazardous waste bin

Educate patients and caregivers on the usage of toilet:

a) To be seated when urinating to reduce the risk of splashes and aerosol contamination.

b) Use full flush and close the toilet lid before flushing

c) When a lid is not present, consider covering the open toilet with a plastic-backed liner prior to flushing to prevent splashing. This covering should be disposed of as cytotoxic waste.

Ways to reduce contamination of linen with cytotoxic waste that can be implemented include:

a) Use incontinence aids or catheterisation for incontinent patients

b) Use plastic- or vinyl-covered mattresses, pillows and chairs for ease of cleaning

c) Encourage ambulatory patients to use the toilet rather than bedpans/ urinals to avoid spilling

Soiled bedding and linen are considered contaminated. Bedding/ linen with small amounts of soiling can be treated as infected linen and handled as per institutional protocol. But those with heavy soiling should be treated and disposed of as cytotoxic waste. Contaminated bed mattresses and pillows should be cleaned with detergent and water in a way that will not generate aerosols.

## 4.9 SPILL AND ACCIDENTAL CONTAMINATION

Everything that come into contact with cytotoxic drugs are considered "contaminated":

a) Any material/ items associated with the administration e.g. sharps, syringes, IV bags and administration sets

b) Patients' bodily fluid and waste

c) Linen, mattresses, etc that had spills on them

Spill may occur due to drugs spilt or leaking during preparation, storage, transport and administration and thereby contaminate nearby

floors, work surfaces, equipment, bedding and clothing. Spill kit (**refer Appendix 2**) should be made available in areas where cytotoxic drugs and related waste are stored, transported, handled and disposed. Spills of cytotoxic drugs and waste must be dealt with immediately as per institutional protocol or MOH guideline (**refer Appendix 3 and 4**).

Accidental personnel exposure may involve contamination of clothing and PPE, penetrating injuries, skin, eye, mucous membranes and other body contact. In the event of contamination by cytotoxic drugs, ask for help whenever possible and the following measures should be taken:

a) All overtly contaminated protective clothing should be removed and disposed of as a cytotoxic waste.

b) All contaminated clothing should be removed and discarded as a cytotoxic waste . Clothing with minimal amount of contamination could be laundered separately in accordance with institutional policy/ procedure.

c) Use a shower if necessary. If an emergency shower is not available, cleanse the affected skin areas with soap and rinse with running water for at least 15 minutes.

d) For needle prick injury, rinse the area with running water (allow the wound to bleed freely to flush out any drug). Do not squeeze the injured finger. Wash the area thoroughly with soap and water and for at least 15 minutes.

e) Flush affected eyes gently with clean water or normal saline or other isotonic eyewashes for 15 minutes. If eyewash station and eyewash bottle are not available, use a large syringe or a small receptacle with a pouring spout. Do not rub affected eyes.

f) Seek medical advice immediately.

g) Document occurrence of the incidence as per institutional incident management and reporting guidelines.

h) Follow up and manage each case as per recommendations from Occupational Safety and Health Unit.

Contaminated Non-Disposable Equipment/ Items should be handled accordingly:

a) Re-usable plastic or metal trays should be rinsed with running water to remove residue of cytotoxic drug/ waste followed by washing with detergent and water.

b) If non disposable equipment or items are to be sent to another department/ unit for terminal cleaning, they must be transported in sealed leak-proof bags or containers clearly labelled with cytotoxic warning signs.

## 4.10 HANDLING AND ADMINISTRATION OF MONOCLONAL ANTIBODIES

Concerns over the handling of monoclonal antibodies (MABs) arose due to the uncertainty over the effects of potential occupational exposure to this diverse group of drugs.

Monoclonal antibodies (MABs) are not inherently cytotoxic unless they are conjugated to a cytotoxic agent, fusion protein or radioisotope (e.g. Trastuzumab Emtansine, Brentuximab Vedotin, etc). The conjugated MABs must be prepared and administered following accepted cytotoxic safe handling precautions and regulations related to the handling of cytotoxic and radiopharmaceuticals.

Non-cytotoxic MABs do not need to be handled with cytotoxic precautions; however, they do require greater handling precautions than

other non-hazardous injectable medications. Non-cytotoxic MABs may be prepared within the sterile production unit or in the clinical area (ward and daycare unit). PPE requirement and precautions for the preparation and administration of non-cytotoxic MABs in the clinical areas are as followed:

a) Use gloves and practice effective hand hygiene to minimise risks of contamination and infection.

b) Gowns are not necessary for either dose preparation or administration of MABs.

c) Wear a respirator mask (N95) and protective eyewear during dose preparation and administration.

d) Dispose contaminated items, including waste and bodily fluids of patients, in accordance with the disposal of clinical biohazardous waste, i.e. not as cytotoxic waste, unless conjugated with a cytotoxic agent.

e) Needle prick injury and spill should be handled as per institutional guideline for managing biohazard substances.

**Note:**

- ❖ Non-cytotoxic MABs which are reconstituted by CDR unit shall be treated as hazardous drug preparations due to the cross-contamination of cytotoxic residues during compounding.

## References:


1. Carrington C, Stone L, Koczwara B, Searle C, Siderov J, Stevenson B, Michael M, Hyde S, Booth A, Rushton S; Clinical Oncological Society of Australia. The Clinical Oncological Society of Australia (COSA) guidelines for the safe prescribing, dispensing and administration of cancer chemotherapy. Asia Pac J Clin Oncol. 2010 Sep;6(3):220-37.
2. Managing hazardous drug exposures: information for healthcare settings, Hodson L, et al, U.S. Department of Health and Human Services, Centers for Disease Control

and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2023-130, https://doi.org/10.26616/NIOSHPUB2023130

3. International Society of Oncology Pharmacy Practitioners Standards Committee. ISOPP standards of practice. Safe handling of cytotoxics. J Oncol Pharm Pract. 2007;13 Suppl:1-81.
4. Goodin S, Griffith N, Chen B, et al. Safe handling of oral chemotherapeutic agents in clinical practice: recommendations from an international pharmacy panel. Journal of Oncology Practice. 2011 Jan;7(1):7-12.
5. Easty AC, Coakley N, Cheng R, Cividino M, Savage P, Tozer R, White RE. Safe handling of cytotoxics: guideline recommendations. Curr Oncol. 2015 Feb;22(1): e27-37.
6. Toolkit for Safe Handling of Hazardous Drugs for Nurses in Oncology. Oncology Nursing Society, 2018.
7. Policy for The Safe Handling and Administration of Cytotoxic Drugs in Adults with Cancer. Thames Valley Cancer Network NHS, Feb 2019.
8. Malaysian Patient Safety Goals, 1st edition, 2015. Ministry of Health Malaysia.
9. MOH Systemic Therapy Protocol, 3rd Edition, 2016. Ministry of Health Malaysia.
10. Guideline of Injection Administration, First Edition 2021.Malaysian Nursing Board.
11. Clinical procedure - administration of anti-cancer drugs - intramuscular and subcutaneous. eviQ Clinical Resources. https://www.eviq.org.au/clinical-resources/administration-of-anti-cancer-drugs/457-administration-of-anti-cancer-drugs-intramus#literature-search (accessed on 13 Jan 2025)
12. Safe Administration of Anti-Cancer drugs. eviQ Clinical Resources. https://www.eviq.org.au/clinical-resources/administration-of-anti-cancer-drugs/5-safe-administration-of-anti-cancer-drugs#post-administration (accessed 13 Jan 2025)
13. Clinical procedure - administration of anti-cancer drugs - intravenous cannula (IVC). eviQ Clinical Resources.https://www.eviq.org.au/clinical-resources/administration-of-anti-cancer-drugs/1087-administration-of-anti-cancer-drugs-intraven#post-procedure (accessed 14 Jan 2025)
14. Clinical procedure - administration of anti-cancer drugs - central venous access device (CVAD). eviQ Clinical Resources. https://www.eviq.org.au/clinical-resources/administration-of-anti-cancer-drugs/1127-administration-of-anti-cancer-drugs-central#procedure (accessed on 14 Jan 2025)
15. Procedure Cytotoxic Drugs Administration and Handling. Sidney Children's Hospital. 7 March 2014.
16. Guidance for administration of tretinoin (ATRA) capsules in haematology patients with swallowing difficulties and NG/PEG tubes, NHS Thames Valley Strategic Clinical Network, 2022.

17. Cohen J, Lee C, Markham R, Szerwo J, Roska M, Bubalo J. Medication use process and assessment of extemporaneous compounding and alternative routes of administration of oral oncology drugs: Guidance for clinical and oncology pharmacists. J Am Coll Clin Pharm. 2022; 5(11): 1176-1228.
18. Tejedor-Tejada E, Nieto-Guindo P, Tejedor-Tejada J, Martínez-Velasco E, Gómez-Sánchez A. A guide for the administration of oral antineoplastic in patients with swallowing disorders. Farm Hosp. 2021 Apr 28;45(3):126-134.
19. Handbook of Drug Administration via Enteral Feeding Tubes, British Pharmaceutical Nutrition Group, Pharmaceutical Press, 2015.
20. How to use your Mitomycin C eye drops - 0.04% or 0.02%. Queen Victoria Hospital, NHS, March 2023.
21. Open Resources for Nursing (Open RN). Nursing Skills [Internet]. Ernstmeyer K, Chrisman E, editors. 2nd ed. Eau Claire (WI): Chippewa Valley Technical College; 2023. PMID: 37906668.
22. Cytotoxic Drugs and Related Waste- Risk Management. NSW Government, 2017.
23. Safe handling and waste management of hazardous drugs. eviQ Clinical Resources.https://www.eviq.org.au/clinical-resources/administration-of-anti-cancer-drugs/188-safe-handling-and-waste-management-of-hazardou#spill-and-accidental-exposure-management (accessed on 14 Jan 2025)
24. Manual for Sterile Preparation 2nd Edition, Sterile Pharmaceutical Services Guideline, Ministry of Health Malaysia.
25. Ryan, M., N. Lam, K. Wright, et al. 2023. "Clinical Oncology Society of Australia Position Statement: 2022 update to the safe handling of monoclonal antibodies in healthcare settings." Asia Pac J Clin Oncol.
26. Safe Handling and Administration of Monoclonal Antibodies Guideline. Western Australia WA Country Health Service. September 2024 (Version 1.02)

# 5.0 HANDLING OF HAZARDOUS DRUGS AT THE OUTPATIENT PHARMACY

Hazardous drugs that are available in the out-patient pharmacy are usually in the forms of tablets, capsules, syrup, topical and eye preparations. Personnel who handle these drugs must be made aware of the hazards and importance of adhering to safe handling procedures. Ensure the use of appropriate PPE (**refer Appendix 1**) for tasks performed at all times. All personnel must be trained to handle leakage/ spill (broken bottle of liquid or powder) (**refer Appendix 2, 3 and 4**). Safety measures taken for work processes at the outpatient pharmacy must include:

**a) Receiving and transporting hazardous drugs from other units**

i) Wear disposable gloves when receiving hazardous drugs from other units within facility (e.g. logistics pharmacy, CDR unit, etc) or from other hospitals

ii) Examine boxes/ containers/ bottles for signs of damage/ leakage.

iii) Trolleys or other vehicles used to transport fragile items (e.g. liquid/ powder in bottles) must be equipped with spill kits, and guards to prevent falling & breakage.

iv) Have designated, sturdy, leak-proof carrier (labelled with warning sign) for the purpose of transporting hazardous drugs.

v) Hazardous drugs must be delivered directly (without detours) to out-patient pharmacy

vi) All personnel involved in the transport of the drugs must receive training on dealing with breakages and spills.

**b) Storage**

i) Designate an area for hazardous drugs storage to separate them from other drugs in a manner that prevents cross contamination and accidental personnel exposure.

ii) Restrict access to authorised personnel only (e.g. pharmacy personnel only).

iii) All hazardous drugs must be made easily identifiable with cytotoxic warning labels (**refer Appendix 5**).

iv) Store hazardous drugs in properly sized bins or on shelves that have guards to prevent accidental falling and breakage.

v) Hazardous drugs must be stored in a designated refrigerator used exclusively for hazardous drugs. When a dedicated refrigerator is unavailable, hazardous drugs must be kept separate from non-hazardous items, contained within individual leak-and break-proof bins.

vi) Spill kits must be kept in close proximity to the location of hazardous drugs stock.

vii) Wear disposable gloves when stocking, conducting inventory and arranging the drug packages.

viii) Unused expired hazardous drugs should be handled and disposed of as per institutional cytotoxic waste management protocol.

**c) Repackaging for dispensing and deliveries to other hospitals/ clinics**

i) Wear disposable gloves when repacking hazardous drugs and surgical mask (if handling loose tablets or capsules (not blistered-packed).

ii) All equipment (e.g. tray, forceps, etc) used in the repackaging process must be designated for use with hazardous drugs only and clearly labelled as such.

iii) Do not use automated counting machines for tablet and capsule forms of hazardous drugs to prevent generation of powdered hazardous contaminants at the work space.

iv) Avoid pouring liquid hazardous drugs whenever possible. When unavoidable, perform the procedure with caution and thoroughly clean all equipment accordingly afterward.

v) All non-disposable materials exposed to hazardous drugs including counting trays, tools, etc should be washed thoroughly with soap and water after use. Rinse the sink and dry with a paper towel after washing. Dispose towel as cytotoxic waste.

vi) Discard used gloves and other PPE, packaging materials and empty containers/ bottles (not to re-use) as cytotoxic waste.

vii) Handle containers with liquid hazardous drugs with extra caution as they may exhibit some spillage during preparation or use. These containers should be dispensed in sealable plastic bags to contain any inadvertent contamination.

viii) Dispensing a complete original container whenever possible to reduce manipulation required. Labelling requirement for hazardous drugs dispensed to patients:

- Envelopes/ containers of the cytotoxic drugs should be clearly labelled to inform handlers of their hazardous nature.
- Stick the “Cytotoxic” hazard symbol (**refer Appendix 5 for example**) on drug envelopes or containers or alternatively, use an envelope/ bag with "Cytotoxic" warning printed on it.
- The back of the drug envelope should be transparent to ease identification of its content without having to remove or open the envelope.

ix) For the delivery of hazardous drugs to other hospitals/ clinics, label envelope/ container as required above. Ensure envelopes/ containers of tablets/ capsules are properly sealed. Pack powdered and liquid hazardous drugs (extemporaneous and commercial products) separately from non-hazardous drugs with sealable plastic bags inside sturdy boxes/ cartons. There must be “FRAGILE” and “Cytotoxic” warnings on the outer box/ carton.

x) For delivery of sterile preparations to other hospitals/ clinics (if any), refer to the latest edition of Manual for Sterile Preparations for guidance on proper transportation.

xi) Spill kit must be readily available to personnel involved in the transport of cytotoxic drug preparations.

**d) Dispensing**

i) Hazardous drugs should be dispensed in the final dose and form whenever possible. Doses and schedules of drug treatment can be adjusted, to match the available commercial strengths, when clinically appropriate.

ii) Perform standard medication safety check and verification (by different person):

- Verify patient's identity
- Verify treatment regime - Drug name, dose, route of administration, frequency, duration, number of cycle or block/ phase of treatment, date start and stop (if applicable), etc
- Ensure quantity is sufficient for a specified timeframe or till next review. Check the physical content of drugs inside the final packages.

iii) Disposable gloves should be worn for dispensing, and with surgical masks if opening envelopes/ bottles of loose tablets/ capsules/ powder.

iv) All patients (caregivers) should receive proper counselling regarding their medication as well as safe handling of the drugs at home as per institutional protocol (if any) (**refer Chapter 6.0 Handling of Hazardous Medications at Home, Cancer Drug Counselling: A Guide for Pharmacists Second Edition (2023), and other references**)

**e) Return and disposal of unused medication**

i) Decision to use returned drugs for other patients (if it is allowed) should be based on criteria set by institutional policy

ii) The causes for drug return should be identified and documented on the patient's pharmacotherapy review record (e.g. on CP2 form, case note, medication return (PhIS), etc) whenever possible.

iii) Disposal of non-injectable hazardous drugs should be performed in the same manner as for cytotoxic injectables and waste, with additional precautionary steps, to reduce risk of environmental contamination:

- Loose tablets/ capsules: Pack in sealed plastic bag before putting them into sharps bin/ cytotoxic waste bag/ bin
- Oral liquids: Close the medicine bottle tightly, put into a sealed plastic bag before discarding it into sharps bin/ cytotoxic waste bag/ bin

iv) Cytotoxic waste bags/ bins must be clearly labelled and properly sealed/ tied/ closed

v) Do not throw hazardous drugs in the trash or down the drain, and don't flush them down the toilet

vi) If cytotoxic waste is mixed with other pharmaceutical waste, it should be handled in the same manner as cytotoxic waste.

vii) Waste should be handled and disposed of as per institutional cytotoxic waste management protocol.

**Note(s):**

❖ The use of gloves does not substitute the need for hand-washing after completion of each task.

- ❖ Risk of exposure is low with intact boxes/ bottles/ blister packs of tablets and capsules.
- ❖ Oral cytotoxic drugs in the form of powder or liquid need to be handled as cautiously as injectable drugs. Handle as spill if bottles/ containers are broken or leaked.
- ❖ Compounding of non-sterile hazardous drugs without a ventilated cabinet should be avoided. Use commercially available ready-to-use products whenever possible.
- ❖ Counsel patients and caregiver accordingly if they need to prepare the medication themselves at home (e.g. split tablets, dissolved capsules, etc) (**Refer institutional protocol or Chapter 6.0 Handling of Hazardous Medications at Home**)

## References


1. International Society of Oncology Pharmacy Practitioners. *Standards for the Safe Handling of Cytotoxics*. International Society of Oncology Pharmacy Practitioners, 2022.
2. Managing hazardous drug exposures: information for healthcare settings, Hodson L, et al, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2023-130, https://doi.org/10.26616/NIOSHPUB2023130
3. Power LA, Coyne JW. ASHP Guidelines on Handling Hazardous Drugs. Am J Health Syst Pharm. 2018 Dec 15;75(24):1996-2031. doi: 10.2146/ajhp180564. Epub 2018 Oct 16.
4. Goodin, Susan and Griffith, Niesha and Chen, Beth and Chuk, Karen and Daouphars, Mikael and Doreau, Christian and Patel, Rinku and Schwartz, Rowena and Tamés, Maria and Terkola, Robert and Vadnais, Barbara and Wright, Debbie and Meier, Klaus. (2011). Safe Handling of Oral Chemotherapeutic Agents in Clinical Practice: Recommendations from an International Pharmacy Panel. Journal of oncology practice / American Society of Clinical Oncology. 7. 7-12. 10.1200/JOP.2010.000068.
5. Easty AC, Coakley N, Cheng R, Cividino M, Savage P, Tozer R, White RE. Safe handling of cytotoxics: guideline recommendations. Curr Oncol. 2015 Feb;22(1): e27-37.

# 6.0 HANDLING OF HAZARDOUS DRUGS AT HOME

Patients who are having chemotherapy infusion, oral chemotherapy or other forms of hazardous drug at home, as well as their caregivers and household members, are potentially at risk of being exposed to hazard via inhalation of contaminated air, skin contact with contaminated surfaces or ingestion of contaminated food or drinks. Pregnant or breastfeeding household members should be protected from all types of contact with hazardous drugs as much as possible.

Hence, it is crucial to provide drug counselling and safe handling education both verbally and in writing to the patient and caregiver. Although similar education might be given by the nursing team, pharmacists have roles in the assessment and reinforcement of patient's and caregiver's awareness and knowledge. Safe handling recommendations from credible sources (e.g. international safe handling guidelines) can be adopted with appropriate adjustments to ensure feasibility within the local home setting and lifestyles. Collaboration between pharmacy and nursing teams in the standardization of education materials and establishment of counselling protocol is strongly recommended.

Generally, safety education provided should cover the following areas:

a) Treatment protocol, potential side effects and management

b) Safe handling of hazardous drugs (storage, administration and disposal)

c) Spill and waste management

## 6.1 ADMINISTRATION OF ORAL CHEMOTHERAPY AND OTHER NON-INJECTABLE HAZARDOUS DRUGS

Advice caregivers and patients who are taking oral and other forms of non-injectable drugs on the following:

**a) Storage**

i) It is generally not recommended to remove the medication from its original/ provided packaging.

ii) Keep out of reach from children and pets.

iii) Store the medication in a container with tight-fitting lid and label it clearly e.g. “Hazard: Do not touch”

iv) Store the medication container in a cool and dry place unless otherwise instructed. Some medications may need to be refrigerated, separate them from other items in the refrigerator.

**b) Preparation and Administration of Medication**

i) Wash hands and clean surfaces before and after handling the medicines.

ii) Wear disposable gloves, and surgical mask (if handling loose tables/ capsule/ powders) and eye/ face protection (if vomit or splash potential).

iii) Avoid preparing food and drinks in the same area where hazardous medicines are handled.

iv) Prepare the medicine on a clean and clutter free surface, such as a table or counter. Use “no-touch” technique (e.g., pour tablets into the cap of the container) whenever possible.

v) All equipment used for medicine preparation and administration e.g. syringes, cups, tablet cutter, scissors, etc should be designated for the use for hazardous medicines only

vi) Do not cut, break, crush or try to dissolve the hazardous medicines with liquid unless otherwise instructed by the healthcare team. Cover the work surface with disposable plastic before preparing the medication. Do not prepare hazardous medicines near/ under fans or air-conditioning units.

vii) If required to cut the tablets, place the tablet cutter inside a zip lock bag, and seal the bag before cutting. Remove content from the bag carefully to prevent spreading of hazardous powder/ residual to the surrounding environment.

viii) In cases where patients have difficulty swallowing, their medication (tablets/ capsules) can be prepared as follows (unless otherwise instructed by the healthcare team):

- Pour warm (not boiling) drinkable water into a cup
- Take a syringe and pull the plunger from the barrel
- Place the tablet(s) or half tablet or capsule(s) inside the syringe. Do not open the capsule. Only dissolve one type of drug in each syringe at a time. Do not mix different types of medications together.
- Place the plunger of the syringe back into the barrel and push it down until close to the opening at the tip without touching

the tablet or capsule. Do not use the plunger to crush the tablet or capsule.

- Place the tip of the syringe in the cup and draw back a small amount of water between 2-5mL.
- Leave a small amount of air in the syringe to facilitate mixing, cap the syringe with a stopper.
- Invert the syringe a few times to allow the drug to dissolve.
- Give the required volume/ dose (check with pharmacist/ nurse) by mouth, NG tube or gastrostomy tube (g-tube, PEG tube). It is best to give the dose immediately (within 30 minutes) after preparation.
- If required to administer the whole content in the syringe, draw back another small amount of water and administer the residue of the drug. Flush the ng tube or g-tube if applicable.
- Wash all equipment use with soap and water and clean the work surface thoroughly when done.
- If the medication is in the form of soft gel, **refer Chapter 4.5.5 Procedure - Administration of Soft Capsules (Tretinoin [ATRA], Isotretinoin)** for the appropriate method of preparation and administration.

ix) For preparation and administration of hazardous eye, ear and topical medication, **refer Chapter 4.7 Administration of Hazardous Drugs via Alternative Routes**.

x) While wearing PPE, wash reusable equipment (e, g, cup, scissor, etc) with soap and water.

xi) Place all contaminated PPE and items (e.g. disposable medication cup, plastic cover, tissue, etc) in a plastic bag, seal/ tied before throwing it into the thrash.

xii) Wash hands with soap and water.

**Note(s):**

- Consider providing patients with syringes and stoppers required for medication preparation and administration.

## 6.2 HOME CHEMOTHERAPY INFUSION

Having intravenous chemotherapy at home is popular among patients and care providers as it helps to reduce hospital visits. The majority of MOH cancer patients are using the elastomeric infuser for their home chemotherapy without needing an infusion pump. An elastomeric infuser is a lightweight, disposable plastic bottle that contains a balloon filled with chemotherapy which is being delivered continuously over 24 hours to 7 days into the patient's body via a central venous access device (CVAD). Comprehensive safe handling education is essential to ensure patients and caregivers are able to handle the infusions at home in the absence of healthcare professionals. Different brands of infuser may differ in their handling and care. Nonetheless, education provided should address the frequently asked questions:

- What is an Elastomeric Infuser and how does it work?
- How to manage daily activities with chemotherapy infusion in-progress?
- How to tell if the infuser is functioning or not functioning well?
- How to handle unwanted situations such as air bubbles in the line, leak and spill, needle/ line dislodges, infuser emptied before appointment, etc?
- How to take care of the infuser and central venous access device (CVAD)?
- What PPE should be worn by the caregivers when tending the patients?

**Note(s):**

- Home chemotherapy services are typically led by nursing teams. Close collaboration between nursing and pharmacy teams is essential to develop patient education materials and safety guides that align with institutional policies and procedures.
- The management of technical complications related to elastomeric infusers may vary by brand and model.

## 6.3 WASTE AND SPILL MANAGEMENT

All equipment and items that have come into contact with hazardous drugs (e.g. containers, used gloves and masks, other items used in the preparation and administration of medicines) are considered contaminated. For disposal, put all contaminated PPE and items in sealed/ tied plastic bags (prefer double bagged) before throwing it into the thrash to avoid inadvertent contact by others. Sharps must be placed in a container with a closed lid before bagging. Empty containers of hazardous drugs should not be recycled or used again to store other medicines or items. Unused medication should be returned to the pharmacy, or treatment centre for safe disposal. It is important to inform patients/ caregivers to never throw unused drugs in the trash and drain or flush them down the toilet.

Small spill that occurs during preparation and administration of oral/ enteral hazardous drugs can be managed as followed:

a) Block off the spill area and keep children and pets away.

b) Wear 2 pairs of gloves to clean up.

c) For liquid spills, use paper towels to soak up the liquid. Start at the outside of the spill and work inward. Place the paper towels into a plastic bag and seal/ tie before throwing away.

d) Clean the area 3 times with a home cleaning product and make sure that no medicine is left on the surface. Rinse the area with water.

e) Remove contaminated clothes, place them in a plastic bag, and seal/ tie. Wash these clothes separately as soon as possible. Always wash contaminated clothing separately from other laundry.

On the other hand, leakage and spill from chemotherapy infusion must be handled as taught by the care team according to institutional protocol. Provision of a spill kit with written instructions to guide the patient/ caregiver is recommended.

Hands should be washed with soap and water after removal of gloves worn for handling hazardous drugs, spill, waste or contaminated items each time. If the hazardous drug, spill or waste gets in the eyes, rinse with clean water for 15 minutes and contact the health care provider for further instructions. For accidental skin contact, wash the affected area with soap and water for 10 minutes. Seek medical attention if there is skin redness or irritation.

## 6.4 HANDLING PATIENT'S BODY FLUID AND WASTE

Patients' body fluids and excreta are hazardous during on-going medication and remain hazardous potentially as long as 7 days after administration of the last dose of medication or completion of chemotherapy infusion. The following precautionary steps may be adopted at home to safeguard all household members:

**a) Wear appropriate PPE**

i) Wear gloves and protective clothing (e.g. disposable apron) when handling patient's vomit, blood, urine, or stool.

ii) Wear gloves when handling soiled laundry or linens.

iii) Wear a face shield or goggles if there is a risk of splashing of body fluids.

iv) Wear gloves and a face shield when changing diapers. Put used diapers in a sealed/ tied plastic bag (preferred double bags) before discarding.

**b) Safe toilet and bathroom usage**

i) Family members should use separate toilets from the patient for 7 days after hazardous drug administration to eliminate the risk of contact with contaminated body waste. In households with only one bathroom, patients can keep disinfecting sanitizing wipes near the toilet to clean the toilet seat and rim after use.

ii) Male patients to be seated when urinating to reduce the risk of splashes and aerosol contamination

iii) Use full flush and close the toilet lid before flushing

iv) When a lid is not present, consider covering the open toilet with a plastic-backed liner prior to flushing

**c) Soiled clothing and linens**

i) Unsoiled clothing and linens can be washed normally.

ii) Soiled linen and clothing should be washed immediately on their own. Do not mix other laundry.

## References


1. Chemotherapy safety at home. eviQ Clinical Resources: https://www.eviq.org.au/clinical-resources/administration-of-anti-cancer-drugs/188-safe-handling-and-waste-management-of-hazardou#patient-education.
2. Toolkit for Safe Handling of Hazardous Drugs for Nurses in Oncology. Oncology Nursing Society, 2018.
3. Safe Handling of Chemotherapy and Hazardous Drugs at Home. St. Jude Children's Research Hospital. Together by St. Jude resources: https://together.stjude.org/en-us/medical-care/medication-management/safe-handling-chemotherapy.html#sectioned_content-34b33c71-e896-4cd5-94dc-c2ae7a56f040--0 (Accessed 31 Jan 2026)
4. Procedure: Cytotoxic Drugs Administration and Handling. Sidney Children's Hospital. 7 March 2014.
5. Having treatment through an Elastomeric Infuser. eviQ Patient information: https://www.eviq.org.au/getmedia/fcbc56ad-49fe-4e79-95bd-ce8209a300d5/ID-502-Having-treatment-through-an-Elastomeric-Infusor-V-5.pdf.aspx?ext=.pdf (Accessed 3 Feb 2026)

# 7.0 APPENDICES

## APPENDIX 1

### TABLE OF CONTROL APPROACHES FOR SAFER HANDLING OF HAZARDOUS DRUGS, BY ACTIVITY AND FORMULATION

**Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation**

| | | Control Approaches | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Engineering Controls | | | Personal Protective Equipment | | | |
| Activity | Formulation | Ventilated engineering control (BSC or CACI)* | Closed system drug transfer device | Other | Double chemotherapy gloves (ASTM rated) | Protective gown (impervious, single use) | Eye, face, hair, sleeve, and shoe protection | Respiratory protection† |
| **Receiving, unpacking, and placing in storage** | All types of hazardous drugs | No, unless a leak is observed or suspected | NA* | NA* | No (Single pair of gloves) | No, unless a leak is observed or suspected | Consider protective sleeves; add additional protection if a leak is observed or suspected | No, unless a leak is observed or suspected |
| **Transportation within facility** | Intact tablets or capsules, manufacturers' prefilled syringes | No | NA* | Transport in containers that minimize the risk of breakage or leakage; Double-bag or place in a sealed container | No (Single pair of gloves) | No | No | No |
| | Cut or crushed tablets or capsules (in containers); powders, liquids, or creams; in-house filled syringes | No | NA* | Transport in containers that minimize the risk of breakage or leakage; Double-bag or place in a sealed container | Yes | No | No | No |

(Continued)

## TABLE OF CONTROL APPROACHES FOR SAFER HANDLING OF HAZARDOUS DRUGS, BY ACTIVITY AND FORMULATION (CONT)

**Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation**

| | | Control Approaches | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Engineering Controls | | | Personal Protective Equipment | | | |
| Activity | Formulation | Ventilated engineering control (BSC or CACI)* | Closed system drug transfer device | Other | Double chemo-therapy gloves (ASTM rated) | Pro-tective gown (imper-vious, single use) | Eye, face, hair, sleeve, and shoe protection | Respiratory protection† |
| **Compounding‡** | Oral liquid drug | Yes§ | NA* | NA* | Yes¶ | Yes | Hair and shoe covers; Add eye and face pro-tection, if not done in a ventilated engineer-ing control | Yes, if not using a ventilated engineering control |
| | Topical drug | Yes§ (Note: some drugs such as carmustine, thiotepa, and mechlore-thamine are volatile) | NA* | NA* | Yes¶ | Yes | Hair and shoe covers. Add eye and face pro-tection, if not done in a ventilated engineer-ing control | Yes, if not done using a ventilated engineering control |
| | Injections withdrawn from a vial | Yes§ | Yes, when dosage form allows | NA* | Yes¶ | Yes | Hair and shoe covers; Add eye and face pro-tection, if not done in a ventilated engineer-ing control | Yes, if not using a ventilated engineering control |
| | Mixing injec-tions from a vial | Yes§ | Yes, when dosage form allows | NA* | Yes¶ | Yes | Hair and shoe covers; Add eye and face pro-tection, if not done in a ventilated engineer-ing control | Yes, if not using a ventilated engineering control |

(Continued)

## TABLE OF CONTROL APPROACHES FOR SAFER HANDLING OF HAZARDOUS DRUGS, BY ACTIVITY AND FORMULATION (CONT)

**Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation**

| | | Control Approaches | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Engineering Controls | | | Personal Protective Equipment | | | |
| Activity | Formulation | Ventilated engineering control (BSC or CACI)* | Closed system drug transfer device | Other | Double chemotherapy gloves (ASTM rated) | Protective gown (impervious, single use) | Eye, face, hair, sleeve, and shoe protection | Respiratory protection† |
| | Solution for irrigation | Yes§ | Yes, when dosage form allows | NA* | Yes¶ | Yes | Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control | Yes, if not using a ventilated engineering control |
| | Powder/solution for aerosol treatments | Yes§ | Yes, when dosage form allows | NA* | Yes¶ | Yes | Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control | Yes, if not using a ventilated engineering control |
| Administering | Intact tablets or capsules from unit dose package | NA* | NA* | NA* | No (Single glove) | No | Eye and face protection if vomit potential** | No |
| | Crushing or manipulating tablets or capsules | Yes§ | NA* | Consider crushing tablets in a pill pouch | Yes¶ | Yes | Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control | Yes, if not using a ventilated engineering control |
| | Cut, crushed, or uncoated tablets or capsules | NA* | NA* | NA* | Yes | Yes | Eye and face protection if vomit potential** | No |

(Continued)

## TABLE OF CONTROL APPROACHES FOR SAFER HANDLING OF HAZARDOUS DRUGS, BY ACTIVITY AND FORMULATION (CONT)

**Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation**

| | | Control Approaches | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Engineering Controls | | | Personal Protective Equipment | | | |
| Activity | Formulation | Ventilated engineering control (BSC or CACI)* | Closed system drug transfer device | Other | Double chemotherapy gloves (ASTM rated) | Protective gown (impervious, single use) | Eye, face, hair, sleeve, and shoe protection | Respiratory protection† |
| | Subcutaneous or intramuscular injections from manufacturer's supplied prefilled syringe or injector | NA* | NA* | NA* | No (Single glove) | Yes | Eye and face protection if liquid likely to splash** | No |
| | Subcutaneous or intramuscular injections from a prepared syringe or injector | NA* | NA* | NA* | Yes | Yes | Eye and face protection if liquid likely to splash** | No |
| | Intravenous injections from prepared syringes†† | NA* | Yes, when dosage form allows | NA* | Yes | Yes | Eye and face protection if liquid that could splash** | No |
| | Intravenous solution for infusion | NA* | Yes, when dosage form allows | NA* | Yes | Yes | Eye and face protection if liquid that could splash** | No |
| | Ophthalmologic applications | NA* | Yes, when dosage form allows | NA* | Yes | Yes | Eye and face protection if liquid likely to splash** | No |

(Continued)

## TABLE OF CONTROL APPROACHES FOR SAFER HANDLING OF HAZARDOUS DRUGS, BY ACTIVITY AND FORMULATION (CONT)

**Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation**

| | | Control Approaches | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Engineering Controls | | | Personal Protective Equipment | | | |
| Activity | Formulation | Ventilated engineering control (BSC or CACI)* | Closed system drug transfer device | Other | Double chemo-therapy gloves (ASTM rated) | Pro-tective gown (imper-vious, single use) | Eye, face, hair, sleeve, and shoe protection | Respiratory protection† |
| | Oral liquid drug: PO*/feed-ing tube/NG* tube | NA* | NA* | NA* | Yes | Yes | Eye and face protection if liquid likely to splash** | Yes, if inhala-tion potential |
| | Topical drug (ointment, cream) | No (Note: some drugs such as carmustine, thiotepa, and mechlore-thamine are volatile and may need to be administered in an enclosure) | NA* | NA* | Yes | Yes | Eye and face protection if liquid likely to splash** | Yes, if inhala-tion potential |
| | Irrigation solution, bladder instil-lation, HIPEC*, limb perfusion | NA* | Yes, when dosage form allows | NA* | Yes | Yes | Eye and face protection | Yes |

(Continued)

## TABLE OF CONTROL APPROACHES FOR SAFER HANDLING OF HAZARDOUS DRUGS, BY ACTIVITY AND FORMULATION (CONT)

**Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation**

| | | Control Approaches | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Engineering Controls | | | Personal Protective Equipment | | | |
| Activity | Formulation | Ventilated engineering control (BSC or CACI)* | Closed system drug transfer device | Other | Double chemo-therapy gloves (ASTM rated) | Pro-tective gown (imper-vious, single use) | Eye, face, hair, sleeve, and shoe protection | Respiratory protection† |
| | Powder/ solution for inhalation/ aerosol treatment | Yes, when applicable; Note that some treatments may need to be administered in an enclosure | Yes, when dosage form allows | NA* | Yes | Yes | Eye and face protection if liquid that could splash** | Yes, full facepiece or PAPR* with combination particulate/ chemical cartridges if inhalation potential |
| **Disposal and Cleaning** | Drugs and metabolites in body fluids | NA* | NA* | Fold soft materials (sheets, hygiene care products) inward to prevent leakage Place in sealed bags | Yes | Yes | Eye and face protection if liquid could splash | Yes, if inhala-tion potential |

(Continued)

## TABLE OF CONTROL APPROACHES FOR SAFER HANDLING OF HAZARDOUS DRUGS, BY ACTIVITY AND FORMULATION (CONT)

**Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation**

| | | Control Approaches | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Engineering Controls | | | Personal Protective Equipment | | | |
| Activity | Formulation | Ventilated engineering control (BSC or CACI)* | Closed system drug transfer device | Other | Double chemo-therapy gloves (ASTM rated) | Pro-tective gown (imper-vious, single use) | Eye, face, hair, sleeve, and shoe protection | Respiratory protection† |
| | Drug-contaminated waste | NA* | NA* | Avoid creating dust; Place in sealed bags; Use caution when closing bags; Pushing waste down may force hazardous drug dust up into face. | Yes | Yes | Eye and face protection if liquid could splash | Yes, if inhala-tion potential |
| **Routine Cleaning** | All types of hazardous drugs | NA* | NA* | Use wet wiping methods; Avoid creating dust; Disinfection, deactivation, or decontami-nation agents may be neces-sary; Place in sealed bags for disposal | Yes | Yes | As needed‡‡ | As needed‡‡ |

(Continued)

## TABLE OF CONTROL APPROACHES FOR SAFER HANDLING OF HAZARDOUS DRUGS, BY ACTIVITY AND FORMULATION (CONT)

**Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation**

| | | Control Approaches | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Engineering Controls | | | Personal Protective Equipment | | | |
| Activity | Formulation | Ventilated engineering control (BSC or CACI)* | Closed system drug transfer device | Other | Double chemotherapy gloves (ASTM rated) | Protective gown (impervious, single use) | Eye, face, hair, sleeve, and shoe protection | Respiratory protection† |
| Spill cleanup | All types of hazardous drugs | NA* | NA* | Limit access to area. Use absorbent pads for liquid spills; Disinfection, deactivation, or decontamination agents may be necessary; Avoid creating dust; Place in sealed bags | Yes | Yes | Yes, as needed | Yes, full facepiece or PAPR* with combination particulate/chemical cartridges may be needed |

**Note.** The Table of Control Approaches provides general approaches that should be adapted to facility-specific conditions. For more detailed information on safe handling practices, see the reference list for this table [ASHP 2006; NIOSH 2004a, 2008; ONS 2011, 2018; OSHA 2016; Power and Cyne 2018].

*Abbreviations: BSC: biological safety cabinet; CACI = compounding aseptic containment isolator; CSTD = closed system drug-transfer device; CVE = containment ventilated enclosure; HIPEC = hyperthermic intraperitoneal chemotherapy; NA = not applicable; NG = nasogastric; PAPR = powered air-purifying respirator; PO = per os (by mouth).

†Respiratory protection must be selected on the basis of the hazardous drug and its physical form (particulate, vapor, etc.) and other exposure factors. For general activities, a N95 may suffice. Use a surgical N95 respirator if there is potential for splashes of bodily fluids or liquid drugs. When performing activities such as cleaning the BSC or CACI or responding to large spills, a combination particulate/chemical cartridge respirator may be needed.

‡Compounding is the process of combining, mixing, or altering ingredients by or under the direct supervision of a licensed pharmacist or physician to create a prescribed medication tailored to the needs of an individual patient. See FDA: https://www.fda.gov/drugs/human-drug-compounding/section-503a-federal-food-drug-and-cosmetic-act and https://www.fda.gov/drugs/human-drug-compounding/compounding-and-fda-questions-and-answers.

§For nonsterile preparations, a ventilated engineering control such as a fume hood, Class I BSC or CVE is sufficient if the ventilated engineering control exhaust is either (1) HEPA-filtered and appropriately exhausted to the outside of the building (preferred) or (2) filtered with redundant HEPA filters in series and recirculated back into the C-SCA. Although these activities are recommended in ventilated engineering controls, they may not be possible under some treatment scenarios (e.g., time-sensitive activities in the emergency department). If the activity is performed in a ventilated engineering control that is used for sterile intravenous preparations, a thorough cleaning and disinfecting is required following the activity.

¶Sterile gloves are required for aseptic drug preparation in a BSC or CACI.

**Needed if the patient might resist (infant, unruly patient, patient predisposed to spitting, patient with difficulty swallowing, or veterinary patient) or if the formulation is hard to swallow.

††Intravenous tubing already attached and primed.

‡‡Activities such as cleaning floors may not require eye or respiratory protection but cleaning a BSC or CACI may require it.

**Reference:**

NIOSH [2023]. Managing hazardous drug exposures: information for healthcare settings. By Hodson L, Ovesen J, Couch J, Hirst D, Lawson C, Lentz TJ, MacKenzie B, Mead K. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2023-130, https://doi.org/10.26616/NIOSHPUB2023130

**Appendix 2**

## CONTENT OF SPILL KIT

| No. | Content of Spill Kit | Quantity |
|---|---|---|
| *1.* | *Disposable Gown* | *1 piece* |
| *2.* | *Surgical Glove* | *1 pair* |
| *3.* | *Chemo Glove* | *1 pair* |
| *4.* | *Shoe Cover* | *1 pair* |
| *5.* | *Head Cover* | *1 piece* |
| *6.* | *Respirator Mask N95* | *1 piece* |
| *7.* | *Sharps Container* | *1 bin* |
| *8.* | *Brush and Dustpan* | *1 set* |
| *9.* | *Cytotoxic Waste Bag* | *2 piece* |
| *10.* | *Gauze and Absorbent Pads* | *10 pieces each* |
| *11.* | *Deactivation Agent* | *120ml* |
| *12.* | *Water* | *500ml* |
| *13.* | *Spill Handling Procedure* | *1* |
| *14.* | *Spill Reporting Form* | *1* |
| *15.* | *Caution Sign* | *1 piece* |

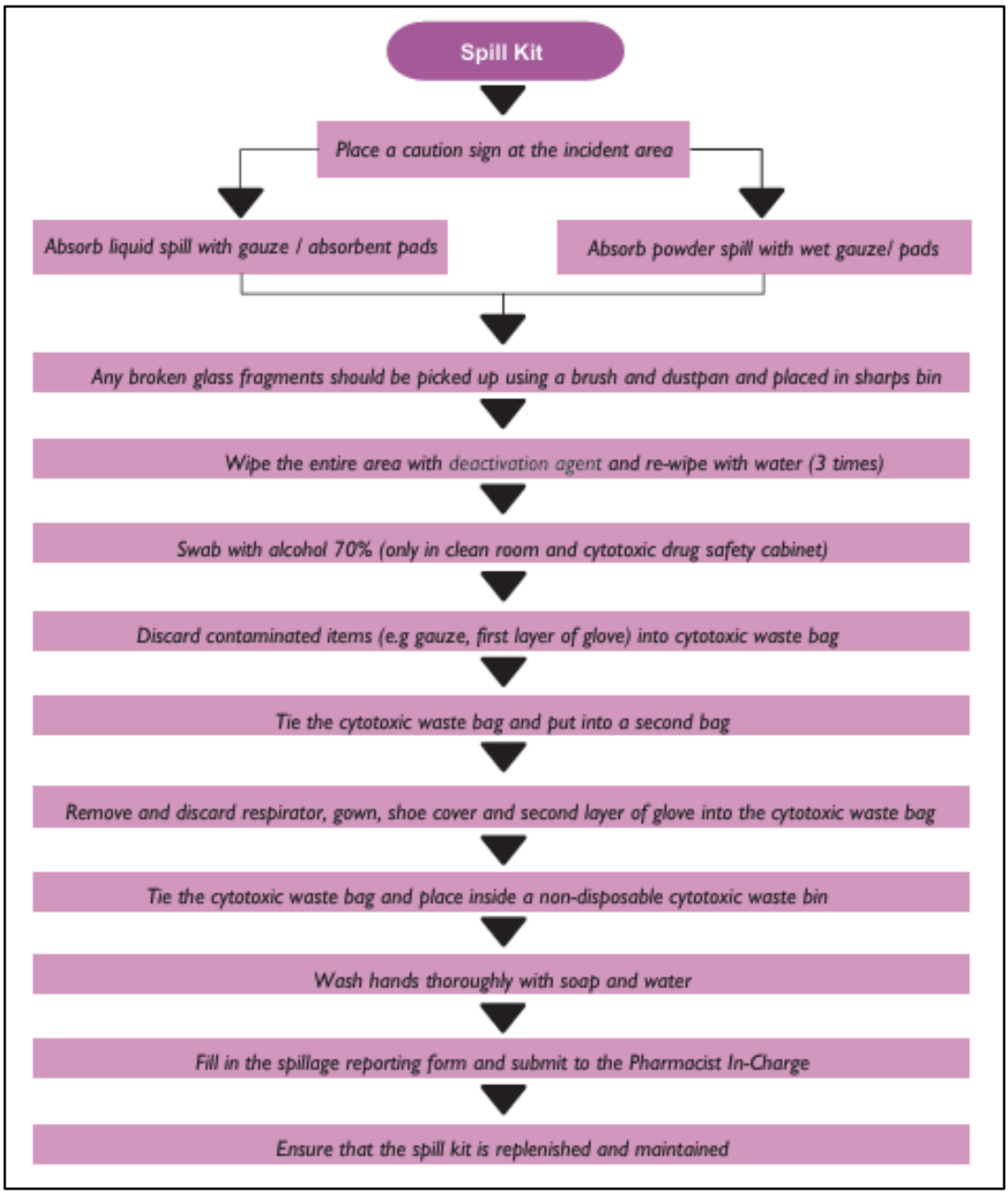
Note:

The kit's content is subject to change based on the user's location and needs, such as inside the CDR cleanroom, in open areas like the logistics pharmacy and wards, or at a patient's home.

**Reference:**
Manual for Sterile Preparations latest edition, Sterile Pharmaceutical Services Guideline, Ministry of Health Malaysia

**Appendix 3**

## FLOW CHART ON THE MANAGEMENT OF CYTOTOXIC SPILL




**Reference:**
Manual for Sterile Preparations latest edition, Sterile Pharmaceutical Services Guideline, Ministry of Health Malaysia

**Appendix 4**

## SPILLAGE REPORTING FORM

*Return to Pharmacy on day of incident*

| *Drug involved* | *Ward/Clinic/area* |
|---|---|
| What form was drug supplied in? | |
| • *liquid - vial/ ampoule*<br>• *dry powder - vial/ampoule*<br>• *syringe*<br>• *plastic bag* | • *vol/amp of drug supplied .....*<br>• *vol/amp of drug supplied .....*<br>• *vol/amp of drug supplied .....*<br>• *vol/amp of drug supplied ..... |
| *Date:* | *Time of incident:* |
| Cause of spill | Location of incident |
| • *Container supplied leaking*<br>• *Container dropped*<br>• *Container faulty*<br>• *Container pierced*<br>• *IV line disconnected*<br>• *Pump problem*<br>• *Others (describe)*<br>..... | • *Patient area*<br>• *Corridor*<br>• *Nursing staff/area*<br>• *Pharmacy area*<br>• *Others .....* |

Description of incident - what happened? To whom? Any precipitating cause?

_____

_____

_____

*Name of witness:*_____

*Pharmacist notified at ext.:*_____

*Spill kit returned to the pharmacy:* _____

*Signature of person completing report::* _____

*Name (in block letters):* _____

*Date of kit returned:*

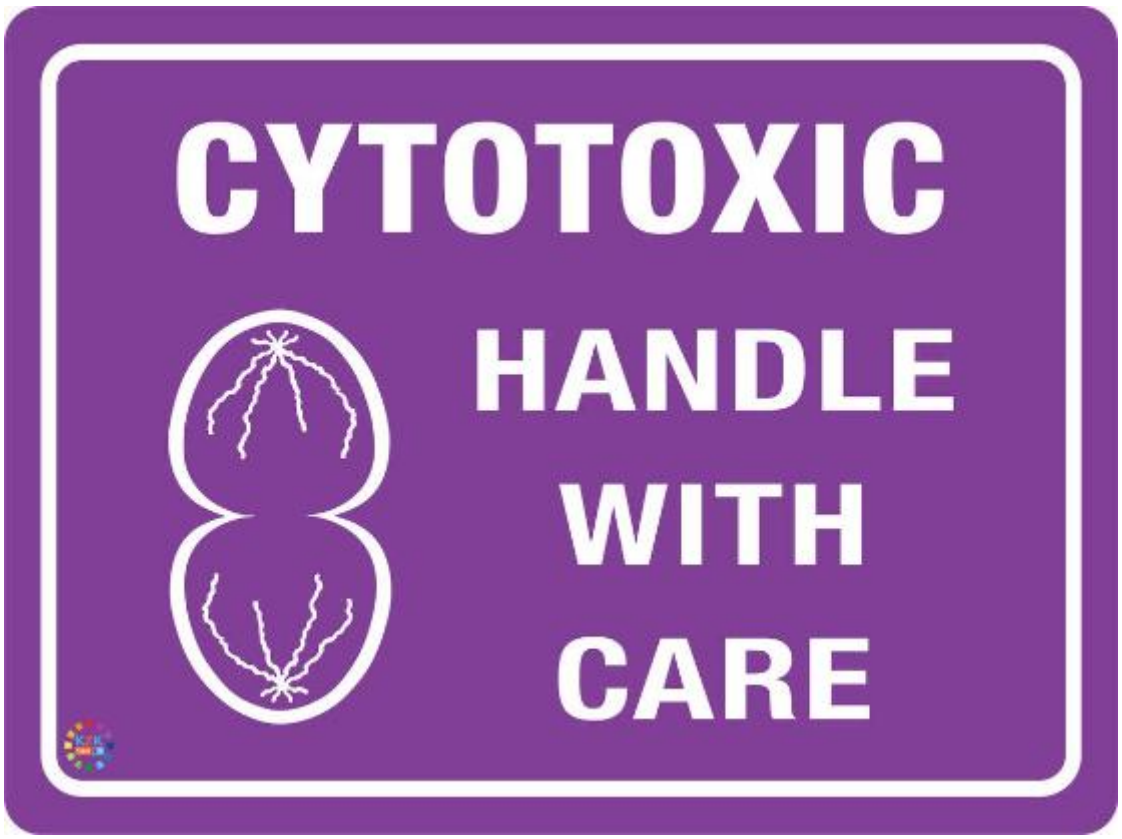
*Comment on incident:*

*Checked by (signature):*
*Date:*

**Reference:**
Manual for Sterile Preparations latest edition, Sterile Pharmaceutical Services Guideline, Ministry of Health Malaysia

**Appendix 5**

## CYTOTOXIC WARNING LABELS






**Appendix 6**

# CRITERIA/ CHARACTERISTICS OF PPE REQUIRED FOR EACH ACTIVITY BEFORE PURCHASE/ USE

| PPE type | Selection criteria |
|---|---|
| Gloves | • Chemotherapy gloves (as tested to American Society for Testing and Materials International (ASTM) standard D6978, or its successor) should be used for all HDs<br>• Powder-free gloves should be made of nitrile, polyurethane, neoprene, or latex material; polyvinyl chloride is not recommended |
| Gowns | • Disposable, lint free, and rated to resist chemotherapy<br>• Do not use cloth laboratory coats, scrubs, or isolation gowns<br>• Should have long sleeves and elastic or knit cuffs, fasten in the back (no open front), and be without seams or closures that could allow HD exposure<br>• Polyethylene-coated polypropylene or other laminate is recommended |
| Eye/face shields | • To be worn any time there is a risk of splashes or spills (e.g., working above eye level, cleaning spills, surgery, bladder treatments), including disposal of contaminated body fluids<br>• Goggles should be worn with face shields when full eye and face protection is needed |
| Respirators | • For most activities requiring respiratory protection, a fit-tested, NIOSH-certified,N95 or more protective respirator is sufficient for airborne particles; however, N95 respirators offer no protection against gases and vapors<br>• An appropriate full-facepiece, chemical cartridge-type respirator or powered air-purifying respirator (PAPR), should be worn when there is a risk of respiratory exposure to HDs, including large spills and known risk of exposure to vapors and gases<br>◦ These are the currently known HDs with the potential to vaporize at room temperature[6]:<br>- Carmustine<br>- Cisplatin<br>- Cyclophosphamide<br>- Etoposide<br>- 5-fluorouracil<br>- Ifosfamide<br>- Nitrogen mustard<br>- Thiotepa<br>• Surgical masks do not provide protection against HD exposure |
| Shoe, sleeve, and hair/facial hair covers (if needed) | • Lint free<br>• Made of disposable materials<br>• Sleeve covers should be polyethylene-coated polypropylene or other laminate, with closed cuffs and no seams, openings, or closures that would allow exposure |

**Reference:**
Toolkit for Safe Handling of Hazardous Drugs for Nurses in Oncology. Oncology Nursing Society, 2018.

**Appendix 7**

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES

**TABLE 3** Summary of extemporaneous oral liquid preparation of oral oncology drugs, stability, and drug properties[a]

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| Abemaciclib[10,11] | • Crush tablet<br>• Disperse in at least 10 mL of water<br>• Administer completely and immediately within 10 minutes of dispersion in water | • Intended for immediate use | • None | • Online resource available for administration instructions for patients unable to swallow<br>• Off-label information notes it is not expected that breaking or crushing of the tablet will alter its effectiveness<br>• The tablet will not dissolve in the water and may taste bitter if swallowed, crushed, or broken |
| Abiraterone[f][12,13] (Zytiga©) | • No data | • No data | • Administer at least 1 hour before or 2 hours after food | • Phase I bioavailability study with liquid formulation using olive oil found 4.5-fold higher AUC compared to tablet<br>• High-fat meal increased Cmax 17-fold and AUC 10-fold<br>• Available in uncoated (250 mg) and film coated (500 mg) formulations<br>  ○ Film coated contain hypromellose<br>• High inter- and intra-subject variability<br>• Yonsa 500 mg comparable to Zytiga 1000 mg in fasting conditions |
| Abiraterone[f][14,15] (Yonsa©) | • No data | • No data | • None | • High inter- and intra-subject variability<br>• Yonsa 500 mg comparable to Zytiga 1000 mg in fasting conditions |
| Acalabrutinib[C][16-19] | • Weak base and requires acidic environment to dissolve. Use standard Coca-Cola with phosphoric acid, do not use other sodas, Diet Coke or Coke Zero<br>  ○ Open the glass bottle. Carefully open one 100 mg acalabrutinib capsule by pulling apart the blue cap and holding the yellow body over the opening of the bottle. Transfer capsule contents into the glass bottle. Discard the capsule body and cap<br>  ○ Add 100 mL of degassed Coca-Cola at room temperature to the glass bottle and cap it<br>  ○ Agitate by shaking the bottle for 20 seconds. Let the bottle rest for at least 15 minutes agitate the bottle for | • Shelf-life is 3 hours after constitution and must be discarded after | • Avoid concomitant use with PPIs<br>• Separate from antacids; may give 3 hours after antacid<br>• Give at least 2 hours before H2-receptor antagonist | • Solubility decreases with increasing pH<br>• Rapid absorption with Tmax within 1 hour |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | 20 seconds at the end of the resting period. There may be fine particles remaining in suspension, but this is normal<br>○ Label the bottle per institutional guideline: "100 mg acalabrutinib dispersion in Coca-Cola—NG for enteral use only"<br>○ Open the NG tube and flush the enteral syringe and NG tube with 15-30 mL of water<br>○ Agitate the bottle for 3 seconds, open it and administer the 100 mg acalabrutinib dispersion via the NG tube, using the enteral syringe portion-wise. Pour directly from the bottle to the enteral syringe. Use either gravity, or the plunger. There may be residues in the bottle after complete transfer, but this is normal. Do not rinse the bottle<br>○ Flush the NG tube with 15-30 mL of water<br>○ Recap the NG tube<br>○ If allowable by [hospital] staff, elevate head of patient's bed to 30° for 1 hour to facilitate gastric emptying of the drug | | | |
| Afatinib[120,21] | • Place tablet into a glass containing 100 mL of noncarbonated drinking water (no other liquids should be used)<br>• Drop tablet into the water without crushing it<br>• Stir occasionally for up to 15 minutes until the tablet is broken up into very fine particles<br>• Drink the suspension immediately or administer via a gastric tube<br>• Rinse the glass with another 100 mL of noncarbonated drinking water and consume/administer the supplementary solution via the gastric-tube again | • Intended for immediate use | • Administer at least 1 hour before or 2 hours after food | • Clinical trial instructions for administration via drinking or GT<br>• Coating contains hypromellose |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| Alectinib[Cc22-26] | Method 1:<br>• Dissolve four 150 mg capsules into 50 mL of water at room temperature<br>• *Note: Instructions described by Bejarano Varas et al for aqueous suspension received from manufacturer off-label information.*<br>Method 2:<br>• Preparation of 10 aliquots (each aliquot consisting of 7150 mg capsules mixed with 10 mL of olive oil)<br>• Add olive oil to contents of 10 aliquots to make a sufficient/total volume of 210 mL (50 mg/mL)<br>• For 600 mg dose: 12 mL of 50 mg/mL suspension were drawn into a 20 mL syringe<br>• Shake prior to administration<br>• After administration, FT was flushed with 30 mL of tube feeds<br>• *Note: instructions described by Bejarano Varas et al* | • Beyond-use date of 4 hours for aqueous solution (*Bejarano Varas et al manufacturer off-label information*)<br>• Olive-oil suspension beyond-use date of 6 months (*Bejarano Varas et al extended dating used per USP 795 nonaqueous formulations*) | • Administer with a meal | • Case reports describe administration via NGT suspended in water<br>• One case report describes clogged syringe catheter tip with attempts to dissolve with water; administered successfully with use of olive oil base<br>• Capsules contain hydroxypropyl cellulose and shell contains hypromellose, carnauba wax |
| Alpelisib[f27-29] | • Add the required number of alpelisib film-coated tablet(s) into an appropriately sized glass<br>• Add approximately 150 mL of water<br>• Let the mixture stand for 5 minutes<br>• Following the 5 minutes, stir and crush the mixture with a spoon to help the disintegration of the tablet(s)<br>• Prolong stirring and/or crushing until the tablet(s) is sufficiently disintegrated for administration. It may take up to 30 minutes for complete disintegration of the tablet(s)<br>• Alpelisib film-coated tablets contain excipients that are insoluble in water. Therefore, the final oral suspension will contain solid particulate material. This has no impact on the treatment.<br>• Gently stir the suspension with the spoon and administer the full amount | • Intended for immediate use | • Administer with a meal | • Co-administration with ranitidine decreased AUC and Cmax by 30 and 51% in the fasted state<br>• Bioavailability is nearly complete if taken with food across dose 30-450 mg. Both high-fat and low-fat meals showed similar results |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • Rinse the glass with approximately 50 mL of water and administer the rinse. Ensure that there are no visible solid residue left in the glass | | | |
| Altretamine[C,99] | • No data | • No data | • Administer with a meal | • Altretamine food-effects and bioavailability poorly characterized<br>• Capsules reported to be well-absorbed |
| Anastrozole[C,31] | • Stop the enteral feed (if applicable)<br>• Flush the enteral FT with the recommended volume of water<br>• Place the tablet in the barrel of an appropriate size and type of syringe<br>• Draw 10 mL of water into the syringe and allow the tablet to disperse, shaking if necessary<br>• Flush the medication dose down the FT<br>• Draw another 10 mL of water into the syringe and also flush this via the FT (this will rinse the syringe and ensure that the total dose is administered)<br>• Finally, flush with the recommended volume of water<br>• Re-start the feed, unless a prolonged break is required (if applicable) | • Intended for immediate use | • None | – |
| Apalutamide[U,32,33] | • Phase 1 study:<br>◦ Recommended dose of apalutamide tablets may be mixed with 4 oz (120 mL) of applesauce<br>◦ Do not crush the tablets. Stir applesauce upon introduction of whole tablets as well as at 15 minutes and 30 minutes afterwards until tablets are dispersed (well mixed with no chunks remaining)<br>◦ Using a spoon, administer the mixture right away<br>◦ Rinse the mixture container with 2 oz of water and immediately administer the contents. Repeat the rinse with 2 oz of water one more time to ensure the whole dose is taken | • Intended for immediate use | • None<br>• Caution use with PPIs (CYP2C19 inducer) | • Tablet contains HPMC<br>• AUC increased by roughly 5% and Cmax increased 27.6% when dispersed in applesauce compared to taking tablet whole under fasting conditions |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • Findings from an additional assessment of dose accuracy and in-use stability of apalutamide in different food vehicles showed apalutamide tablets were comparable in purity and dose accuracy when mixed in 50-200 g of applesauce or yogurt or 50-200 mL of orange juice or green tea and dose accuracy for all food vehicles was found to be within the 85.0%-115.0% criteria with no food vehicles (fasting) appearing to impact the availability of apalutamide<br>○ Tablets were dispersed in food vehicles by gently mixing contents with a spatula for 10 seconds, repeated after 15 minutes and again after another 15 minutes | | | |
| Avapritinib[34] | • No data | • No data | • Take on empty stomach, ≥1 hour before or 2 hours after a meal or snack | • Cmax and AUC increased 59% and 29% when taken with high-fat meal |
| Avatrombopag[35,36] | • One stability trial showed drug was stable after being crushed and sprinkled with yogurt or pudding for up to 30 minutes | • Intended for immediate use | • Take with food | • One study suggests high-fat may increase AUC by 21% |
| Axitinib[4,b,37] | • Place tablets (for doses 2-10 mg) in the barrel of a 20 mL syringe (do not crush tablets and protect from light)<br>• Add/draw up 15 mL of USP grade water to form a suspension<br>• Allow 10 minutes for tablets to dissolve<br>• Fill 2 clear syringes with 15 mL each of USP grade water for prerinsing and flushing FT<br>• Prerinse FT with 15 mL of USP grade water<br>• Gently invert syringe with axitinib several times to mix suspension prior to administration<br>• Rinse now empty axitinib syringe with 10 mL of USP grade water and invert several times to mix | • Intended for immediate use | • None | • Only administer via NGT made of either polyurethane, polyvinyl chloride, or silicone<br>• Other types of FT not specified |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • Administer suspension with residual axitinib<br>• Repeat prior step 5 more times<br>• Rinse FT with 15 mL of USP grade water | | | |
| Azacitidine[C,38] | • No data | • No data | • None | • Formulation contains hypromellose |
| Bexarotene[C,Ln5] | • Cut a 75 mg bexarotene capsule in half<br>• Rinse the interior of the capsule and suspend the contents in 75 mL of water<br>• Suspension must be consumed immediately and the glass refilled halfway with water to ensure administration of a full dose | • Intended for immediate use | • Administer with a meal | • Oral suspension and swallowed capsules are bioequivalent |
| Bicalutamide[C,31] | • Stop the enteral feed (if applicable)<br>• Flush the enteral FT with the recommended volume of water<br>• Place the tablet in a suitable crushing syringe and crush to a fine powder<br>• Add a few mL of water and mix to form a paste<br>• Add up to 15 mL of water and mix thoroughly, ensuring that there are no large particles of tablet<br>• Flush the medication dose down the FT<br>• Draw another 15 mL of water into the syringe and stir to ensure that any remaining drug is rinsed from the container and flush this via the FT (this will rinse the syringe and ensure total dose is administered)<br>• Finally, flush the enteral FT with the recommended volume of water<br>• Re-start the feed, unless a prolonged break in feeding is required (if applicable) | • Intended for immediate use | • None | — |
| Binimetinib[C,39-42] | • Crossover study comparing bioavailability with liquid formulation vs tablets in 22 healthy individuals<br>○ Liquid suspension was prepared by dissolving tablets in a vehicle of (Ora-sweet/Water) at a conc. of 1 mg/mL<br>○ Peak plasma conc. Was slightly higher for the liquid formulation, and total | • No data | • None | • Phase I/II pediatric study describes use of oral suspension (no information provided for administration or preparation instructions) |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | exposure was similar for both formulations | | | |
| Bosutinib[43-45] | • *Syringe preparation*<br>◦ Step 1: Select appropriate number of tablets for a single patient dose<br>◦ Step 2: Take one (1) 10 mL syringe, remove the plunger<br>◦ Step 3: Add the tablets required for the dose to the oral syringe from Step 2 Example: 600 mg dose (6 × 100 mg tablets)<br>◦ Step 4: Fit the plunger into the syringe<br>◦ Step 5: Attach the tip cap to the syringe<br>◦ Step 6: Prepare the dissolution media by preparing 2 beakers/containers of water one heated and one at room temperature<br>◦ Step 7: Take a separate beaker/container and add the room temperature water and boiling water in roughly equal amounts (ie, approximately 50 mL of boiling water to 50 mL of room temperature water)<br>◦ Step 8: Remove the tip cap from the syringe from step 5. Draw the water from step 7 into oral syringe until the plunger is level with the 10 mL measuring line and replace the tip cap. *Note that there will be an air pocket in the syringe due to the space created by the tablets*<br>◦ Step 9: Shake the syringe for approximately 1 minute and then store the syringe on its side for a further 4 minutes (approximately). Repeat the process twice more leaving the syringe for approximately 10 minutes after the final shake to ensure that the tablets have disintegrated fully and to allow the | • Intended for immediate use (only tested with 100 and 500 mg tablets) | • Administer with a meal<br>• Avoid concomitant use with PPIs (if possible)<br>• Take 2 h before or after locally acting antacids or H2RAs | • Highly variable bioavailability. High-fat meal increased bosutinib AUC 1.7-fold and Cmax 1.8-fold |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | solution in the syringe to cool to an appropriate temperature<br>• *Oral syringe administration*<br>○ Take the prepared syringe from Step 9 above. Shake the syringe immediately prior to administration (approximately 10 seconds) to redistribute contents of the syringe *Note: The syringe nozzle should not be blocked by the components. If the syringe nozzle is blocked after this step, discard this syringe and repeat the preparation from Step 1 above*<br>○ Hold the syringe upright (tip end up)<br>○ Release the tip cap to reduce the pressure and push the plunger to expel excess air<br>○ Administer the contents of the syringe rapidly<br>• *Administration via NG tube*<br>○ Draw 10 mL of room temperature water into a separate NG syringe and flush the NG tube<br>○ Take the prepared syringe from Step 9 above. Shake the syringe immediately prior to administration (approximately 10 seconds) to redistribute contents of the syringe. *Note: The syringe nozzle should not be blocked by the components. If the syringe nozzle is blocked after this step, discard this syringe and repeat the preparation from Step 1 above*<br>○ Hold the syringe upright (tip end up)<br>○ Release the tip cap to reduce the pressure and push the plunger to expel excess air<br>○ Attach the syringe to the nasal-gastric tube<br>○ Administer the contents of the syringe<br>○ Rinse the syringe by drawing approximately 10 mL of room | | | |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | temperature water into the syringe. Attach the syringe to the NG tube and administer the solution | | | |
| Brigatinib[44,47] | • No data | • No data | • None | • Oral brigatinib is dependent on the rate of brigatinib absorption in the GI tract rather than being limited by disintegration of the dosage form or dissolution of the active substance in the stomach |
| Busulfan[7,55] | • Crush 120 × 2 mg busulfan tablets into a fine powder using a mortar<br>• Add a small amount of simple syrup and levigate into a uniform paste<br>• Add simple syrup to almost 120 mL and transfer contents into a graduated cylinder<br>• Rinse the mortar with simple syrup and transfer that to the graduated cylinder<br>• Add simple syrup to make a final volume of 120 mL (2 mg/mL)<br>• Transfer the contents of the graduated cylinder to an amber prescription bottle<br>• Label the bottle with "Shake Well," "Refrigerate" | • 30 days under refrigeration | • None | • Busulfan tablets may also be crushed, mixed with water, and administered via a NGT (intended for immediate use) |
| Cabozantinib[C48] (Cometriq) | • No data | • No data | • Administer at least 1 hour before or 2 hours after food | • High-fat, high-calorie meal increased Cmax by 41% and AUC by 57%<br>• Phase 1 dose escalation study found capsule 2-fold higher dose-normalized AUC after single dose compared to powder-in-bottle suspension<br>• Similar exposure (AUC) found following a single 140 mg dose of tablet and capsule formulations<br>• Very variable PK parameters, extended half-lives and long Tmax (up to 120 hours) suggest enterohepatic recirculation or multiple sites of absorption |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | | | | • Mass balance study estimated AUC of capsule 74%-97% |
| Cabozantinib[149] (Cabometyx) | • No data | • No data | • Administer at least 1 hour before or 2 hours after food | • Food-effect on absorption extrapolated from capsule information (Cometriq)<br>• Similar exposure (AUC) found following a single 140 mg dose of tablet and capsule formulations<br>• Very variable PK parameters, extended half-lives and long Tmax (up to 120 hours) suggest enterohepatic recirculation or multiple sites of absorption<br>• Mass balance study estimated mean AUC of tablet 97% compared to solution (suggests high bioavailability)<br>• Tablets contain hydroxypropyl cellulose and coating contains hypromellose |
| Capecitabine[16] | • Place four 500 mg capecitabine tablets in 200 mL of lukewarm water (50 mL/500 mg capecitabine)<br>• Stir for 15 minutes<br>• Consume immediately<br>• Rinse the glass with half a glass of water and consume to ensure administration of a full dose<br>• Solution can be flavored with fruit juice (not grapefruit juice) or squash | • Intended for immediate use | • Administer with a meal<br>• Caution concomitant use with a PPI | • The solution may also be administered through a NGT or other enteral tube |
| Capmatinib[150] | • No data | • No data | • None | • Formulation contains hypromellose |
| Ceritinib[C,16,51-54] | • Open and empty the appropriate number of capsules into a glass bowl. Ensure that the capsule is completely empty<br>• Add at least 40 mL of water (20 mL if dose is 200 mg or less)<br>• Mix the ingredients carefully with a spoon. Draw up solution with a syringe and administer via NG or G tube<br>• The interior of the container used should be rinsed with 20 mL (10 mL for doses | • Stable for 4 hours at room temperature | • Administer with a meal | • Case report describes opening capsule and mixing with normal saline. Patient experienced elevated liver enzymes after administration via NGT requiring ceritinib to be held (received 600 mg)<br>• Phase I pediatric study with instructions to mix capsule contents with applesauce or non-fat yogurt<br>• *Note: case report and phase I pediatric study describe using capsule formulation* |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | 200 mg or less) of water twice and administered to the patient | | | • Decreased solubility with increasing pH<br>• Absolute bioavailability not characterized (expected to be low)<br>• High-fat/high-calorie meal increased AUC by 73% and Cmax by 41%<br>• Low-fat meal increased AUC by 58% and Cmax by 43%<br>• Administration with meals may improve GI tolerability but risk of increased AE<br>• Capsule contains low substituted hydroxypropyl cellulose (insoluble in water)<br>• Tablet contains hypromellose |
| Chlorambucil[55] | • Place 60 × 2-mg chlorambucil tablets in a mortar and crush to a fine powder<br>• Transfer the powder to an amber glass bottle<br>• Mix with 30 mL of 1% methylcellulose<br>• Add a sufficient quantity of simple syrup for a final volume – 60 mL (transfer to a graduated cylinder, rinse mortar and pestle with simple syrup, and add quantity of vehicle sufficient to make 60 mL (2 mg/mL)<br>• Label the bottle with "Shake Well," "Refrigerate," and "Protect from Light" | • 7 days under refrigeration | • Administer preferably on an empty stomach | — |
| Cobimetinib[55-57] | • No data | • No data | • None | • Clinical trial permitted use of an oral solution (no information provided for administration or preparation instructions)<br>• PK studies of the commercial tablet were comparable to the powder-in-capsule formulation utilized in the dose escalation trial<br>• Powder-in-capsule and powder-in-bottle thought to have similar AUC and Cmax<br>• Absolute bioavailability of a single 20 mg dose of cobimetinib is 46% |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| Crizotinib[C,b61,58,59] | • Capsules suspended in warm water (50°C) prior to administration via FT<br>• Capsules mixed in 20 mL syringe with warm water (capsules not opened or crushed)<br>• Mix/invert syringe for 4 minutes<br>• Let syringe rest for 10 minutes after mixing<br>• Flush syringe after use 4 times with 10 mL of water as well as pre/post line flushes (compatible with polyurethane, PVC, and silicone) | • Intended for immediate use | • None | • Case reports describing administration via NGT and PEG<br>• One case report describes observed response with use of 250 mg daily via NGT (followed by 200 mg twice daily after PEG placement)<br>• Clinical trial instructions for NGT administration |
| Cyclophosphamide[b5] | Method 1:<br>• Dissolve 1 g of lyophilized cyclophosphamide for injection in 50 mL of 0.9% sodium chloride injection solution. Tablets can be crushed, but the manufacturer recommends injection powder for reconstitution for making oral liquid<br>• Add a sufficient quantity of either simple syrup or Ora-Plus to a final volume of 100 mL (10 mg/mL) and place in an amber bottle<br>• Label the bottle with "Shake Well"<br>Method 2:<br>• Dissolve the desired amount of lyophilized cyclophosphamide for injection in a sufficient amount of normal saline. Tablets can be crushed, but the manufacturer recommends injection powder for reconstitution for making oral liquid<br>• Compound 1:1 with either simple syrup or Ora-Plus and transfer to an amber bottle (20 mg/mL)<br>• Label the bottle with "Shake Well," "Refrigerate"<br>Method 3: | Method 1:<br>• 10% degradation in 10.6 days (simple syrup) and 6 days (Ora-Plus) at room temperature<br>Method 2:<br>• Stable for 56 days under refrigeration<br>• Stable for 8 days (simple syrup) and 3 days (Ora-Plus) at room temperature<br>Method 3:<br>• 14 days under refrigeration | • Administer with a meal | – |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • Dissolve cyclophosphamide for injection in Aromatic Elixir, N.F. in a glass container | | | |
| Dabrafenib[LCI60-66] | • Case report of 35-year-old BRAF (+) metastatic melanoma, patient was given dabrafenib and trametinib through suspension.<br>◦ Dabrafenib was dispersed through 1.5% carboxymethylcellose (cannot be dispersed in water) and trametinib was dispersed in water and both were immediately given through G-tube | • Intended for immediate use | • Administer at least 1 hour before or 2 hours after a meal | • Ongoing clinical trials describing use of oral suspension (10 mg/mL) (no information provided for administration or preparation instructions)<br>• HPMC capsule increased Cmax 2.0-fold and AUC 1.8-fold compared to gelatin capsule<br>• Administered as a 95 mg suspension in PK study; suspension resulted in faster absorption (Tmax 1.0 hour) and higher Cmax, but similar exposure when compared to HPMC capsules<br>• Absorption of 150 mg doses was nearly complete with HPMC capsules<br>• Unpublished workflow describing successful administration via G-tube after dissolving capsule in a 10 mL syringe with 5 mL of room-temperature water for irrigation |
| Dacomitinib[54,58] | • Tablet disintegrated in 60 mL syringe with 15 mL water and 30 mL Ora-Plus (for 45 mg dose)<br>• Four 50 mL water rinses of syringe administered after dose (total volume administered ~245 mL) | • Intended for immediate use | • Avoid concomitant use with PPIs<br>• Take 6 or more hours before or 10 hours after H2RA<br>• Concomitant antacid use may be used | • Phase I study with instructions for GT administration to a patient in a supine position on an empty stomach (ambulatory permitted after administration)<br>• Cmax and AUC noted to be reduced with suspension compared to historical data |
| Darolutamide[167,68] | • No data | • No data | • Administer with food | • Absolute oral bioavailability of darolutamide is 98.9% (21.3%) as an oral solution and 29.9% (19.4%) as an oral tablet, both at fasted state.<br>• Oral absorption increases 2-2.5× when taken with low- or high-fat meal. Oral absorption may be saturated at 700 mg BID |
| Dasatinib[61,5,A] | • Add the dose of dasatinib to 30 mL of chilled 100% preservative-free orange | • Stable for 60 minutes after preparation | • Avoid concomitant use with PPIs | |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | juice or apple juice and let stand. Do not use grapefruit juice<br>• After 5 minutes, swirl the contents for 3 seconds; repeat every 5 minutes until 20 minutes have elapse from the time the dasatinib was added to the juice<br>• Swirl one last time and administer immediately<br>• Rinse the glass with 15 mL of juice and administer to ensure administration of the full dose. At the discretion of the physician, the suspension may be used through a NGT | | • Separate from antacids; at least 2 hours before or after an antacid<br>• Administer at least 2 hours before or 10 hours after an H2RA | • Evaluation in pediatric patients found 36% lower exposure with use of suspension<br>• Use in healthy adults found comparable AUC (0.84) and geometric mean ratio (0.97) between suspension and intact tablet |
| Decitabine plus cedazuridine[69] | • No data | • No data | • Do not consume food 2 hours before and 2 hours after dose | • Formulation contains hypromellose |
| Duvelisib[LC70-72] | • No data | • No data | • None | • Manufacturer notes that capsules are not enteric coated or sustained release<br>• High-fat meal decreased Cmax by 37%, AUC by 6% (intact capsule)<br>• Absolute bioavailability approximately 42% |
| Elrombopag[173,74] | • No data | • Refer to package insert | • Administer at least 1 hour before or 2 hours after a meal<br>• Separate at least 2 hours before or 4 hours after polyvalent cations | • Study evaluating use in ICU patients; tablets were crushed into a slurry and administered orally or via NGT; no significant adverse effects reported<br>• Tablets contain hypromellose<br>• Commercial suspension available |
| Enasidenib[175,76] | • Place tablet in container with water<br>• Allow to completely dissolve until a homogenous mixture is reached<br>• Withdraw with syringe<br>• Rinse products used with purified water | • Intended for immediate use | • None | • Manufacturer notes dissolving until a homogenous mixture is attained (no time parameters outlined)<br>• Tablets contain hydroxypropyl cellulose and hypromellose |
| Encorafenib[LC77,78] | • No data | • No data | • None | • PK studies suggest no significant difference in total exposure between intact capsule and when capsule contents are sprinkled in applesauce<br>• Animal (canine) study found 25.2% increase in total exposure between intact capsule and suspension made from 3 g satchet (450 mg active encorafenib) mixed with Ora-Blend. |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | | | | Suspension must be administered within 15 minutes of use due to potential crystallization |
| Entrectinib[C79,80] | • During clinical trials, patients that required NG or gastric administration were given a 20 mg/mL suspension<br>○ Capsule contents were emptied into a glass container and homogenized with water (*adapted to be 20 mg/mL per institutional protocol/internal review*) by repeated stirring or shaking for approximately 30 minutes (turbidity due to inactive ingredients)<br>○ Immediately given via FT after preparing<br>○ Tube was flushed w/ adequate amount of water to completely flush the dose through | • Intended for immediate use | • None | • Formulation contains hypromellose |
| Enzalutamide[I,C81-83] | • Extemporaneous liquid preparation of capsules for oral and enteral administration (>95% of dose was recovered with extemporaneous preparation and stable up to 4 hours at room temp):<br>○ Prepare 40-50 mL of 90% v/v ethanol:water. Transfer 30 mL to a container. Cover if not used immediately. Use as reservoir for subsequent steps<br>○ Swipe-clean the dosing container, tweezers and scissors with alcohol wipes<br>○ Using tweezers and scissors carefully cut a small vent, ~2 mm long, through a soft gel capsule wall- just enough to vent internal pressure. *Note: cut vent over dosing cup since some material may flow out of the vent hole. Place vented capsule in dosing cup. Repeat for remaining 3 capsules*<br>○ Using tweezers and scissors, slowly cut each capsule in half laterally. | • Intended for immediate use | • None | • Liquid-filled capsule contains fully dissolved enzalutamide; formulation circumvents the typical dissolution issues associated with Biopharmaceutics Classification System (BCS) Class 2 compounds, and allows for rapid dissolution of the capsule/release of solubilized enzalutamide into the gut lumen |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

**TABLE 3** (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | Allow capsule contents (enzalutamide in Labrasol) to empty into dosing cup (fill material flows out easily). Repeat for all capsules<br>*Note: all 8 capsule shell pieces and fill contents will be in in the dosing cup*<br>○ Hold each capsule shell piece with tweezers and rinse the inside and outside into the dosing cup using 90% ethanol. Use 1-2 mL per capsule half (2-3 mL syringe). Discard rinsed capsule shells<br>○ Withdraw 10 mL of ethanol solution and rinse the tweezers and scissors into the dosing cup<br>○ Withdraw and dispense solution back into dosing cup at least 5 times to ensure a homogeneous mixture<br>○ Withdraw the solution into the dosing syringe<br>○ Slowly dispense through the NG tube<br>○ Withdraw the remaining ~10 mL of 90% ethanol, rinse dosing cup, withdraw into dosing syringe, cap and shake, and dose through the NG tube<br>○ Flush tube with 6 mL of water | | | |
| Erdafitinib[194] | • No data | • No data | • None | • Avoid co-administration of serum phosphate level-altering agents |
| Erlotinib[†,160,5,A] | Method 1:<br>• 10 mg/mL oral suspension prepared from commercially available 150-mg tablets in a 1:1 mixture of Ora-PlusOra-Sweet<br>Method 2:<br>• Dissolve tablets in 100 mL of water. Do not disperse in grapefruit juice<br>• Rinse the container twice with 40 mL of water to ensure delivery of the full dose<br>• The suspension may either be swallowed or delivered via gastric tube | Method 1:<br>• 28 days at room temperature (22-25°C)<br>• Sedimentation may occur if left undisturbed (stability unaffected, mix/shake to re-suspend)<br>• Do not refrigerate (discard if refrigerated due to observed increase in viscosity at 4°C)<br>Method 2:<br>• Intended for immediate use | • Administer at least 1 hour before or 2 hours after food<br>• Avoid concomitant use with PPIs (if possible)<br>• Separate from antacids; at least 3 hours after an antacid<br>• Administer at least 2 hours before or 10 hours after an H2RA | • One case report describes tablet dissolved in water; patient stopped therapy after 3 weeks due to pneumatosis intestinalis |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| Estramustine[C85] | • No data | • No data | • Administer at least 1 hour before or 2 hours after food<br>• Avoid dairy products or other calcium-rich food or drugs (including calcium-containing antacids) | — |
| Etoposide[85,A] | Method 1:<br>• Dilute the desired amount of etoposide 20 mg/mL injectable solution with NS 0.9% solution for injection to 10 mg/mL<br>• Store in oral syringes or an amber bottle<br>Method 2:<br>• 50 mg oral solution of etoposide can be prepared by adding 2.5 mL of IV etoposide 20 mg/mL solution to 100 mL of water<br>Method 3:<br>• Mix etoposide with orange juice, apple juice, or lemonade to concentration of 0.4 mg/mL | Method 1:<br>• 22 days at room temperature<br>Method2:<br>• Not provided<br>Method 3:<br>• Less than 1% loss of potency over 3 hours in orange juice (1 mg/mL)<br>• No loss of potency over 3 hours in apple juice or lemonade (1 mg/mL)<br>• Precipitate observed at 1 mg/mL (no loss of potency)<br>Other:<br>• 7-day BUD may be recommended (no preservative) | • None | — |
| Everolimus[B86] | • Disperse tablet in ~30 mL (1 oz) of water; gently stir<br>• Administer and rinse container with additional 30 mL (1 oz) water and administer to ensure entire dose is administered | • Intended for immediate use | • None | • Instructions for preparation of liquid suspension from everolimus tablet (Afinitor)<br>• Commercial tablet for oral suspension available (Afinitor Disperz) |
| Exemestane[87] | • No data | • No data | • Administer with a meal | • A high-fat breakfast increased AUC by 59% and Cmax by 39% |
| Fedratinib[C88] | • No data | • No data | • None | • Administration with fatty food may decrease nausea/vomiting, but food did not affect drug exposure |
| Flutamide[C31] | • Stop the enteral feed (if applicable)<br>• Flush the enteral FT with the recommended volume of water<br>• Place the tablet in the barrel of an appropriate size and type of syringe<br>• Draw 10 mL of water into the syringe and allow the tablet to disperse, shaking if necessary<br>• Flush the medication dose down the FT<br>• Draw another 10 mL of water into the syringe and also flush this via the FT | • Intended for immediate use | • None | • Only capsules available (instructions for liquid formulation specify use of tablet formulation) |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | (this will rinse the syringe and ensure that the total dose is administered)<br>• Finally, flush with the recommended volume of water<br>• Restart the feed, unless a prolonged break is required (if applicable) | | | |
| Fostamatinib[1,88,90] | • No data | • No data | • None | – |
| Gefitinib[7,85,86,91,92] | Method 1:<br>• Immerse tablets in 4-8 oz of water and stir for about 15 minutes<br>• Rinse container with another 4-8 oz of water and give immediately via NGT<br>Method 2:<br>• Dissolve a 250 mg tablet (without crushing) in hot water (55°C) for 10 minutes | • Intended for immediate use | • Avoid concomitant use with PPIs (if possible). If use is required, administer at least 12 hours before or after PPI<br>• Administer at least 6 hours before or after antacids or an H2RA | • Case report describes administration via gastrostomy tube<br>• PK study found comparable bioavailability between suspension and intact tablet |
| Gilteritinib[81,92] | • Stability Study 1: Suspension was prepared by warming 20 mL water to 55°C and adding 1 or 5 tablets and stability was measured 0, 30, and 120 minutes after preparation. More than 97% of gilteritinib was detected at each time point and was stable throughout 120 minutes<br>• Dissolution Study 2: Gilteritinib 40 mg (one and five tablets) were placed inside of a syringe, 20 mL of city water (20°C, 40°C, 50°C or 55°C) was drawn into the dispenser and the tip was locked with a cap, the dispenser was left at room temperature for 0 to 120 minutes with the cap returned back onto the tip (static hold time), the dispenser was shaken by hand at about 2 strokes per second. Results showed less shaking was required to disintegrate tablets at higher temperatures (20 minutes to dissolve at 55°C)<br>• Enteral FT pass- ability study 3: 1, 3 and 5 gilteritinib tablets were used to prepare a suspension with 20 mL 55°C hot city water under special predefined | • Intended for immediate use | • None | • Tablet contains hydroxypropyl cellulose, low-substituted hydroxypropyl cellulose, and hypromellose |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | laboratory conditions in a dispenser. An 8 Fr enteral tube (New Enteral Feeding Tube 8 Fr) was rinsed with 10 mL city water, provided by a clean dispenser. Following this, the drug suspension was injected into the tube using the dispenser. Finally, the tube was washed with 10 mL tap water twice. This procedure was repeated 3 times. No residue of the suspension in the enteral tube was observed | | | |
| Glasdegib[59,94] | • Dissolve tablets in 10 mL of water<br>• Invert continuously for 3 minutes<br>• Dilute further with 10 mL Thick-It (maltodextran) for total volume 20 mL.<br>• Rinse/flush syringe used and administer via FT | • Stable for 2 hours when stored in the syringe at room temperature<br>• Intended for immediate use | • None | • Clinical trial instruction for creation of extemporaneous suspension<br>• Tablet coating contains hypromellose |
| Hydroxyurea[85,95,96] | Method 1:<br>• Place the contents of 20 hydroxyurea capsules (500 mg each) into 50 mL of room temperature sterile water (200 mg/mL)<br>• Stir this solution for several hours<br>• Filter the solution to removed insoluble excipients<br>• Add 50 mL of flavored syrup to the filtered solution for a final concentration of 100 mg/mL<br>• Store in an amber plastic bottle<br>Method 2:<br>• Tablets (Siklos) may be dispersed in water | Method 1:<br>• Stable for 1 month at room temperature<br>• 5% loss of chemical activity in 3 months with no additional loss for up to 9 months<br>Method 2:<br>• Intended for immediate use | • None | • Chemical stability reduced by 40% with use of heated water (41°C) |
| Ibrutinib[C11,97,98] | • Open 3 capsules and pour contents into mortar<br>• Mix and swirl with ~15 mL of sterile water for injection<br>• Wait 5 minutes and then draw entire contents into a 20 mL oral syringe (contents may not be completely dissolved) | • Intended for immediate use | • None | • Case reports describing administration via NGT and PEG tube by opening the capsule contents and flushing the contents down the tube(s) with water<br>• Capsule and tablet formulations available |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • *Note: preparation instructions not well defined by case reports. These instructions stem from OHSU preparation and experience* | | | |
| Idelalisib[99-101] | • No data | • No data | • None | • In vitro/drug properties suggests that use of ARAs that increase gastric pH to 6 or higher may decrease bioavailability<br>  ○ PK data did not show significant difference in AUC/Cmax<br>  ○ Observed decrease in AEs related to surmised difference in bioavailability with use of ARA (ie, increased tolerability with decreased exposure)<br>• Withdrawn pediatric clinical trial noted use of 10 mg dispersible tablets for oral suspension<br>• Tablets contain hydroxypropyl cellulose |
| Imatinib[7,63,102] | Method 1:<br>• Tablets may be dispersed in water or apple juice (using ~50 mL for 100 mg tablet, ~200 mL for 400 mg tablet)<br>• Stir until dissolved<br>• To ensure the full dose is administered, rinse the glass and administer residue<br>Method 2:<br>• Crush desired number of 400 mg tablets in a glass mortar and triturate to a fine powder (estimated powder volume for each imatinib 400 mg tablet is 0.4 mL)<br>• Measure the necessary volume of Ora-Sweet (to make a 40 mg/mL suspension) and add to the powder by geometric dilution until a smooth suspension is created<br>• Transfer to an amber plastic bottle | Method 1:<br>• Intended for immediate use<br>Method 2:<br>• Stable for 14 days at room temperature or refrigerated (4°C) | • Administer with a meal | — |
| Ivosidenib[103,104] | • Place appropriate number of ivosidenib tablets (max 500 mg dose) into a glass bottle (instructions specify a 50 mL glass | • Suspension should be administered within 90 minutes of preparation | • Do not administer with a high-fat meal | • Gently mix/shake to avoid excessive foam generation (Do not shake vigorously). If foam is observed let settle prior to administration |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | bottle with an unlined [ie, no cap liner, insert] plastic cap)<br>• Add 20 mL of sterile water for injection<br>• Allow the bottle to stand for at least 5 minutes to ensure full disintegration of tablet(s)<br>• Mix the suspension in the bottle by gently inverting the bottle manually at least 10 times or until a uniform suspension is formed (no visible agglomerates)<br>• Instructions specify use of a 10 mL syringe to administer bottle contents via NGT<br>• To ensure that all contents are delivered, rinse the bottle with 10 mL of sterile water for injection at least twice using the same syringe used in prior step | | | • Tablet and coating contain hypromellose |
| Ixazomib[C105,106] | • No data | • No data | • Administer at least 1 hour before or 2 hours after meals | • Absolute bioavailability was estimated to be 58% based on population PK<br>• High-fat meal decreased ixazomib Cmax by 69% and AUC by 28% |
| Lapatinib[b3] | • 50 mg/mL oral suspension prepared from commercially available 250-mg tablets in a 1:1 mixture of Ora-Plus:Ora-Sweet | • Stable for 28 days at room temperature<br>• Do not refrigerate (discard if refrigerated due to observed increase in viscosity at 4°C) | • Caution use with acid-suppressing agents (may decrease lapatinib serum concentration) | • Suspension is highly viscous and adheres to prescription bottles (dose syringe recommended to ensure delivery of full dose) |
| Larotrectinib[C107] | • No data | • Refer to package insert | • None | • Capsules or solution may be used interchangeably<br>• Commercial suspension available |
| Lenalidomide[C,bc108] | • Place 5 intact capsules (5 mg each) in 20 mL (1.25 mg/mL) of hot water (55°C)<br>• Do not grind, open, or crush the lenalidomide capsules | • Stable for 24 hours | • None | • Scarce adsorption onto tubes made of polyurethane or polyvinyl chloride.<br>• 96.8%-100.6% recovered from the suspension<br>• 92%-114.5% of lenalidomide passable through a PEG tube (PEG tube French 8, 12, 20, and 24) |
| Lenvatinib[C,bc6,109] | • May dissolve capsules in 1 tablespoonful of water or apple juice<br>• Do not break or crush capsules and allow to sit for 10 minutes<br>• Stir for at least 3 minutes | • Stable for 24 hours | • None | — |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • To ensure that all contents are delivered, rinse containers or devices used with an additional tablespoon of water or juice and administer accordingly | | | |
| Letrozole[1,4,6,10,111] | • Place 1 × 2.5 mg letrozole tablet in a 10 mL oral syringe<br>• Draw up 5 mL of purified water into a 10 mL oral syringe and transfer to the 10 mL oral syringe containing 2.5 mg letrozole tablet using a syringe connector. Remove the empty 20 mL syringe and connector from the oral syringe<br>• Cap the oral syringe<br>• Shake the mixture until tablet is completely dissolved into solution<br>• Let solution sit and shake periodically until tablet completely dissolved<br>• Draw up patient specific dose, labels, and cap the oral syringe<br>• Add LOT number and BUD time to Epic label<br>• *Note: these instructions stem from OHSU preparation and experience* | • Intended for immediate use | • None | • Pharmacokinetic studies found oral and intravenous plasma profiles almost identical within 2-4 hours after administration, suggests that PK variability likely not related to absorption<br>• Tablet contains hypromellose |
| Leucovorin[65] | Method 1:<br>• Crush 24 tablets (25 mg each) in a glass mortar and reduce to a fine powder<br>• Transfer powder to amber bottle<br>• Add 30 mL Cologel and shake mixture thoroughly<br>• Add a quantity of syrup mixture (2:1 mixture of simple syrup and wild cherry syrup) sufficient to make 120 mL (5 mg/mL)<br>Method 2:<br>• Drop tablets into an 8 oz glass of water and let stand for 5 minutes<br>• Stir the solution with a spoon (tablets should readily go into solution) | Method 1:<br>• Stable for 28 days under refrigeration (rapid degradation with storage at room temperature)<br>Method 2:<br>• Stable for 2 hours at room temperature | • None | • Doses greater than 25 mg should not be administered orally |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| Lomustine[c,112,113] | • Quantities may vary—instructions for lomustine 10 mg/mL suspension<br>• Empty contents of lomustine capsules into a small plastic med cup<br>• Add __mL of simple syrup and mix well<br>• Withdraw the lomustine suspension into an amber 20 mL oral syringe<br>• Add __ mL more of simple syrup to the med cup and then withdraw into the oral syringe<br>• Cap syringe and label<br>• *Note: these instructions stem from OHSU preparation and experience* | • Intended for immediate use | • Administering on an empty stomach may reduce the incidence of nausea and vomiting | • Animal studies/compounded prescriptions for animals use sesame or other oils for suspension due to insoluble nature in water |
| Lorlatinib[c,58,114] | • Put the tablet into 20 mL—35 mL oral syringe. Do not break or crush them<br>• QS syringe to 10 mL with sterile water for irrigation<br>• Leave the tablet in the liquid for at least 10 minutes<br>• Invert syringe repeatedly to mix contents for up to 3 minutes | • Stable for at least 3 hours within the oral/enteral syringe<br>• Intended for immediate administration | • None | • Clinical trial instructions for administration via NGT<br>• Tablet coating contains HPMC 2910/ hypromellose |
| Lusutrombopag[f,115] | • No data | • No data | • None | • Formulation contains hypromellose and hydroxypropyl cellulose |
| Melphalan[h,5] | • Not recommended | • Highly subject to hydrolysis<br>• Preparation in methylcellulose and simple syrup resulted in loss of >80% at room temperature and >50% within 7 days at 5°C<br>• Complete hydrolysis when prepared in water (30 µg/mL) at 37°C after 8 hours | • Administer at least 1 hour before or 2 hours after meals | • Preparation in an acidic environment reduces rate of hydrolysis; potency with preparation in more acidic conditions is not well characterized |
| Midostaurin[C,c,116,117] | • Begin with 100 °F tap water in beaker-water bath. (Use thermometer)<br>• Turn magnetic stirrer/hot plate on lowest heat setting<br>• Place the 4 midostaurin capsules into a 20 mL amber syringe and QS to 10 mL with sterile water for injection<br>• Cap syringe<br>• Heat syringe in water bath until gelatin capsule has dissolved (approximately 60 minutes) | • Intended for immediate use | • Administer with a meal | • AUC increased by 22% and 59%, Cmax reduced by 20% and 27%, Tmax delayed to 2.5 hours and 3 hours, with a standard meal and a high-fat meal, respectively<br>• Capsule contains castor oil, glycerin 85%, corn oil mono-di-triglycerides, hypromellose 2910 |

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## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • *Note: these instructions stem from OHSU preparation and experience* | | | |
| Mitotane[c,118–121] | Method 1:<br>• Micronize (grind to a fine powder) mitotane with mortar and pestle<br>• Carefully place that—the micronized mitotane—in a shaker container with a top (preferably glass)<br>• Do not use this shaker for anything else except mitotane preparation<br>• Add 1 tablespoon of flax oil to the container<br>• Add 2 teaspoons of Nestle Nesquik (or other powdered chocolate product) powdered chocolate<br>• Add 8 oz of cold 2% milk<br>• Place the top on the container and shake vigorously for 30–60 seconds<br>• Pour in glass and drink the emulsion<br>• Clean all utensils utilized and store away from children for next dosage. Do not use these utensils for anything else except mitotane preparation<br>Method 2:<br>• Cut 500 mg tablet into quarters and transfer pieces to 6 mL oral syringe<br>• Draw up 1 mL of medium chain triglyceride (MCT) oil into a 3 mL oral syringe and transfer to the 6 mL oral syringe containing 500 mg mitotane tablet (use syringe connector)<br>• Push MCT oil between syringes till tablet pieces have been dissolved<br>• QS to 2 mL with MCT oil<br>• Transfer to appropriate oral syringe and discard excess | • Intended for immediate use | • None | • Manufacturer recommendations and institutional practices (Michigan Medicine "Milkshake recipe"<br>• Manufacturer suggests mixing with yogurt or other fat-containing food (ex. Chocolate spread) to improve bioavailability (lipophilic)<br>• "Milkshake recipe" consists of flax oil, powdered chocolate (or other powdered milk flavoring), and 2% milk (or soy milk)<br>• Pediatric administration instructs crushing/dissolving in MCT oil then mixing with fat-containing food (ie, milk or yogurt) |
| Mercaptopurine[b,85] | • Place 30 tablets (50 mg each) in a mortar and grind into a fine powder<br>• Transfer the powder to an amber glass bottle and add 5 mL of sterile water for irrigation | • Stable for 35 days at room temperature<br>• Stable for 77 days at room temperature with addition of ascorbic acid 0.1% (weight/volume) | • Administer preferably on an empty stomach<br>• Avoid concomitant dairy products if possible | • Commercial suspension available |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • Shake the mixture to create a uniform paste<br>• Add 10 mL of simple syrup. Add wild cherry syrup to a quantity sufficient for 30 mL (50 mg/mL) | | | |
| Mesna[65] | • Dilute solution for injection to 20 mg/mL or 50 mg/mL with orange or grape syrup<br>• Prior to administration, syrup-diluted solutions may be diluted to a final concentration of 1, 10, or 50 mg/mL with any of the following: Carbonated beverages, apple juice, orange juice, or milk | • Stable for at least 9 days undiluted in polypropylene syringe at 5°C, 24°C, 35°C<br>• Stable for 7 days after dilution to 1:2 or 1:5 with syrups at 24°C<br>• Stable for 24 hours after dilution to 1:2, 1:10, or 1:100 in orange/apple juice, milk, or carbonated beverages at 5°C | • None | – |
| Methotrexate[65,122] | Method 1:<br>• Dissolve sodium bicarbonate 0.6 g in sterile water in a mortar or in a beaker with a magnetic stirrer to insure adequate stirring<br>• Slowly incorporate Ora Sweet(R) 7.5 mL<br>• While continuing to stir, add 2.4 mL of methotrexate for injection 500 mg/20 mL injectable solution (Mylan(R))<br>• *Note: do not use methotrexate powder for injection*<br>• Add sufficient sterile water to reach a final volume of 30 mL (2 mg/mL)<br>Method 2:<br>• Tablet may be added into a syringe and suspended in water | • Stable for 120 days at 4°C or 25°C in a 30 mL amber type 1 glass bottle<br>• Tablet suspension intended for immediate use | • None | • Commercial suspension available<br>• No significant difference in bioavailability between extemporaneous oral solution and commercial oral tablet |
| Neratinib[123,124] | • No data | • No data | • Administer with a meal<br>• Avoid concomitant use with PPIs<br>• Separate from antacids; at least 3 hours after an antacid<br>• Administer at least 2 hours before or 10 hours after an H2RA | • Clinical trial outlining inclusion criteria of pediatric patients with existing GT (no information provided for administration instructions)<br>• pH-dependent aqueous solubility (insoluble at pH ≥ 5.0) |
| Nilotinib[65,125] | • No data | • No data | • Administer at least 1 hour before or 2 hours after meals<br>• Avoid concomitant use with PPIs | • Capsule contents may be added to 5 mL of applesauce<br>• Solubility of nilotinib in an aqueous solution decreases with increasing pH |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | | | • Separate from antacids; at least 2 hours before or after an antacid<br>• Administer at least 2 hours before or 10 hours after an H2RA | • A crossover study found that administration of opened capsule contents with yogurt increased Cmax, AUC(0-tlast), and AUC(0-inf) by 31%, 11%, and 8%, respectively<br>• Similar exposure found with use of applesauce |
| Nilutamide[126] | • No data | • No data | • None | — |
| Niraparib[C,127,128] | • No data | • No data | • None | • Absolute bioavailability of approximately 73%<br>• Niraparib is unlikely to be altered in the presence of gastric acid reducing agents (in vitro solubility information) |
| Olaparib[C,F,129-132] | • Not recommended | • No data | • None | • Olaparib tablets dissolve via an eroding mechanism. Therefore, if the surface area is greater, the dissolution rate will increase. Crushing the tablet would result in a greater surface area which could directly affect olaparib pharmacokinetics by increasing the Cmax and decreasing the Tmax. Increased Cmax could potentially increase drug toxicity. Crushing the tablet is therefore not recommended<br>• Due to differences in dosing and bioavailability, do not substitute the 50 mg capsules for the 100/150 mg tablets on a mg-per-mg basis (capsules discontinued in August 2018)<br>• Tablet higher bioavailability than capsule (AUC 300 mg tablet twice daily 77% higher than 400 mg capsule twice daily). Increased bioavailability attributed to improved solubility with tablet vs capsule formulation<br>• Tablet coating contains hypromellose |
| Osimeritinib[H,133] | • Disperse tablet in 15 mL of noncarbonated water<br>• Stir to disperse into small pieces<br>• Do not crush, heat, or ultrasonicate tablets | • Intended for immediate use | • None | • PK study found no difference between AUC and Cmax between suspension and intact tablets |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • *Note: the tablet will not completely dissolve*<br>• Use an additional 15 mL of water to transfer any residues to the syringe (total volume ~ 30 mL) | | | |
| Palbociclib[C98] | • Add 15 mL of warm water to syringe with capsules (half boiling and half room temperature)<br>• Let sit for 10 minutes<br>• Invert to ensure mixed<br>• *Normal for trace amounts of capsule shell or powder to remain*<br>• Flush syringe used with water and administer (repeat 4 times) | • Stable for 2 hours at room temperature<br>• Intended for immediate use | • Administer with a meal<br>• Take with food if taken with a PPI (capsule); minimal interaction expected with use of tablet formulation | • Clinical trial instructions for administration via NGT or PEG<br>• PEG or NGT diameter range from 12-28 and <8 French tested, respectively |
| Panobinostat[C134,135] | • No data | • No data | • None | • Absolute bioavailability estimated to be 21% based on a population PK |
| Pazopanib[LF,b136-140] | • Crush tablets and mix with applesauce or yogurt | • Intended for immediate use | • Administer at least 1 hour before or 2 hours after meals<br>• Avoid concomitant use with PPIs<br>• Avoid concomitant use with H2RAs<br>• Caution concomitant use with antacids; separate from antacids by several hours | • Case reports of 2 patients describing administration after crushing tablets and mixing with applesauce (one patient mixed with yogurt as well due to preference). Applesauce used due to low drug solubility in aqueous medium. Starting doses were reduced (400 mg and 200 mg), and increased as tolerated. Doses were later adjusted to account for AEs<br>• Phase I pharmacokinetic study found administration of a single pazopanib 400 mg crushed (5 mL of applesauce) tablet increased AUC by 46% and Cmax by approximately 2-fold and decreased Tmax by approximately 2 hours<br>• Phase I Pharmacokinetic study in pediatric patients describe use of suspension using pazopanib powder and Ora-Sweet (50 mg/mL). Dose escalation conducted at 50% MTD based on adult data showing increased bioavailability with suspension/ crushed tablet |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | | | | • The most frequently reported AEs (>20%) in patients who received the crushed tablet (n = 9) included:<br>◦ Erythema, vomiting, and fatigue (22% each)<br>• Population analysis showed that food increased bioavailability of pazopanib by 160%<br>• Film coating contains hypromellose |
| Pemigatinib[141] | • No data | • No data | • No meaningful effect of administration with food | • pH dependent solubility, no concerning inactive ingredients |
| Pexidartinib[C142] | • No data | • No data | • Take on empty stomach, ≥1 hour before or 2 hours after a meal or snack<br>• Avoid concomitant use with PPIs<br>• Separate from antacids; at least 2 hours before or after an antacid<br>• Administer at least 2 hours before or 10 hours after an H2RA | • Formulation contains hypromellose |
| Pomalidomide[C,c75] | Method 1:<br>• Suspend 3 mg capsules in 0.5% carboxymethylcellulose<br>• Admix 0.5 mL of Tween 80 to facilitate dilutions<br>Method 2:<br>• Put the capsule into 20-35 mL oral syringe. Do not break or crush them<br>• QS syringe to 15 mL with sterile water for irrigation<br>• Leave the capsule in the liquid for at least 10 minutes<br>• Invert syringe repeatedly to mix contents for up to 3 minutes<br>• *Note: these instructions stem from OHSU preparation and experience* | • Intended for immediate use | • None | • Case report describing desensitization recipe using 0.5% carboxymethylcellulose and 0.25% tween 80 (dose 0.00025-1 mg; volume 0.25-5 mL); concentration 0.001-1 mg/mL) |
| Ponatinib[f143,144] | • No data | • No data | • None | • Case report of inadvertent administration of an entire bottle of study medication via NGT causing significant QTc interval prolongation (nonfatal, patient later deceased in setting of pneumonia/sepsis) |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | | | | • Bioavailability may decrease with use of ARAs |
| Pralsetinib[C145] | • No data | • No data | • Take on empty stomach, ≥1 hour before or 2 hours after a meal or snack | • Following administration with high-fat meal, Cmax increased by 104% and AUC by 122%<br>• Formulation contains hypromellose |
| Procarbazine[b5] | • Empty the contents of 10 capsules (50 mg each) into a mortar<br>• Add a 2 mL of glycerin and levigate the mixture to a thick paste<br>• Add 10 mL of strawberry syrup by geometric proportion and levigate until the mixture is uniform<br>• Transfer the mixture to an amber glass bottle and add a quantity of strawberry syrup sufficient for a final volume of 50 mL (10 mg/mL) by repeatedly rinsing the mortar and pestle with small amounts of syrup | • Stable for 7 days at room temperature | • Do not drink alcohol and avoid high-tyramine-containing foods | • Protect from light |
| Regorafenib[J146,147] | • No data | • No data | • Administer after a low-fat meal containing <600 cal and <30% fat | • Does escalation study describes mean relative bioavailability of tablets compared to oral solution (60 mg) is 69% (20 mg tablet) to 83% (100 mg) in the fasted state (no information provided for administration or preparation instructions) |
| Ribociclib[J148–150] | • No data | • No data | • None | • Moderate absorption estimated to be around 60% based on human pharmacokinetic data with 600 mg dose<br>• Ongoing phase I study describing use of ribociclib liquid formulation (no information provided for administration or preparation instructions) |
| Ripretinib[151,152] | • No data | • No data | • None | • AUC and Cmax increased by 30% and 22% following administration with a fatty meal<br>• Formulation contains hypromellose |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| Rucaparib[153,154] | • No data | • No data | • None | • Mean oral bioavailability at doses > 480 mg were 51.7% with a high-fat meal, 32.6% under fasted conditions, and 37.2% with a meal of patient's choice<br>• High-fat meal increased AUC by 38% and Cmax by 20%, delayed Tmax by median of 2.5 hours |
| Ruxolitinib[b,c,155] | • Place one tablet inside of a 60 mL syringe<br>• Draw up 40 mL of sterile water into syringe and cap<br>• Suspend and stir tablet over approximately 10 minutes by inverting and shaking syringe | • Administer within 6 hours after dispersion | • None | • Tablet contains hydroxypropyl cellulose |
| Selinexor[f,b,156-161] | • Compounded as 5 mg/mL suspension; must be compounded with Ora-Blend in a polyethylene terephthalate (PET) or glass amber bottle; do NOT shake suspension at anytime; resuspend any solids by gentle and repeated inverting<br>◦ 20 mg tablets (total volume: 50 mL or 100 mL)<br>• Place 12 or 24, 20 mg tablets, in 4 oz PET amber vial<br>• Add 12 or 24 mL of water to disintegrate tablets (about 20 minutes)<br>• Cap the bottle and intermittently swirl the solution and inverted gently to disperse the particles for 20 minutes<br>• Add 36 or 72 mL of Ora-Blend to disintegrated tablets respectively<br>• Invert the solution 20 times for final suspension<br>◦ 40 mg tablets (total volume: 50 mL or 100 mL)<br>• Place 6 or 12, 40 mg tablets, in 4 oz PET amber vial | • Should be stored in 2-8°C if not used within 24 hours<br>• May be stored up to 42 days under refrigeration (2-8°C)<br>• May be stored up 28 days at room temperature (≤25°C) | • Administration with food or nutrition may reduce nausea | • Similar PK parameters found between tablet, capsule, and suspension in preclinical and phase I studies<br>• Oral nasogastric toxicity study of monkeys showed dose proportional increases with no clinically relevant accumulation when looking at overall Cmax and AUC<br>• No clinical difference between absorption (Cmax and AUC) between TF2.2 tablets (second gen tablet formulation) and suspension formulation GMR<br>• Manufacturer also provides guidance for pediatric dosing based on body surface area (not described here) |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • Add 12 or 24 mL of water to disintegrate tablets (about 20 minutes)<br>• Cap the bottle and intermittently swirl the solution and inverted gently to disperse the particles for 20 minutes<br>• Add 36 or 72 mL of Ora-Blend to disintegrated tablets respectively<br>• Invert the solution 20 times for final suspension<br>◦ 50 mg tablets (total volume: 50 mL or 100 mL)<br>• Place 5 or 10, 50 mg tablets, in 4 oz PET amber vial<br>• Add 12 or 25 mL of water to disintegrate tablets (about 20 minutes)<br>• Cap the bottle and intermittently swirl the solution and inverted gently to disperse the particles for 20 minutes<br>• Add 38 or 75 mL of Ora-Blend to disintegrated tablets respectively<br>• Invert the solution 20 times for final suspension<br>◦ 60 mg tablets (total volume: 50 mL or 100 mL)<br>• Place 4 or 8, 60 mg tablets, in 4 oz PET amber vial<br>• Add 12 or 24 mL of water to disintegrate tablets (about 20 minutes)<br>• Cap the bottle and intermittently swirl the solution and inverted gently to disperse the particles for 20 minutes<br>• Add 36 or 72 mL of Ora-Blend to disintegrated tablets respectively | | | |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | • Invert the solution 20 times for final suspension<br>• *Note: Selinexor tablets should NOT be crushed (increased risk of dermatologic toxicity [eg rash] from exposure to powder)*<br>• *Note: Do not shake suspension due to substantial foaming (risk of impacting dose uniformity). If shaken/foaming occurs, allow 12-24 hours for foaming to subside prior to administering patient dose. Gentle and repeated inverting of capped bottle recommended for resuspension.* | | | |
| Selpercatinib[C162,163] | • Administration with natural water, pureed/juiced carrots, and regular unflavored whole milk:<br>◦ Heat the liquid until warm<br>◦ Add 10-15 mL into a glass or plastic cup with a smooth inside<br>◦ Add 1 dose of unopened capsules and stir with wooden utensil until the outer shell dissolves<br>◦ Stir well, may add more warmed liquid if needed<br>◦ Dose must be given within 30 minutes after prepared. May add warm liquid to scrape off remaining medication stuck to the cup<br>◦ Do not mix with acidic drinks as it causes an unpleasant taste<br>◦ Avoid preparing with metal cups/ utensils as the medication can stick to it<br>• Preparation through NG or G-tube:<br>◦ Add 10-15 of heated, warm water (MUST BE WATER) to a glass or plastic cup with a smooth inner surface<br>◦ Add unopened capsules and stir with wooden or plastic utensil until capsule shells fully dissolve and no medication is stuck on the surfaces, may add more water as needed | • Intended for immediate use | • Avoid concomitant use of a PPI (if possible)<br>• Administer with food if taken with a PPI<br>• Separate from antacids; at least 2 hours before or after an antacid<br>• Administer at least 2 hours before or 10 hours after an H2RA | – |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | ▫ Draw up contents into syringe and give within 30 minutes after preparing<br>▫ Recommended to rinse FT with water before administration. Also recommended to rinse FT after with a minimum of 20 mL, but no more than 30 mL of water to ensure the full dose was given<br>• Do NOT open capsules, even when preparing extemporaneously with food | | | |
| Selumetinib[C164-167] | • No data | • No data | • Take on empty stomach, ≥1 hour before or 2 hours after a meal or snack | • Comparison of free base oral suspension and hyd-sulfate capsule showed 2-fold AUC and 2.5-fold Cmax in capsule compared to free base suspension<br>• Capsules are not permeability or dissolution limited. Tmax was quickly reached after 1-2 hours across pediatrics, adult, and healthy patients<br>• Absolute oral bioavailability after a single dose was about 62% in healthy adult<br>• Phase 2 open-label trial found similar outcomes between groups receiving selumetinib free base suspension and capecitabine<br>• Phase 1 clinical trial evaluated patients receiving capsule and free base suspension showed favorable PK and safety/tolerability with the capsule<br>• Formulation contains hypromellose |
| Sonidegib[LC168169] | • No data | • No data | • Administer at least 1 hour before or 2 hours after meals | • The population PK analysis suggests that geometric mean sonidegib steady-state AUC is 34% lower in cancer patients taking an ARA with a sonidegib dose of 200 mg compared to patients not concomitantly taking an ARA<br>• The mass balance study suggests that <10% of the dose is absorbed |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| Sorafenib[6,85] | • Place 2 tablets (200 mg each) into a glass with 60 mL of water<br>• Wait 5 minutes<br>• Stir until the tablets are completely dissolved in a fine particular suspension<br>• The suspension is ready for consumption after 10 minutes<br>• Rinse the glass several times, with a total of 6 oz of water, to ensure consumption of the full dose<br>• *Note: The tablet coating may form a thin film which has no bearing on the accuracy of dosing* | • Intended for immediate use | • Administer at least 1 hour before or 2 hours after meals<br>• Caution concomitant use with a PPI | — |
| Sunitinib[86,6] | Method 1:<br>• Mix the contents of capsules (50 mg each) with 15 mL (10 mg/mL) of a 1:1 mixture of Ora-Plus:Ora-Sweet solution<br>• Transfer to an amber plastic bottle<br>Method 2:<br>• Capsule contents (max 750 mg) may be mixed with 75 mL of apple juice<br>Method 3:<br>• Empty contents of the capsule into a container<br>• Add 5 mL of normal saline and swirl for 60 seconds<br>• Attach barrel of a syringe to G-tube connector and then pour suspension into the syringe to administer<br>• Rinse the container with 5 mL of normal saline twice, administering each rinse via G tube<br>• Flush syringe and tube with 5 mL of water twice after rinses | Method 1:<br>• Stable for 60 days at room temperature and 4°C<br>Method 2:<br>• Must be consumed/administered within 2 hours (intended for immediate use)<br>Method 3:<br>• Intended for immediate use | • None | — |
| Talazoparib[2,43,170] | • Unpublished study regarding extemporaneous suspension preparation for FT administration:<br>  ○ Step 1: Place two drinking glasses (such as juice glasses) on the work surface. Mark the glasses as Glass A and Glass B using the marking pen | • Intended for immediate use (within 60 minutes)<br>• Stable up to 2 hours at room temperature | • None | • HPMC capsule |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | ○ Step 2: Obtain 3 20-mL syringes. Mark them as Syringe 1, 2, and 3 using the marking pen<br>○ Step 3: Transfer 1 Cup (8 oz) of room temperature water to Glass A. Bottled water should be used. The water in Glass A will be used for rinsing<br>○ Step 4: Using Syringe 1, draw up water from Glass A to the 15 mL mark. Expel any excess air by pointing the syringe upward and away from people, and slowly depressing the syringe plunger. Stop before expelling liquid. Cap the syringe with the syringe cap and set aside<br>○ Step 5: Repeat step 4 with Syringe 2. There should be two syringes, each with 15 mL of water in them. Syringe 1 will be a prerinse of the FT and Syringe 2 will be used to flush the tube immediately after administration of the dose<br>○ Step 6: Remove the plunger of Syringe 3 and set it on a clean working surface<br>○ Step 7: Transfer the correct number and strength of capsules into the open Syringe 3 barrel. Return the plunger until it is just touching the capsules being careful not to crush the capsules<br>○ Step 8: Draw up water from Glass A into Syringe 3, until the plunger reaches the 15 mL line<br>○ Step 9: Invert Syringe 3 (nozzle up), cover the tip with a syringe cap and leave to stand for 10 minutes, or until all the capsules have disintegrated. The syringe may be placed in the second (empty) drink vessel for the 10 minutes duration | | | |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | ◦ Step 10: After 10 minutes, grasp the barrel in fist with the thumb tightly over the cap. Gently mix with inversions continuously for a minimum of 3 minutes. The capsule(s) should be completely disintegrated<br>◦ Step 11: Take Syringe 1 (prerinsing syringe) which was prepared in Step 4 and remove the syringe cap. Remove the FT port cap, and firmly attach Syringe 1 tightly to the FT port. Administer the Syringe 1 contents completely to the FT. Remove Syringe 1 from the FT port and set aside<br>◦ Step 12: Gently invert Syringe 3 containing the active dose several times to ensure that the suspension is well mixed. Remove the syringe cap and firmly attach Syringe 3 tightly to the feeding port. With the syringe tip angled upward, administer the contents to the FT<br>◦ Step 13: Remove Syringe 3 from the FT port, replace the syringe cap and set aside. Immediately take Syringe 2 (post-dose syringe) which was prepared in step 5 and remove the syringe cap. Firmly attach Syringe 2 tightly to the FT port. With the syringe tip angled upward, administer the contents to the FT. This step should be completed within 3 minutes from performing Step 12. Remove Syringe 2 from the FT port, replace the syringe cap and set aside<br>◦ Step 14: Remove the cap from Syringe 3 and pull up water from Glass A until it just reaches the 15 mL mark. Replace the cap on Syringe 3; invert three times to mix the contents with thumb tightly over cap. Remove the syringe cap and firmly attach | | | |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | Syringe 3 tightly to the FT port. Administer the contents to the FT<br>*Note: it is normal for a trace amount of powder to remain inside the syringe. Remove Syringe 3 from the FT port, replace the syringe cap and set aside*<br>• Step 15: Using Syringe 2, draw up water from Glass A to the 15 mL mark. Firmly attach Syringe 2 tightly to the FT port. Administer the Syringe 2 contents completely to the FT as a final rinse of the tubing. Remove Syringe 2 from the FT port and replace the port cap to the FT<br>• Step 16: Clean all materials carefully and dispose of all consumables as directed. Utilize appropriate disposal procedures | | | |
| Tamoxifen[5,171] | • Place 2 tablets (10 mg each) into 40 mL of water and let stand.<br>• Stir until the tablets are completely disintegrated and a fine particular suspension is formed<br>• Rinse the glass with adequate water to ensure administration of the full dose<br>• *Note: dispersion of 10 mg tablets is 2-5 minutes* | • Intended for immediate administration | • None | • Rate and extent of absorption are bioequivalent between tablet and oral solution when administered under fasting conditions<br>• Commercial suspension available |
| Tazemetostat[172] | • No data | • No data | • None | • Formulation contains hypromellose and hydroxypropyl cellulose |
| Temozolomide[b,C5,173] | Method 1:<br>• Mix the contents of 10 capsules (100 mg each) and 500 mg of povidone K-30 powder in a glass mortar<br>• Add 25 mg anhydrous citric acid dissolved in 1.5 mL purified water and mix to a uniform paste<br>• Mix while adding 50 mL Ora-Plus in incremental proportions.<br>• Transfer to an amber plastic bottle<br>• Rinse mortar 4 times with small portions of either Ora-Sweet or Ora-Sweet SF, and add quantity of Ora-Sweet or Ora- | Method 1:<br>• Stable for 7 days at room temperature<br>• Stable for 60 days under refrigeration<br>Method 2:<br>• All 10 mg/mL formulations evaluated suggest BUD of 30 days stored at 4°C<br>*Note: crystals were observed in all samples* | • Administer consistently either with or without meals (absorption affected by food)<br>• Administration at bedtime and/or on an empty stomach may reduce nausea and vomiting | • Povidone K-30 is essential to prevent crystal growth and to improve solubility/stability with extended shelf-life<br>• Suspension may have pinkish color when refrigerated or may appear darker when stored at room temperature |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | Sweet SF sufficient to make 100 mL (10 mg/mL)<br>Method 2:<br>• Reference describes 10 mg/mL suspension using several formulations consisting of Oral Mix-SF and Ora-Blend-SF with different amounts of PK-30 and citric acid | | | |
| Thalidomide[b174] | • Empty the contents of 12 capsules (100 mg) into a glass mortar<br>• Add small portions of the vehicle (1:1 mixture of Ora-Sweet and Ora-Plus) and mix to a uniform paste<br>• Mix while adding the vehicle in incremental proportions to almost 60 mL<br>• Transfer to an amber calibrated bottle<br>• Rinse mortar with vehicle, and add quantity of vehicle sufficient to make 60 mL (20 mg/mL) | • Stable for 35 days under refrigeration | • Administration at bedtime is preferred<br>• Administer at least 1 hour after meals | • Protect from light |
| Thioguanine[b175] | Method 1:<br>• Crush 15 tablets (40 mg each) in a mortar and reduce to a fine powder<br>• Add 5 mL of Ora-Plus in incremental proportions and mix to a uniform paste<br>• Transfer to a graduated amber glass bottle, rinse mortar with Ora-Sweet and add sufficient quantity to make 30 mL (20 mg/mL)<br>Method 2:<br>• Crush 15 tablets (40 mg each) in a mortar and reduce to a fine powder<br>• Add 3.33 mL of methylcellulose 1% in incremental proportions and mix to a uniform paste<br>• Transfer to a graduated amber glass bottle, rinse mortar with simple syrup and add sufficient quantity to make 30 mL | • Stable for 63 days at room temperature (both methods) | • None | – |
| Topotecan[b176] | • Reconstituted topotecan solution for injection (1 mg/mL concentration) may be mixed with up to 30 mL of acidic fruit juice (eg, apple, orange, grape) | • Intended for immediate use | • None | – |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| Toremifene[177] | • No data | • No data | • None | • Reported to be well-absorbed<br>• Tablet contains copovidone |
| Trametinib[b,60,62,178] | • Case report of 35-year-old BRAF (+) metastatic melanoma, patient was given dabrafenib and trametinib through suspension.<br>○ Dabrafenib was dispersed through 1.5% carboxymethylcellose (cannot be dispersed in water) and trametinib was dispersed in water and both were immediately given through G-tube | • No data | • Administer at least 1 hour before or 2 hours after meals | • Tablet coating contains hypromellose<br>• Ongoing phase IV trial using trametinib powder for oral solution (0.05 mg/mL) (no information provided for administration or preparation instructions) |
| Tretinoin[b,179-182] | Method 1:<br>• Cutting open capsules and aspirating the highly viscous contents via a 19-gauge needle into a syringe that had been primed with 1 mL of soya bean oil<br>• The capsules retained approximately half of the original volume of drug. Small amounts of soya bean oil were then mixed with the capsule contents, which resulted in a reduction in viscosity and allowed for more of the ATRA to be drawn up into the syringe<br>• The remaining liquid was flushed out with fresh soya bean oil and stirred until uniform, placed in a glass syringe<br>Method 2:<br>• Begin with 100 °F tap water in beaker-water bath. (Use thermometer)<br>• Turn magnetic stirrer/hot plate on lowest heat setting<br>• Place the 4 tretinoin capsules into a 20 mL amber syringe and QS to 10 mL with sterile water for injection<br>• Heat syringe in water bath until gelatin capsule has dissolved (approximately 30-40 minutes) | Method 1:<br>• Administer within 24 hours of preparation<br>Method 2:<br>• Intended for immediate use | • Administer with a meal | • After 14 days of daily NG-tube administration, ATRA plasma levels rose from 1.4 to 2.2 μmol following administration of a dose<br>• Tretinoin has also been administered sublingually by squeezing the capsule contents beneath the tongue<br>• Low plasma concentrations have been reported when tretinoin has been administered through a FT, although patient-specific impaired absorption or a lack of excipient (eg, soybean oil) may have been a contributing factor |
| Trifluridine/tipiracil[b,183,184] | • No data | • No data | • Administer within 1 hour of completing meals | • The mean relative bioavailability of TAS-102 tablets compared to oral solution was 100% for trifluridine and 96% for tipiracil |

(Continues)

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

TABLE 3 (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | | | | • A high-fat, high-calorie meal decreased trifluridine Cmax, tipiracil Cmax and AUC by approximately 40%, but did not change trifluridine AUC compared to those in a fasting state in cancer patients taking single dose of 35 mg/m$^2$ TAS-102<br>• Tablet contains hypromellose |
| Tucatinib[185,186] | • No data | • No data | • None | • Administration after fatty meal increased AUC 1.5-fold and extended Tmax to 4 hours<br>• Study compared administration 300 mg tucatinib PO in 4 formulations: (1) capsules (PIC), (2) micronized PIC, (3) aqueous suspension, (4) 20% Captisol/apple juice solution<br>• Relative AUC higher with micronized PIC and aqueous suspension; lower with 20% Captisol/apple juice solution compared to capsule (PIC) |
| Vandetanib[f,b187] | • A dispersion can be made with 2 oz of noncarbonated water only<br>• Stir for approximately 10 minutes (will not fully dissolve)<br>• To ensure full dose is received, rinse glass again with 4 oz of noncarbonated water and administer contents | • Intended for immediate use | • None | • Tablet coating contains hypromellose 2910 |
| Vemurafenib[b,c6,55,188-191] | • Dissolve capsule in 15 mL of water and remove cellulose precipitate after dissolution<br>• Flush with 30 mL of water per every capsule given | • Intended for immediate use | • None | • Case reports/series using NGT or oral administration of dissolved tablet (one case describes holding tube feeds for at least 60 minutes after administration)<br>• One case report experienced complications with tube patency after administration<br>• Tablet contains hypromellose acetate succinate, hydroxypropyl cellulose |
| Venetoclax[f,c192-194] | • No data from literature or manufacturer—administered via aqueous median per OHSU MUP | • No data | • Administer with a meal | • Manufacturer reports that similar tablet formulations exhibited as much |

## EXTEMPORANEOUS ORAL LIQUID PREPARATION OF ORAL ONCOLOGY DRUGS, STABILITY AND DRUG PROPERTIES (CONT)

**TABLE 3** (Continued)

| Drug | Extemporaneous oral liquid formula or instructions for administration via feeding tube | Storage, stability, and label information | Administration instructions in regard to meals/intake | Comments/notes |
|---|---|---|---|---|
| | | | | as 50% reduced plasma concentration when crushed<br>• When administered after a standard breakfast, single doses of 50 mg film-coated and uncoated tablets were found to be bioequivalent |
| Vismodegib[C,b6,22] | • Dilute capsule in 50 mL of warm water<br>• Other specific instructions for opening capsules not reported | • Intended for immediate use | • None | • Phase I pharmacokinetic study found similar drug activity with use of suspension for PEG administration<br>• Case reports of opening capsule contents for administration with a soft diet |
| Vorinostat[b5] | • Add 20 mL Ora-Plus into a glass bottle (≥4 oz)<br>• Add the contents of 20 capsules (100 mg each) and shake thoroughly to disperse (may take up to 3 minutes)<br>• Add 20 mL Ora-Sweet and shake to disperse (50 mg/mL) | • Stable for 14 days at room temperature. | • Administer with a meal | — |
| Zanubrutinib[C195,196] | • No data | • No data | • None | • Coadministration with low-fat meal increased Cmax by 51%, 3% with high-fat meal (PI recommends taking without regard to food) |

Abbreviations: AE, adverse events; ARA, acid reducing agent; AUC, area under the curve; C, capsule; Cmax, maximum concentration; f, film-coated, specific ingredients that may influence suspension appearance/consistency noted specifically in comments (ie, hypromellose); FT, feeding tube; GI, gastrointestinal; GT, gastrostomy tube; H2RA, histamine-2 receptor antagonist; HPMC, hydroxypropyl methylcellulose; I, insoluble in water; IV, intravenous; MTD, maximum tolerated dose; MUP, medication use process; NGT, nasogastric tube; OHSU, Oregon Health & Science University; OGT, orogastric tube; PEG, percutaneous endoscopic gastrostomy; PI, package insert; PK, pharmacokinetic; PPI, proton pump inhibitor; SF, sugar-free; Tmax, time to max concentration; USP 795, United States Pharmacopeia chapter <795>.

[a]Available information for extemporaneous formulations or alternative routes of administration for oral oncology drugs gathered from literature (published guidance, tertiary resources, case reports, etc) and unpublished resources (ie, manufacturer drug information resources). Case reports from institutional experience at OHSU are included in the table to contribute to a growing repository of reports currently published for specific agents. Drugs without any available guidance (from literature, unpublished/manufacturer data, institutional experience) are noted to have "No data."

[b]Published or tertiary information available for extemporaneous compounding or administration via feeding tube.

[c]Evidence/case reports of administration via FT or extemporaneous compounding from study retrospective review at OHSU.

**Reference:**

Cohen J, Lee C, Markham R, Szerwo J, Roska M, Bubalo J. Medication use process and assessment of extemporaneous compounding and alternative routes of administration of oral oncology drugs: Guidance for clinical and oncology pharmacists. J Am Coll Clin Pharm. 2022; 5(11): 1176-1228. doi:10.1002/jac5.1698

**Appendix 8**

## HANDLING OF BODY WASTE AFTER HAZARDOUS DRUG ADMINISTRATION

| Drug | Urine | Excretion rate | Faeces | Excretion rate | Other |
|---|---|---|---|---|---|
| Amsacrine | 3 days | 20% in 1st 8hrs | 2 days | | |
| Asparaginase | Trace amounts | | | | |
| Bleomycin | 3 days | Up to 68% in 1st 24hrs | | | |
| Busulphan | 12–24hrs | | Trace amounts | | |
| Capecitabine | 1 day | | | | |
| Carboplatin | 1–2 days | 60–80% in 1st 24hrs | | | |
| Carmustine | 4 days | 60–70% as metabolites | | 1% of dose | 10% as CO2 |
| Chlorambucil | 2 days | | | | |
| Cisplatin | 7 days | | | | |
| Cladribine | 3 days | | | | |
| Cyclophosphamide | 3 days (IV) | 25% unchanged drug in 1st 48hrs, total of 62% over 48hrs | 5 days after PO dose | 4% excreted after IV | In sweat and saliva for 72hrs |
| Cytarabine | 1 day | | | | |
| Dacarbazine | 6hrs | | | | |
| Dactinomycin | 5 days | 20% in 1st 24 hrs | 7 days | | |
| Daunorubicin | 2 days | 20% in 1st 24 hrs | 7 days | | 20% excreted via gallbladder in 1st 24hrs |
| Docetaxel | 7 days | | 7 days | 80% in 1st 48hrs | |
| Doxorubicin | 6 days | | 7 days | | Bile 5 days |
| Doxorubicin liposomal | 5 days | | 7 days | | |
| Epirubicin | 7 days | | 5 days | | |
| Etopophos | 5 days | | | | |

| Drug | Urine | Excretion rate | Faeces | Excretion rate | Other |
|---|---|---|---|---|---|
| Etoposide | 4 days | 40–60% mainly unchanged | 7 days | 15% excreted in faeces | |
| Fludarabine | 2 days | Bolus: 60% in 1st 24hrs<br>Infusion: 40% metabolised in 24hrs and 60% in 72hrs | | | |
| Fluorouracil | 2 days | Bolus: 15% unchanged in 1st 24hrs<br>Infusion: 4% unchanged over 24hrs | 5 days | | |
| Fotemustine | 4 days | 30–40% in 1st 24 hrs | | 50% excreted in faeces | |
| Gemcitabine | 7 days | Almost complete elimination in form of metabolites in 24hrs | | 1% excreted in faeces | |
| Hydroxyurea | 1 day | 50–80% in 24hrs | | | |
| Idarubicin | 4 days | | 7 days | | |
| Ifosfamide | 2 days | 62% unchanged with another 20% as metabolites | | | |
| Imatinab mesylate | 7 days | | 7 days | | |
| Irinotecan | 2 days | | | | |
| Liposomal Doxorubicin | Unknown | Plasma clearance slower than for Doxorubicin | | | |
| Lomustine | 1 day | 66% in 1st 24 hrs | | | |
| Melphalan | 2 days | 28% in 1st 24hrs after PO, 56% in 1st 24hrs after IV | 7 days | 20–50% after PO administration | |
| Mercaptopurine | 2–3 days | 50% in 1st 24 hrs | 5 days | | |
| Methotrexate | 3 days | Majority in 1st 8 hours,<br>low dose: 40–50%,<br>high dose: up to 90% in 48hrs | 7 days | 9% after IV | |
| Mitomycin | 1 day | 10% as active drug | | | Small amount in bile |
| Mitoxantrone | 6 days | 6.5% unchanged drug, 3.6% metabolised drug | 7 days | 18% over 5 days | |
| Nimustine | 4 days | | | | |
| Oxaliplatin | 3 days | 40–50% of the dose in 1st 24 hrs | | | |
| Paclitaxel | 1 day | 13% unchanged drug | 5 days | | |

| Drug | Urine | Excretion rate | Faeces | Excretion rate | Other |
|---|---|---|---|---|---|
| Pemetrexed | 3 days | 70–90% of dose unchanged in urine in 1st 24 hrs | | | |
| Procarbazine | 2 days | 5% as unchanged drug and 70% as metabolites in 1st 24 hrs | | Good absorption from GIT, 12% of dose eliminated from GIT in 4 days | |
| Raltitrexed | 8 days | | | | |
| Streptozocin | 3 days | | | | |
| Temozolomide | Unknown | 10% of dose in 1st 24 hrs | | | |
| Teniposide | 5 days | 10% of dose in 1st 24 hrs | 2 days | | |
| Thioguanine | 1 day | 85% unchanged and metabolites | | | |
| Thiotepa | 3 days | 60% as metabolites in 1st 24 hrs | | | |
| Topotecan | 2 days | | | | |
| Vinblastine | 4 days | | 7 days | | |
| Vincristine | 4 days | | 7 days | | |
| Vindesine | 4 days | | 7 days | | |
| Vinorelbine | 4 days | | 7 days | | |

*This list contains cytotoxic drugs currently used. However this listing is not exhaustive. The information provided is current at the time of writing the guidelines. When any new cytotoxic drug enters the workplace, it must be listed and risks be managed.

**Disclaimer:** The compilation of information shown here is the data derived from the references cited below. The information shown on this site is not complete, current, accurate or free from error. For current and complete information contact the appropriate agency or refer the current medical journals.

Reference:

Cass Y & Musgrave CF, August 1992, Am J Hosp Pharmacy, vol 49, pp 1957-1958, *Guidelines for the safe handling excreta contaminated by cytotoxic agents.*

Oncology Nursing Society, 2003, p28, *Safe handling of hazardous drugs.*

Gullo Shirley, 1995, *Safe handling of antineoplastic drugs: Translating the recommendations into practice,* Oncology Nursing Forum, vol 22 no 3, pp517-525.

Quapos 3, Quality Standard for the Oncology Pharmacy Service (English translation), published by the Institute for Applied Healthcare Sciences for the German Society of Oncology Pharmacy Jan 2003 – http://www.esop.li/downloads/library/Quapos-en-with-commentary.pdf

Workplace Health and Safety Queensland. October 2014. Guide for handling cytotoxic drugs and related waste.

**Reference:** NSW Government. CYTOTOXIC DRUGS AND RELATED WASTE – RISK MANAGEMENT (JULY 2017)

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