# NATIONAL POLICY ON CHEMOTHERAPY SAFETY (CHEMOSAFE)

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# FOREWORD

Cancer is one of the leading causes of morbidity and mortality worldwide. According to the World Health Organization (WHO), the number of cancer patients is expected to double in the next two decades with a commensurate number of healthcare workers required to care for them. Sequel to increased awareness of cancer across the country, improved diagnostic capacity and documentation, there has been a progressive increase in the number of cancer cases in Nigeria. The majority of these cancers are treated with chemotherapy. Other treatment options available in Nigeria include Surgery and Radiotherapy.

The Federal Ministry of Health is committed to making all forms of cancer treatment more accessible and affordable in Nigeria. This underscores the collaboration currently in place to increase access to quality cancer care services at markedly reduced cost across the country. The Ministry is also paying particular attention towards improving access to radiotherapy services as well as improved expertise for surgical interventions nationwide.

Cancer chemotherapy refers to use of medicines that destroy or kill cancerous cells including biologics and other immune modulators in the treatment of different types of cancers. Studies have shown that Similar to the effects of radiation, chemotherapeutic agents also affect healthy normal cells of the patients as well as health workers and other people who are exposed to them. The effects may vary depending on the type of medicine, dose, duration of exposure and other underlying conditions and states such as pregnancy.

This National Chemotherapy Safety (ChemoSafe) Policy was developed to provide actionable direction in the implementation of strategies to improve the safe handling and administration of chemotherapy in cancer treatment centres in Nigeria. This policy document prescribes stepwise approach that starts when chemotherapy agents are received by the facility and considers every potential point of exposure to hazardous medicines, including transportation within the facility, compounding, administration, home care, housekeeping and waste collection and disposal. At each point where patients and health workers may be exposed to chemotherapy, steps are taken to reduce the potential for harm, including adopting safe work practices, improving infrastructure, and using personal protective equipment (PPE).

Several hospitals, states and even other countries may have initiated some safety protocols in addressing the potential harm of chemotherapy, this policy is the first of its kind in Africa, where government is taking the lead in ensuring systematic and documented guidelines in

protecting our environment, health workers and even patients from the adverse effects of cytotoxic medicines. It is my hope that all the oncology stakeholders at all levels will find this policy very useful in their practice.

I therefore, recommend this National Policy on Chemotherapy Safety to students, teachers, academia, governmental and non-governmental organizations and stakeholders in the various oncology subspecialties as it will add an immeasurable value to knowledge, work, safety and policy making.

**Dr. E. Osagie Ehanire,** MD, FWACS
Honourable Minister of Health
June 2021

# ACKNOWLEDGEMENT

The Federal Ministry of Health highly appreciates the unrelenting efforts of all the stakeholders in the oncology space in Nigeria. The enthusiasm and passion of the oncology experts despite all odds have continued to give hope to the cancer patients across the country. This policy was developed to protect both the patients and the practitioners from the adverse effects of chemotherapy.

The inestimable contributions of all the oncology stakeholders, pharmaceutical companies, governmental and non-governmental organizations is well acknowledged and appreciated. Specifically, the support of the American Cancer Society, the Clinton Health Access Initiative and Pharmasymbiosis is too obvious to be ignored.

The commitment of the entire staff of the National Cancer Control Programme and the Department of Food and Drugs Services of the Federal Ministry of Health in the development of this policy is also appreciated.

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# ACRONYMS / ABBREVIATIONS

| | |
|---|---|
| **ACS** | American Cancer Society |
| **API** | Active Pharmaceutical Ingredient |
| **BSC** | Biological Safety Cabinet |
| **CAP** | Chemotherapy Access Partnership |
| **CHAI** | Clinton Health Access Initiative |
| **CNS** | Central Nervous System |
| **DNA** | Deoxyribonucleic Acid |
| **EGFR** | Epithelial Growth Factor Receptor |
| **FMOH** | Federal Ministry of Health |
| **GnRH** | Gonadotropin-Releasing Hormone |
| **HEPA** | High-Efficiency Particulate Air "or Arrestor" |
| **HVAC** | Heating, Ventilation and Air-conditioning |
| **IV** | Intravenous |
| **NIOSH** | National Institute of Occupational Safety and Health |
| **NSCR** | Nigeria National System of Cancer Registries |
| **PPE** | Personal Protective Equipment |
| **TKI** | Tyrosine Kinase Inhibitor |
| **VTE** | Venous Thromboembolism |
| **WHO** | World Health Organization |

# 1.0 BACKGROUND

## 1.1 Introduction

The current treatment modalities for cancers include surgery, radiotherapy, chemotherapy and targeted therapy, gene therapy and stem cell transplantation. [1] These modalities can be used singly or in combination depending on the type of cancer and the stage at diagnosis. The most widely and readily available modality in Nigeria is chemotherapy. This has been further expanded through the chemotherapy access partnership (CAP) programme of the Federal Ministry of Health (FMOH), American Cancer Society (ACS) and the Clinton Health Access Initiative (CHAI). [1] [2]

The term Chemotherapy, as used in this document refers to systemic anti-cancer agents that destroy or kill cancerous cells including biologics and other immune modulators. A wide variety of chemotherapeutic medicines are available and may be delivered by various routes (Intravenous, intramuscular, intrathecal, intraperitoneal, orally, etc) depending on individual cancer cases. Similar to the effects of radiation, chemotherapeutic agents also affect healthy normal cells of the patients as well as health workers and other people who are exposed to them. The effects may vary depending on the type of medicine, dose, duration of exposure and other underlying conditions and states such as pregnancy. [3]

The concept of chemotherapy safety also known as 'ChemoSafe' was developed to improve the safe handling and administration of chemotherapy in cancer treatment centres. It uses a "life-cycle" approach that starts when chemotherapy agents are received by the facility and considers every potential point of exposure to hazardous medicines, including transport within the facility, compounding, administration, home care, housekeeping and waste collection and disposal. At each point where patients and health workers may be exposed to chemotherapy, steps are taken to reduce the potential for harm, including adopting safe work practices, improving infrastructure, and using personal protective equipment (PPE)

According to the World Health Organization (WHO), the number of cancer patients is expected to double in the next two decades with a commensurate number of healthcare workers required to care for them [3]. Sequel to increased awareness of cancer across the country, improved diagnostic capacity and documentation, there has been a progressive increase in the number of cancer cases in Nigeria. According to the National System of Cancer Registries (NSCR), a total of 13,312 cancer cases (Age Standardized incidence Ratio = 53.7 per 100,000 per year) were documented by the population-based cancer Registries (PBCR) between 2009 and 2016. Of these cases, 8051 (60.5%; ASR = 66.5 per 100,000 per year) were reported in females and 5,261 (39.5%; ASR = 40.9 per 100,000 per year) were reported in males. [4]

The distribution of cancers by year within eight years (2009-2016) is as in figure 1 below.

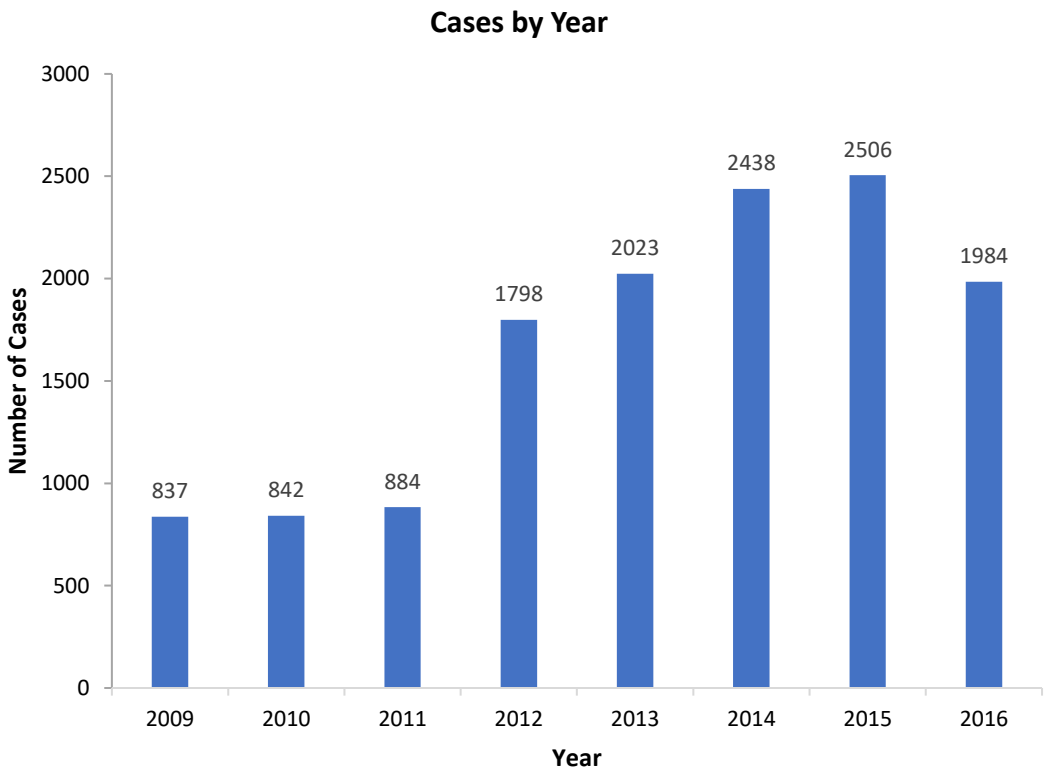


*Figure 1: Distribution of Cancer Cases by Year (2009 - 2016)*[1]

## 1.2 Rationale for ChemoSafe Policy

Currently, there are no organized chemotherapeutic safety activities in our hospitals where these cancer cases are treated.

The majority of these cancers are treated with conventional cytotoxic medicines without an institutionalized guideline on chemotherapy safety. This may have resulted in unnecessary exposure of patients and health care workers and other people to the negative effects of these medicines. There is also the paucity of data on the hazards of chemotherapy among health workers in Nigeria.

However, available literature has shown significant effects of chemotherapy agents on health care professionals which makes it imperative that practitioners become knowledgeable and adhere to these safety measures regarding the handling of these medicines. According to the National Institute for Occupational Safety and Health (NIOSH), close to 8 million health care workers are potentially exposed to hazardous effects of antineoplastic drugs. [3] [5]

The risk to health care professionals from handling a hazardous drug stems from its inherent toxicity and the extent to which workers are exposed to the medicines. The primary routes of exposure are by direct skin contact and through inhalation of aerosolized medicine products.

[1] Adapted from Cancer in Nigeria (2009-2016- NSCR)

Another potential exposure occurs during the disposal of the chemotherapeutic agents, disposal of the items used in medicine preparation and administration, and when caring for patients who have received these medicines. [6] [10]

**Definition of medicine as Hazard Based on Pharmacology/Toxicology**

The following factors are considered in designating medicines as hazardous:

i. Therapeutic Category 10:00 (Antineoplastic Agent) in the American Hospital Formulary Service Drug Information.
ii. Manufacturer's suggestion of the use of special isolation or other techniques in its handling, administration, or disposal.
iii. The drug is known to be a human mutagen, carcinogen, teratogen, or reproductive toxicant.
iv. The drug is known to be carcinogenic or teratogenic in animals or mutagenic in multiple bacterial systems or animals.
v. The drug is known to be acutely toxic to an organ/ system. [6]

**Mechanism of Action of cytotoxic medicine**

While most commonly used cytotoxic medicines are members of several chemically unrelated classes of agents, most of those used for anti-cancer chemotherapy exert their action by binding to cellular macromolecules, including deoxyribonucleic acid (DNA), or through disruption of DNA and protein synthesis. The potential fate of a cell exposed to cytotoxic agents includes transformation to malignant potential, mutation and/or cell death. However, through repair, an affected normal cell may remain. It is important to note that most anti-cancer medicines do not distinguish between normal and cancerous cells, thus normal cells are often affected during treatment or exposure. [6]

It is difficult to set safe levels of exposure to cytotoxic medicines based on current scientific information because the degree of absorption that takes place during work, and the significance of early biological effects on each individual, are difficult to assess and may vary depending on the drug. However, several lines of evidence support the toxic potential of these medicines if handled improperly. Also, most health care workers are exposed to multiple agents during any work shift, yielding a "mixed exposure" scenario. Therefore, it is essential to minimize exposure to all cytotoxic medicines. [6]

Some effects of cytotoxic medicines that have been documented include:

i. Cytogenetic effects including chromosomal aberrations.
ii. Reproductive effects which include congenital malformations and spontaneous abortions. Male mediated reproductive effects have also been documented. Besides, the secretion of cytotoxic medicines in the breast milk of treated patients suggests an additional concern for exposed and pregnant workers who plan to breastfeed.
iii. There is potential for cancer development in exposed health care workers similar to the risk of therapy-related malignancies (such as leukaemia observed in treated patients),

iv. Apart from reproductive concerns or cancer development, it is important to note that acute exposure effects, such as nausea and vomiting, skin rashes, and hair loss, have been reported in health care workers who were exposed. Symptoms such as light-headedness, dizziness, nausea, headache, and allergic reactions have also been reported in employees who prepared and administered antineoplastic medicines in unventilated areas. Anti-cancer medicines are known to be toxic to the skin and mucous membranes, including the cornea in occupational settings. [6]

Although the absolute risk cannot be eliminated, much can be done to reduce the relative risks associated with the handling of chemotherapy agents. Health care professionals who handle chemotherapy agents are expected to be well informed of the potential health hazards, be familiar with safe handling and disposal of these agents, utilize appropriate protective equipment and ventilation cabinets as well as strict adherence to available written policies, procedures and guidelines. Patients who are to receive chemotherapy should be properly counselled on the hazards of these medicines and informed consent obtained.

This policy document is intended to facilitate the standardization of institutional practice guidelines for the safe handling of chemotherapy agents in both private and public health institutions in Nigeria. Strict adherence to the provisions of this policy will assist in minimizing unnecessary exposure and maximizing safety.

## 1.3 Goal and Objectives

### *1.3.1 Goal*

The goal of this policy is to institutionalize chemotherapeutic safety activities in Nigeria by providing a clear framework that would guide professionals and institutions that are involved in cancer management in Nigeria to minimize hazards attributable to handling chemotherapy.

### *1.3.2 Objectives*

This policy is aimed at achieving the following objectives:

i. To standardise the safe handling of chemotherapeutic agents in cancer treatment centres.
ii. To provide comprehensive instructions on the safety measures that would protect oncology practitioners, patients, and other hospital users from the hazards of chemotherapy agents.
iii. To improve the knowledge base of health workers on the safe use of chemotherapy in cancer management.
iv. To define clear cut responsibilities of various players in the cancer space in the use of chemotherapy in cancer care.

## 1.4 Scope of the Policy

This policy covers 7 thematic areas which include:

i. The Environment
ii. Supply Chain

iii. Patient Care
iv. Practitioner's Responsibilities
v. Capacity Building
vi. Monitoring & Evaluation
vii. Funding

## 1.5 Policy Development Process

The process of developing this policy involved consultation with relevant documents and stakeholders to ensure that it is widely accepted and conforms to the international best standard. A zero draft of this policy was developed by a team of experts from the National Cancer Control Programme and the Department of Food and Drug Services of the Federal Ministry of Health. This was reviewed by the National Technical Working Group on cancer chemotherapy and a first draft was produced and presented to a forum of cancer stakeholders to obtain their input and buy-in. The final draft policy was approved by the Honourable Minister of Health as a National Policy on Chemotherapy Safety (ChemoSafe Policy).

## 1.6 Updating

This policy will be reviewed every five years and updated as required to reflect evidence-based changes and new trends in the practice of oncology in Nigeria.

# 2.0 POLICY FRAMEWORK ELEMENTS / THEMATIC AREAS

## 2.1 The Environment

Healthcare workers may be occupationally exposed to cytotoxic medicines in many different types of settings. Preparation of cytotoxic agents can take place in pharmacies (hospital, retail, mail-order, or compounding) or clinic settings. Administration of these agents occur in hospital inpatient and outpatient units, operating rooms, interventional radiology departments, respiratory therapy departments, treatment centres, physician clinics, extended care facilities, and home care agencies. [5] [6]

Exposure potential is related to the manipulations required to prepare and administer antineoplastic medicines, the type of equipment available in the specific setting, the work practices, and personal protective equipment used by the personnel. [6]

Specialized settings such as an operating room or interventional radiology departments may infrequently be involved in cytotoxic drugs handling. However, procedures should be evaluated step-by-step for the likelihood of the drugs being released into the environment so that exposure can be minimized.

Settings, where cytotoxic medicines are administered by inhalation or nebulizer, should be equipped with appropriate engineering controls to prevent workers' inhalation of ‘fugitive’ aerosols. It is also important to note that drug aerosols may be deposited on skin and surfaces, resulting in dermal complications. Chemotherapeutic agents **must** only be stored, processed, reconstituted, delivered and administered in an environment considered appropriate to do so with right equipment, suitable cold chain facility and optimal ventilation. [5]

### *2.1.1 Segregation of Chemotherapy Administration Area*

Patients that require inpatient care should receive chemotherapy only in a designated ward that has the facility to safely care for this group of patients. The wards and/or chemotherapy suites should be safe and free of clutter. Institutional guidelines/standard operating procedures for accidental exposures and emergency facilities including access to a telephone are imperative. All necessary equipment for safe administration and disposal of the chemotherapeutic agents should be accessible at the time of chemotherapy delivery. [5] [6]

### *2.1.2 Infrastructure (safety cabinets and compounding equipment)*

Appropriate ventilated equipment for compounding sterile and non-sterile antineoplastic medicines should be available. Special requirements for heating, ventilation and air-conditioning (HVAC) systems should be provided within the oncology pharmacy.

All mixing and preparation of cytotoxic medicines should be performed in one centralized area in a specially designated class II type B biological safety cabinet (BSC). The biological safety cabinet must be installed with the following features:

i. Exhaust with a High-Efficiency Particulate Air "or Arrestor" (HEPA) filter to the outside atmosphere in a manner that prevents recirculation into any inside area.
ii. Exhaust and ventilation systems that remain in operation for a sufficient period are to ensure that no contaminants escape from the biological safety cabinet into the workplace.
iii. Continuous monitoring device to permit confirmation of adequate airflow and cabinet performance.
iv. Airlocks should be considered if there are particular concerns about the propagation of airborne cytotoxic drugs.
v. The layout of the compounding room should allow for an unimpeded cleaning of all surfaces (walls, floors, ceilings, doors, diffusers, windows)
vi. The furniture and equipment in the sterile preparation room should be kept to a bare minimum and there should be a visual link (e.g., a window as a way to communicate between the sterile preparation room and the pharmacy, to view the work in progress)
vii. Access to the sterile room must be limited to trained and authorized workers.

The facilities should include an emergency eyewash that may or may not be hooked up to the airlock sink. As a minimum, the emergency eyewash should be able to provide 15 minutes of flushing to both eyes. It is strongly recommended that a full shower be accessible nearby.

It is important to note that closed-drug transfer systems are not a substitute for class II type B biological safety cabinets. In the non-sterile drug preparation process (e.g., oral preparations), it is strongly recommended that the same level of worker protection should be adhered to.

Protocols should be established to ensure preventive maintenance, monitoring, certification and the optimal use of facilities and equipment. [6]


*Figure 2: Prototype of Biological safety cabinet type 2*[2]

[2] lamsystems BSC 2B

## 2.2 Supply Chain

Handling procedures need to begin with safely receiving antineoplastic agents into the hospital as there may be a possibility of broken vials. Health workers receiving packaged cytotoxic agents should be protected to the same degree recommended for those preparing and administering chemotherapy.

Chemotherapy spill kits should be available in the Pharmacy and departments where chemotherapy is being prepared, dispensed, and administered.

In the event of a spill or untoward exposure, an intervention based on the SOP should be instituted and appropriate authorities notified. [2]

### *2.2.1 Transportation*

Transportation of cytotoxic drugs should be done in a manner to prevent breakage and contamination of the environment. During transportation, these drugs should, therefore, be placed in a rigid, shock-resistant, leak-proof container made of a material that can easily be cleaned and decontaminated. The bottom of the container should be covered with absorbent, plastic-backed material. The transport container should be labelled with the "Cytotoxic" hazard symbol and be cleaned regularly [3].

### *2.2.2 Receiving and storage of Chemotherapy*

Some cytotoxic drugs may be reconstituted, transferred from one container to another, from one part/department of the hospital to another or manipulated before administration to patients. There is a risk of absorption through inhalation or direct eye or skin contact.

Packaging can have high levels of contamination; therefore, it is strongly recommended that: there be an unpacking area in the pharmacy limiting exposure risks. The unpacking area should be a separate dedicated space, away from eating area. There should be a receptacle for cytotoxic waste in the unpacking area and workers at risk of exposure wear a protective gown and two (2) pairs of gloves when unpacking and cleaning cytotoxic drugs.

Storage areas for antineoplastic drugs requiring manipulation other than counting or repackaging of final dosage forms and any drug active pharmaceutical ingredients (API) should be separated from non-hazardous drugs in a manner that prevents contamination and personnel exposure. These should be stored in an externally vented, negative-pressure room with regular air changes.

Storage of prepared chemotherapy must include storage in a manner that ensures the correct control and security, especially from children and other unauthorised persons.

Storage must also involve a method that does not increase the likelihood of incorrect patient identification and/or incorrect administration.

Within the clinical area, the prepared chemotherapy that should be kept refrigerated should be stored in the designated chemotherapy refrigerator. Non-refrigerator items should be stored in the designated area within the clinical utility room.

All chemotherapy drugs that have not been used should be returned to the pharmacy immediately.

### *2.2.3 Handling – compounding and dispensing*

**Compounding**

When compounding chemotherapy agents, Pharmacists and pharmacy technicians should wear appropriate PPE (a cap, surgical/procedure mask, shoe covers, a protective gown and two (2) pairs of gloves) to make sterile preparations of cytotoxic drugs in biological safety cabinets.

The work surface should be covered with a disposable, absorbent, sterile, plastic-backed pad to absorb any liquid contamination that may occur. The pad should not cover the front and rear grilles of the BSC and should be changed regularly or in the event of a spill or contamination. The pad should be disposed of in a cytotoxic waste receptacle.

The quantity of supplies and cytotoxic drugs in the cabinet should be limited, to avoid adversely affecting the laminar flow and to facilitate regular cleaning of the work surface. The sterile products should be placed at the centre and the non-sterile products (e.g., waste receptacle) along the sides of the cabinet.

There is a need to adhere to the aseptic technique for sterility when necessary. Handling techniques that limit the risk of injury or accidental exposure should always be used. Overfilling of drug containers should be avoided.

All cytotoxic drugs must be labelled to inform those handling these preparations of the nature of the drugs and the precautions to be taken. Cytotoxic drugs must display the “Cytotoxic” hazard symbol or the word “Cytotoxic”. [3] [6]

**Dispensing**

Pharmacists and pharmacy technicians should wear appropriate PPE and ensure that the right medication is dispensed in the right leak-proof container. The container should be appropriately labelled. The pharmacist should also provide adequate information on dosage regimen, storage conditions and possible side effects.

### *2.2.4 Checks required before Chemotherapy Administration*

All Cytotoxic drugs and containers should have an appropriate label to alert handlers of special precautions needed for handling.

Workers should check the integrity of all packaging at every step of the unpacking process and damaged contents treated as a spill. The primary and/or secondary packaging should be cleaned before storage with a regular cleaning protocol in place. It is recommended that there be

adequate ventilation in the area, negative pressure and preferably vented to the outside. Establish a dedicated negative-pressure storage area for cytotoxic medicines that minimizes the risk of contamination.

## 2.3 Patient Care

### *2.3.1 Patient safety*

For the safety of the patient, clinicians must ensure the following conditions are met:

i. The correct diagnosis of the type and stage of cancer has been established;
ii. Chemotherapy is prescribed as per the treatment protocol for the cancer type;
iii. The chemotherapy prescribed is calculated at the correct dose;
iv. For patients commencing chemotherapy for the first time, a hypersensitivity test should be conducted/ascertained;
v. Regular monitoring of response to chemotherapy; and
vi. Assessment of treatment toxicities and complications from the previous cycle should be done and documented.

**Patient identification**

A patient undergoing chemotherapy must be correctly identified before delivery of the treatment. The patient identification verification/check should be made by a registered practitioner who has undergone the relevant chemotherapy training and has been deemed competent to administer chemotherapy. The identity of the patient MUST be established to ensure that an active response is made by the patient and not a passive response e.g. “please could you tell me your name and date of birth?” Not “is your name and date of birth…” The patient check must match the chemotherapy prescription and the details on the chemotherapy that is to be administered. If the patient check, patient prescription, and the chemotherapy drugs do not all match then the chemotherapy should NOT be administered.

**Patient information**

It is important to offer a pre-chemotherapy assessment to all patients receiving chemotherapy. Written and verbal information about the chemotherapy medicines should be given to the patients before the delivery of the first chemotherapy treatment.

**Consent**

All patients treated with chemotherapy should have signed the appropriate chemotherapy consent form. The managing oncologist should obtain informed consent from the patient. The practitioner administering the treatment should check that written consent has been given. It is advisable that the practitioner checks the patient’s understanding of the treatment and gains their verbal consent before continuing with the chemotherapy administration.

### *2.3.2 Sources of exposure to cytotoxic medicines on health workers*

Administration of cytotoxic drugs to patients is generally performed by nurses or physicians. The potential for occupational exposure exists for every route of drug administration. Common

methods include injection (e.g., intravenous, intra-arterial, intramuscular, subcutaneous), IV infusion, oral or enteral tube, intracavitary (e.g., intravesicular, intraperitoneal, or intrapleural), topical, intraspinal, and inhalation. Exposure may occur by absorption when liquid forms of cytotoxic medicines leak or spill during connecting or disconnecting tubing or syringes, spiking IV containers, priming air from infusion sets or syringes, or accidental disconnection in any drug delivery system. Work area surfaces that are contaminated with drug residues have been reported to be common sources of dermal exposure. Exposure may occur by inhalation when antineoplastic medicines dust or droplets are generated during drug administration. The dust may result from crushing solid oral forms. Aerosols can be produced during inserting of or removing tubing from IV containers, expelling air from syringes, or clipping or crushing needles or syringes.

Exposure may occur by accidental ingestion when foods or beverages are consumed in drug administration areas, or by hand-to-mouth transfer of drug residue from cytotoxic medicines contaminated surfaces.

Exposure may also occur by accidental injection from needle sticks or other sharps contaminated by cytotoxic medicines.

Excreta from patients who have received cytotoxic drugs is another source of exposure to health care workers. Patients' urine, stool, vomitus and sweat contain varying concentrations of drugs or their hazardous metabolites. For example, patients receiving cyclophosphamide excrete up to 36% of the drug dose as well as mutagenic metabolites in their urine. Temsirolimus is eliminated in faeces and is present in the stool for up to 14 days. Methotrexate has been found in vomitus and sweat of patients leading to worker exposure.

### *2.3.3 Disposal of Drug Contaminated Materials*

As a best practice, cytotoxic drugs and contaminated materials including discarded antineoplastic medicines generated at the pharmacy, clinics, wards and chemotherapy suites should be treated as hazardous waste.

These items should be disposed of in properly labelled, covered, and sealed disposal containers and handled by trained and protected personnel. Since sharps and potentially infectious materials may also be included in the trace contaminated materials, such containers should be managed as biohazardous waste in line with the Bloodborne Pathogens Standard.

Treatment of contaminated materials should occur at a regulated medical waste incinerator rather than an autoclave or microwave to prevent aerosolization. Spills involving cytotoxic drugs can also represent a hazard, and employers should ensure that all employees are familiar with appropriate spill management procedures.

## 2.4 Practitioner’s Responsibilities

Various health professionals involved in oncology must possess the basic qualifications for their various cadre and possess a valid practising license from the appropriate regulatory body.

Parenteral chemotherapy should only be administered by health care professionals who have been specially trained in parenteral chemotherapy administration. Standardized courses and curricula for chemotherapy administration should be developed at tertiary institutions and postgraduate medical colleges.

### *2.4.1 Training and Information Dissemination*

All staff handling antineoplastic drugs must be fully trained in the receipt, storage, handling, and disposal of these medicines. All personnel involved in any aspect of the handling of cytotoxic drugs (physicians, nurses, nursing assistants, pharmacists, pharmacy technicians, housekeepers, and other employees involved in receiving, transporting, storage, compounding, administering, waste handling and other forms of handling) must receive relevant information and training to keep them abreast of the hazards of cytotoxic drugs present in the work area. Such information shall be provided by the employer at the time of an employee's initial assignment to a work area where antineoplastic and other hazardous medicines are present, and before assignments involving such drugs. Information about new cytotoxic medicines must be provided when they are introduced into the work area. [6] [7]

It is hereby recommended that:

i. Knowledge and competence of personnel shall be evaluated after the first orientation or training session, and then regularly. Direct observation of an individual's performance on the job may be used as the basis for evaluation.
ii. Training should occur before preparing or handling cytotoxic medicines, and its effectiveness should be verified by testing specific cytotoxic medicine preparation techniques. Such verification should be documented for each person regularly. This training may include a didactic overview of hazardous drugs, including mutagenic, teratogenic, and carcinogenic properties, and it should include ongoing training for each new cytotoxic medicine.
iii. Training for compounding personnel should include at least safe aseptic manipulation practices; proper use of biological safety cabinets and other containment measures.

### *2.4.2 Recommended safety precautions for practitioners (Oncology Doctors, Pharmacists, Nurses, Assistants and Hygienists)*

**A. Drug Preparation**

The following recommendations apply to the preparation of all cytotoxic medications including parenteral, oral, and topical, both sterile and non-sterile preparations.

i. A dedicated work area for preparation with conspicuously displayed standard operating procedures including the use of appropriate PPE, appropriate ventilation and other automated equipment for packaging.
ii. Pharmacists or pharmacy technicians should wear PPE (a cap, surgical/procedure mask, shoe covers, a protective gown and 2 pairs of gloves if the right specification 0.007 inches is not available) to make sterile preparations of cytotoxic drugs in biological safety cabinets.

iii. Organize the procedure to limit microbial and environmental contamination.
iv. Work surfaces should be covered with a disposable, absorbent, sterile, plastic-backed pad to absorb any liquid contamination that may occur. The pad should not cover the front and rear grilles of the preparation cabinet and should be changed after 4 hours of continuous use; for a new batch of preparations or in the event of a spill or contamination.
v. The pad should be disposed of in a cytotoxic waste receptacle. The quantity of supplies and cytotoxic medicines in the cabinet should be limited to avoid adversely affecting the laminar airflow and to facilitate regular cleaning of the work surface. The sterile products should be placed at the centre and the non-sterile products (e.g., waste receptacle) along the sides of the cabinet.
vi. Remove the packaging, when applicable, and clean all of the drug containers before taking them into the preparation cabinet. For sterile preparations, adhere to the aseptic technique for sterility. Use handling techniques that limit the risk of injury or accidental exposure.
vii. Spiking of bags and priming of tubing should occur before the addition of cytotoxic medicine unless the clinical protocol requires otherwise.

**B. Cytotoxic drugs reconstitution in the pharmacy**

i. The drug containers should not be overfilled to avoid compromising their integrity.
ii. Air bubbles should never be removed from the IV tubing with a solution containing the drug.
iii. IV tubing should be primed, and air removed in the pharmacy, before adding the cytotoxic medicines to the infusion solution.
iv. Cytotoxic medicines should be labelled to inform those handling these preparations of the nature of the agents and the precautions to be taken. Cytotoxic medicines must display the “Cytotoxic” hazard symbol or the word “Cytotoxic”. [6]


**C. Transport and Storage Following Preparation**

Transportation of cytotoxic drugs should be done in a manner that will prevent contamination of the environment in the event of breakage. It is hereby recommended that:

i. Transportation of the cytotoxic agent from the pharmacy should be in a rigid, shock-resistant, leak-proof container made of a material that can be easily cleaned and decontaminated. The bottom should be covered with absorbent, plastic-backed material.
ii. Mechanical transport systems, such as pneumatic tubes, should not be used because of the stress they put on the contents, and the whole transport system would be compromised if a leak occurs.
iii. The transport container (e.g. trolley) should be designated and identified with the “Cytotoxic” hazard symbol and cleaned regularly.

## D. Preparation for the Administration of Chemotherapy

i. Protective Clothing Recommendations
- All protective clothing and equipment (gowns, gloves, goggles, face shields), should be impermeable to chemotherapy agents. Research has shown that gowns made of high-density polyethene provide the most protective barrier against spillage or aerosolization of cytotoxic medicines.
- Gowns must be worn wherever chemotherapy agents are being handled and administered. The gown should be disposable, impermeable/low permeability fabric, lint-free, with back closure and long cuffed sleeves, which should be tucked into the gloves.
- The gown should be changed within 1hour of an obvious spill as it is known that the time to the permeability of a vesicant is 1 hour.

ii. Gloves:
- It is advisable to use gloves that have been tested to protect against permeations by chemotherapy agents.
- Hand washing should occur before donning gloves and after removing gloves.
- The minimum acceptable standard is powder-free surgical latex gloves (0.007 inches). Some newer products may be thicker and provide more protection. Other suitable materials include polyurethane, neoprene or nitrile.
- In the event of latex sensitivity, equivalent surgical nitrile gloves should be used.
- Gloves should be changed every 60 minutes on the same patient, after each administration or if contamination or puncture occurs.

iii. Masks:
- Masks must be worn throughout the process of chemotherapy drug handling and administration.
- Surgical masks are not acceptable. Masks that are designated to protect against aerosolized particles by the manufacturer such as fit-tested respirators, NIOSH certified N95 or N100 should be used to protect against airborne powder or aerosolized particles. [5] [6]
- Masks with obvious contamination should be changed as well as when it no longer seals the face.

iv. Eye and Face Protection:
- Plastic Face Shields must be worn wherever chemotherapy agents are being handled and administered.
- It is recommended that contact lenses should not be worn because of the risk of absorption.
- Safety glasses or regular eyeglasses are not adequate.
- Eye protectors should be cleaned after each use according to the manufacturer's recommendations.
- In the event of contamination, appropriate spill procedures must be followed

**E. Drug Preparation Area for Nursing Personnel**

i. A dedicated area with restricted access is required.
ii. This area should not be used for food storage or eating and drinking. Chewing of gum in this area should not be allowed.
iii. Signs that restrict access to authorized personnel only should be displayed.
iv. Appropriate warning labels must be placed on all chemotherapy drug storage areas.
v. A sink, an eyewash station and a spill kit should be available in this space. A less desirable alternative is the availability of large volumes of saline solution for eye washing purposes.
vi. A plastic-backed absorbent pad should be used under tubing, syringe or sites of a potential leak.
vii. Leak-proof and puncture-proof biohazard containers should be available. All needles, syringes and other disposable items should be disposed of properly.
viii. Preparation for the Administration of Oral Chemotherapy: Examples: Mercaptopurine, Thioguanine.
    - It is recommended that all health care professionals administering oral chemotherapy adhere to the protective clothing guidelines as outlined in section 2.4.2D above.
    - Chemotherapy tablets/powder should be transferred into empty syringe barrel without touching them (wear gloves).
    - Capsules should be opened in a biohazard hood.
    - It is preferable to dissolve tablets in water instead of crushing them.
    - Prepare each dose on an absorbent pad on an uncluttered surface.
    - Discard materials that have been in contact with the tablets/capsules (medicine cups, oral syringes, absorbent pad, etc.) as hazardous waste.
ix. Regular handwashing with soap especially after preparing medication is recommended.
x. In children who cannot swallow tablets (e. g. methotrexate, mercaptopurine and thioguanine), the following procedures should be used:
xi. Reconstitute the required number of tablets into a liquid formulation immediately before dose time as follows:
    - Remove the plunger of a 10 mL oral syringe;
    - Place the required number of tablets into the barrel of the oral syringe;
    - Replace the plunger and draw up 5 - 10 mL of drinking water (not hot water) into the syringe;
    - Cap oral syringe with blue syringe tip;
    - Wait for 5-15 minutes to allow the tablets to dissolve (gently rock back and forth; shake syringe occasionally);
    - Give the dose in the usual manner;
    - Draw up another 5 mL of drinking water into the oral syringe, cap syringe and shake well to dislodge any remaining particles and give the dose in the usual manner; and
    - Rinse the dissolve and dose device after each use. [5] [7]
    - In children who cannot swallow capsules (e.g. procarbazine, temozolomide, hydroxyurea) or where the dose is less than one capsule, the contents of the capsule

can be emptied into a Dissolve and Dose container and made into a solution using the following procedure:

- ✓ Knock the powder down into one end of the capsule;
- ✓ Take the top off the capsule and empty the contents into the Dissolve and Dose device;
- ✓ Add 10 mL of drinking water (not hot);
- ✓ Cap the device, shake well and allow for 2 minutes to settle; and
- ✓ Measure the appropriate dose using an oral syringe.

xii. In children who cannot swallow capsules (e.g. lomustine, temozolomide, hydroxyurea, procarbazine) where the dose is one or more capsules, the contents of the capsule may be removed and mixed with food or liquid immediately before dose time as follows:

- Put the food or liquid you will mix the drug within a small medication cup;
- Knock the powder down into one end of the capsule;
- Take the top off the capsule and empty the contents into the medication cup;
- Mix the powder and the food/liquid that is in the cup; and
- Draw liquid mixed with the drug into a syringe. [5]

**F. Administration of Chemotherapy Agents**

i. There should be no open food in the patient room when the IV system is opened to administer chemotherapy agents, as there is a potential for the food to be contaminated. In cases where food is used to help with taste aversions or as a comfort measure, exceptions can be made by the administering physician or nurse to give the chemotherapy agents with caution as per his/her discretion. [3] [5]
ii. PPE should be used as outlined above;
iii. Plastic-backed absorbent pads should be placed under tubing and syringes;
iv. Only syringes and tubing with Luer-Lok connections should be used; and
v. Infusion bags should be changed at waist level.

**G. Disposal of Equipment /Personal Protective Equipment used to Administer Chemotherapy Agents:**

i. All syringes and needles should be discarded in containers that are puncture-resistant, leak-proof, with a lid that seals securely and appropriately labelled;
ii. Bags and solution administration sets should be discarded intact inappropriately labelled resealable containers that are both leak and puncture-proof; and
iii. PPE used during handling and administration should be disposed off in an appropriately labelled container.

**H. Nursing Care and Management of Patients Who Have Received Chemotherapy Agents**

i. Potential duration of excretion for all chemotherapy agents and their metabolites are not well defined. While there is data derived from the adult population, the extent to which this applies to children is unclear. Therefore, there is a real potential risk to health care professionals and parents who are caring for children following the administration of chemotherapy agents. It is suggested that PPE should be worn while attending to patients who have received intravenous (IV) chemotherapy agents for up to 48 hours and 7 days for oral chemotherapy agents.

ii. PPE must be worn when handling any patient's blood or body fluids;
iii. Plastic Face Shields should be worn when there is a risk of a splash, e.g., flushing toilet, changing diapers, frequent or unpredictable vomiting;
iv. Parents must be gloved when handling excreta and diapers up to 7 days post-treatment;
v. Gloves should be discarded after each patient use, and when soiled or contaminated with body fluids, in an appropriately labelled container; and
vi. Gloves and gowns should not be worn outside of the drug administration area.
vii. Flushing of Toilets
viii. The toilet bowl should be covered with a plastic-lined, absorbent pad (the absorbent side facing down) before flushing. These pads should be disposed of in biohazard containers after each use.
ix. The toilet should be flushed at least twice and covered.
x. Disposal of Diapers
xi. Used diapers should be disposed of in a biohazard container for up to 7 days after chemotherapy administration.
xii. Disposal of Contaminated Linen:
    - Contaminated, non-disposable, linen should be handled with gloves and gowns and should be dealt with in a manner consistent with institutional policies regarding handling and disposal of infectious linens.
    - Parents should not clean up contaminated linens or clothing. This should be done by gowned and gloved health care personnel.

**I. Patients who go to Other Areas of the Hospital**

i. Personnel in other areas of the Hospital (e.g., Diagnostic Imaging, Echocardiography) should observe these safety precautions when handling patients who have received chemotherapy agents.
ii. This policy should be disseminated to all hospital personnel who may care for oncology patients in other areas.

**J. Disposal of Biohazardous Contaminated Materials**

i. All areas where chemotherapy drugs are handled should have specific disposable containers close at hand for easy and safe disposal;
ii. Needles and syringes should be disposed of intact;
iii. Sharps and breakable items e.g. vials, ampoules should be disposed of in leak-proof, puncture-resistant containers with labels indicating chemotherapy (cytotoxic) waste;
iv. Non-sharp chemotherapy drug waste, e.g. plastic IV bags and tubing, personal protective equipment, should be sealed in leak-proof, puncture-resistant containers with appropriate labels; and
v. These containers should be of a different colour from the regular disposal of hazardous waste containers.

**K. Accidental Contamination and Chemotherapy Spills**

i. Every institution should have an SOP in place for the management of accidental contamination and chemotherapy spills. All health care professionals who handle chemotherapy agents should be oriented and familiar with these procedures.

ii. It is recommended that a spill management kit be readily available within the work area. [5]

### *2.4.3 Pregnancy, nursing or planning to become pregnant*

Since 50 out of the 52 essential medicines for cancers, as listed in annexe 3.2, have negative foetal effects at different stages of pregnancy, it is hereby recommended that pregnant female doctors, nurses, pharmacists and hospital attendants should not be involved in handling, compounding, administration, nursing and attending to patients on chemotherapy. Such staff can be on safety posting within the period of pregnancy and breastfeeding. Alternatively, they must wear personnel protective equipment (PPE) clothing if they must handle chemotherapy. Male and female staff intending to achieve pregnancy are also advised to consistently wear PPE while handling chemotherapy or patients on chemotherapy.

### *2.4.4 Employee Information*

Employees must be informed of the requirements of the Hazard Communication Standard as follows:

i. Any operation/procedure in their work area where drugs that present a hazard are present;
ii. Availability and location of the written hazard communication program;
iii. Availability and location of the list(s) identifying cytotoxic drugs present in the work area; and
iv. Availability and location of safety data sheets for all cytotoxic drugs in the work area.

### *2.4.5 Record Keeping*

Employee exposure records, including workplace monitoring, biological monitoring as well as employee medical records related to drugs posing a health hazard must be maintained and accessible to employees when the need arises. Records created in connection with the handling of cytotoxic drugs shall be kept, transferred, and made available for at least 30 years, and medical records shall be kept for the duration of employment plus 30 years.

## 2.5 Capacity Building

i. Various categories of health workers involved in chemotherapy administration must possess a basic professional certificate and an up-to-date practising licence from their various regulatory bodies.
ii. Oncology practitioners must also participate in a continuous medical education annually either in the hospital or outside the hospital to keep abreast of current chemotherapy administration practices.
iii. Each institution must have a functional tumour/oncology board, which must have at least quarterly academic meeting on oncology practice. This tumour board will be responsible for organizing an orientation course on chemotherapy for new employees and interns in oncology-related departments.
iv. The Federal Ministry of Health through the National Cancer Control Programme in conjunction with relevant partners shall routinely organize workshops and continuing

medical education at the hospitals as well as national levels on chemotherapy/oncology practice.

v. Steps shall be taken to institutionalize chemotherapy safety in the training curricula for various categories of health workers both at the undergraduate and postgraduate levels.

### *2.5.1 Employee Training*

Training should include at least the following elements:

i. The properties of the antineoplastic drugs located in the work area;
ii. The techniques and safe handling practices that have been implemented in the work area to protect employees from exposure to cytotoxic drugs, such as identification of drugs that should be handled as hazardous, appropriate work practices as well as emergency procedures for managing spills or employee exposure;
iii. The details of the hazard communication program developed by the employer, including an explanation of the labelling and cytotoxic drugs identification system used by the employer and how employees can obtain and use the appropriate hazard information;
iv. Proper use of safety equipment such as biological safety cabinets, compounding aseptic containment isolators, and closed system transfer devices; and
v. Proper donning and doffing of PPE.

## 2.6 Monitoring and Evaluation

Monitoring and evaluation is a key thematic area of this policy. This would provide a framework for continuous assessment of the effectiveness of the chemotherapy safety measures in each institution. The Monitoring and evaluation framework covers the following key activities:

i. Infrastructure;
ii. Capacity building compliance;
iii. Safety; and
iv. Quality improvement

***Table 1: Monitoring and Evaluation Framework***

| SN | ACTIVITY | STRATEGY | EXPECTED OUTCOME | RESPONSIBLE ORGANIZATION |
|---|---|---|---|---|
| ***Thematic Area 1: Environment*** | | | | |
| **1.** | Infrastructure/ consumables<br>i. Dedicated chemotherapy wards<br>ii. BSC<br>iii. PPE | Provision of dedicated chemotherapy wards with all the complementary facilities for handling, compounding and | Number of oncology centres with functional dedicated oncology building/chemotherapy wards with complementary facilities built | Individual institutions, State governments, Federal government, Development Partners and good spirited individuals |

| SN | ACTIVITY | STRATEGY | EXPECTED OUTCOME | RESPONSIBLE ORGANIZATION |
|---|---|---|---|---|
| | | administration of chemotherapy | | |
| **2.** | Capacity building of health workers | Training of various categories of oncology practitioners (doctors, nurses, pharmacist, technicians etc | Number of trained oncology practitioners | Individual institutions, state governments, federal government, development partners and good spirited individuals |
| **3.** | Handling | Number of chemotherapy spills, needle pricks, skin contacts, broken vials or contamination of surfaces | Reduced number of accidental exposures | Individual institutions, state governments, federal government, development partners |
| **4.** | Safety<br>Annual report of the number of health workers exposed to each category of chemotherapy. | Report on the number of health workers exposed to chemotherapy and those who had complications related to chemotherapy exposure. | Reduced number of health workers manifesting chemotherapy-related toxicity | Individual institutions, state governments, federal government, development partners and good spirited individuals |
| **5.** | Quality improvement<br>Clinical auditing of chemotherapy administration and compliance to safety protocol | The number of health workers practising safe and efficient chemotherapy administration. | Improved safe and efficient chemotherapy administration. | Individual institutions, state ministries of governments, federal Ministry of Health, development partners and good spirited individuals |

## 2.7 Funding

A major challenge of cancer management especially in developing countries such as Nigeria is the cost of chemotherapy. This is further compounded by the cost of supportive care. It is envisaged in this document that the provision of safety measures including proper use of PPE

by the health workers will increase the overall cost of cancer management. It is imperative to provide for a safety net to address this challenge.

Currently, the chemotherapy access partnership programme of the Federal Ministry of Health, CHAI and ACS has reduced the unit cost of the drugs in the portfolio. It may be necessary for collaboration of governments at all levels and non-governmental organizations to assist in the provision of chemotherapy infrastructure, consumables, PPEs and cost of workshops and capacity building activities for health workers. This may serve as an incentive for more health workers to specialize in the various fields of oncology. Proper and regular training and retraining of health care professionals involved in chemotherapy administration will help to reduce the number of professionals that may be affected by the hazards of chemotherapy.

The cost sharing protocol (Table 2) is hereby recommended:

***Table 2: Estimated cost of executing ChemoSafe programme in Nigeria over a period of five years***

| SN | Activity | Estimated Cost Per Annum (₦) | Estimated Cost Over 5 Year Period (₦) | Recommended Source of Funding |
|---|---|---|---|---|
| **1.** | Provision of dedicated chemotherapy wards with complementary infrastructure (12 hospitals per year) | 1,200,000,000.00 | 6,000,000,000.00 | FMOH (National budgetary allocation), ACS, CHAI & other Donors |
| **2.** | Provision of Biosafety cabinets, personal protective equipment | 250,000,000.00 | 1,250,000,000.00 | FMOH, ACS, CHAI & other donors |
| **3.** | Capacity building including trainings, workshops, support for tumour boards meetings for all the participating hospitals | 10, 000, 000 | 50, 000, 000 | FMOH, ACS, CHAI & other donors |
| **4.** | Monitoring and Evaluation | 50,000,000.00 | 250,000,000.00 | FMOH, ACS, CHAI & other donors |

# 3.0 ANNEXURES

## 3.1 Definition of terms

*Table 3: Pregnancy categories of cytotoxic medicines*

| PREGNANCY CATEGORY | DESCRIPTION |
|---|---|
| **A** | Generally acceptable. Controlled studies in pregnant women show no evidence of foetal risk |
| **B** | May be acceptable. Either animal studies show no risk but human studies not available or animal studies done and showed no risk |
| **C** | Use with caution if benefits outweigh risks. Animal studies show risk and human studies not available or neither animal nor human studies done. |
| **D** | Use in life-threatening emergencies when no safer drug available. Positive evidence of human foetal risk. |
| **X** | Do not use in pregnancy. Risks involved outweigh potential benefits. Safer alternatives exist. |
| **NA** | Information not available. |

## 3.2 Essential Medicine List for Cancers

*Table 4: WHO Essential medicines for cancer (which are also used in Nigeria), 2015 and their common toxicities [8] [9].*

| S/N | MEDICINE | DRUG CLASS | KNOWN TOXICITY | PREGNANCY & LACTATION CATEGORY |
|---|---|---|---|---|
| **1.** | Asparaginase | Antineoplastic; Enzyme | Allergy, CNS toxicity | C: |
| **2.** | Bleomycin | Antineoplastic; antibiotic | Pulmonary fibrosis | D: |
| **3.** | Leucovorin | Reduced folic acid; supportive | Enhances side effects of 5-Fu | A: |
| **4.** | Carboplatin | Antineoplastic; alkylating, agent | Nephrotoxicity, CNS toxicity | D: |
| **5.** | Chlorambucil | Antineoplastic; alkylating agent | Myelosuppression, neurotoxicity, infertility, hepatotoxicity | D: Potentially mutagenic, carcinogenic and teratogenic. Avoid in pregnancy |

| S/N | MEDICINE | DRUG CLASS | KNOWN TOXICITY | PREGNANCY & LACTATION CATEGORY |
|---|---|---|---|---|
| **6.** | Cyclophosphamide | Antineoplastic; alkylating agent | Myelosuppression, haemorrhagic cystitis | X: foetal malformation, miscarriage, foetal growth retardation |
| **7.** | Cytarabine | Antineoplastic; antimetabolite | Myelosuppression, oral ulceration | D: avoid in pregnancy |
| **8.** | Dacarbazine | Antineoplastic; alkylating agent | Myelosuppression, hepatic necrosis | D: avoid in pregnancy |
| **9.** | Dactinomycin | Antineoplastic; antibiotic | Alopecia, myelosuppression, risk of secondary malignancy | D: risk of foetal harm |
| **10** | Daunorubicin | Antineoplastic; anthracycline | Myocardial toxicity, myelosuppression | D: |
| **11** | Docetaxel | Antineoplastic; antimicrotubular | Hepatotoxicity | D: |
| **12** | Doxorubicin | Antineoplastic; anthracycline | Myocardial toxicity, myelosuppression | D: |
| **13** | Etoposide | Antineoplastic; podophyllotoxin | Severe myelosuppression | D: oligospermia, azoospermia, permanent infertility |
| **14** | Fluorouracil | Antineoplastic; antimetabolite | Mucositis, myelosuppression, alopecia | D: avoid in pregnancy |
| **15** | Hydroxycarbamide | Antineoplastic; antimetabolite | Myelosuppression, hyperpigmentation, genetic mutation and secondary malignancy on long term use | NA: mutagenic |
| **16** | Ifosfamide | Antineoplastic; alkylating agent | Alopecia, haematuria, neurotoxicity, CNS toxicity, nephrotoxicity | D; excreted in breast milk, avoid during pregnancy |
| **17** | Mercaptopurine | Antineoplastic; antimetabolite | Myelosuppression, hepatotoxicity, nephrotoxicity | D: avoid in pregnancy. Potential for infertility |
| **18** | Mesna | Uro-protectant; protects against cyclophosphamide and ifosfamide | Hypersensitivity | NA: |

| S/N | MEDICINE | DRUG CLASS | KNOWN TOXICITY | PREGNANCY & LACTATION CATEGORY |
|---|---|---|---|---|
| | | induced haemorrhagic cystitis | | |
| **19** | Methotrexate | Antineoplastic; antimetabolite | Ulcerative stomatitis, demyelinating encephalitis, myelosuppression | X: teratogenic |
| **20** | Paclitaxel | Antineoplastic; antimicrotubular | Myelosuppression, alopecia, Hypersensitivity | D: |
| **21** | Procarbazine | Antineoplastic; alkylating agent | Neuropathy/toxicity, myelosuppression | D: excreted in breast milk, impairment of fertility |
| **22** | Tamoxifen | Hormone; anti-oestrogen | Risk of uterine cancer, stroke, pulmonary embolism | D: Carcinogenic |
| **23** | Tioguanine | Antineoplastic; antimetabolite | Myelosuppression, hepatotoxicity, mucositis | D: teratogenic |
| **24** | Vinblastine | Antineoplastic; vinca alkaloids | Tissue necrosis, peripheral neuropathy | D: |
| **25** | Vincristine | Antineoplastic; vinca alkaloids | Tissue necrosis, peripheral neuropathy | D: |
| **26** | All-trans retinoic acid | Antineoplastic; retinoid | Shortness of breath, neuropathy, depression | D: |
| **27** | Aromatase inhibitors | Hormone; anti-oestrogen | Osteoporosis, cardiomyopathy, carcinogenic | D: carcinogenic |
| **28** | Bendamustine | Antineoplastic; alkylating agent | Myelosuppression | D: foetal harm, impaired male fertility |
| **29** | Bicalutamide | Antineoplastic; antiandrogenic agent | Hepatotoxicity, impaired spermatogenesis | foetal harm, impaired male fertility |
| **30** | Capecitabine | Antineoplastic; antimetabolite | Myelosuppression, potentiates warfarin anticoagulant effect, cardiomyopathy | D: foetal harm |

| S/N | MEDICINE | DRUG CLASS | KNOWN TOXICITY | PREGNANCY & LACTATION CATEGORY |
|---|---|---|---|---|
| **31** | Cisplatin | Antineoplastic; alkylating agent; platinum analogue | Severe nephrotoxicity, myelosuppression | X: foetal harm |
| **32** | Fludarabine | Antineoplastic; antimetabolite | Myelosuppression, neurotoxicity | D: |
| **33** | Gemcitabine | Antineoplastic; antimetabolite | Pulmonary toxicity | D: potential for genotoxicity |
| **34** | Granulocyte colony-stimulating factors | Growth factor | Hypersensitivity | B |
| **35** | Imatinib | Antineoplastic; Targeted therapy; tyrosine kinase inhibitor | Myelosuppression, Hypopigmentation, fluid retention, hepatotoxicity | C: avoid in early pregnancy, excreted in breast milk |
| **36** | Irinotecan | Antineoplastic; topoisomerase inhibitor | Severe myelosuppression, alopecia, hepatotoxicity | D: impaired female and male fertility |
| **37** | Leuprolin class | Antineoplastic; GnRH agonist | Neuropathy, vasodilation | D: |
| **38** | Oxaliplatin | Antineoplastic; alkylating agent; platinum analogue | Severe nephrotoxicity, myelosuppression | X: foetal harm |
| **39** | Rituximab | Antineoplastic; Biologic; targeted therapy, Monoclonal antibody | Angioedema, neuropathy, myelosuppression (hypoplasia), fatal infusion reaction (Sc now available | D: foetal B cell lymphocytopenia |
| **40** | Trastuzumab | Antineoplastic; anti HER2; targeted therapy, | Neuropathy, cardiomyopathy, pulmonary toxicity | X: Embryo foetal toxicity |
| **41** | Vinorelbine | Antineoplastic; vinca alkaloid | Myelosuppression, neuropathy, hepatotoxicity and pulmonary toxicity | D: may cause foetal harm |
| **42** | Arsenic trioxide | Antineoplastic; other | Myelosuppression, hepatotoxicity, encephalopathy | C: potential for foetal harm and testicular toxicity |
| **43** | Dasatinib | Antineoplastic; Targeted therapy; tyrosine kinase inhibitor | Myelosuppression, Hypopigmentation, fluid retention, hepatotoxicity | C: avoid in early pregnancy, excreted in breast milk |
| **44** | Diethylstilboestrol | Hormone agonist; non-steroidal | Cardiomyopathy, VTE | X: |

| S/N | MEDICINE | DRUG CLASS | KNOWN TOXICITY | PREGNANCY & LACTATION CATEGORY |
|---|---|---|---|---|
| **45** | Erlotinib | Antineoplastic; targeted therapy, TKI | Hepatotoxicity, pulmonary toxicity | D: foetal harm |
| **46** | Gefitinib | Antineoplastic; targeted therapy, EGFR inhibitor | Interstitial lung disease | D: foetal harm |
| **47** | Nilotinib | Antineoplastic; Targeted therapy; tyrosine kinase inhibitor | Myelosuppression, Hypopigmentation, fluid retention, hepatotoxicity | C: avoid in early pregnancy, excreted in breast milk |
| **48** | Prednisolone | Glucocorticoid; | Hyperglycaemia, gastric ulcers, adrenal insufficiency (withdrawal effect) | A, C or D: birth defect (cleft palate) |
| **49** | Dexamethasone | Corticosteroid; anti-inflammatory | Anaphylactoid reaction, angioedema | Crosses the placenta and may cause orofacial cleft |
| **50** | Immunomodulators e.g. bortezomib | Antineoplastic; proteasome inhibitor | Peripheral neuropathy, cardiac tamponade, encephalopathy | C: risk of foetal harm |
| **51** | Thalidomide | Antineoplastic; immunomodulator | Peripheral neuropathy, VTE | X: absolutely contraindicated teratogenic |
| **52** | Lenalidomide | Antineoplastic; immunomodulator | Peripheral neuropathy, VTE | X: teratogenic |

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