



# PPUKM PHARMACY BULLETIN

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## CHALLENGES IN COMPOUNDING EXTEMPOREANEOUS CANCER DRUGS by PRP Farid

Studies have shown that of all cancer therapies, 20-25% are expected to be in oral form. Pharmacists in oncology and pediatric setting often face challenges in dealing with oral anticancer drugs that are not available in liquid dosage forms, hence extemporaneous preparation of these agents are deemed necessary. Improper technique of preparing extemporaneous oral chemotherapeutic agents may increase the risk of over or underdosing; leading to increased risk of adverse events or decreased effectiveness, respectively.

Oral anticancer drugs are not only potentially carcinogenic, but also teratogenic. Although limited data are available to evaluate the adverse effects on reproductive health in female family members or caregivers resulting from the exposure to anticancer drugs, studies have associated between occupational exposure of drugs and miscarriages/stillbirths among nurses and pharmacists. Based on these data, caregivers who are pregnant or are breastfeeding should avoid direct contact with, or the handling of, these drugs, especially when an extemporaneous preparation method needs to be used for. However, multiple barriers exist that prevent safe practice of handling oral anticancer drugs such as lack of proper counseling and education, as well as limited access to personal protection equipment (PPE) gears.

Although most oral anticancer agents are not controlled-released or enteric coated, majority of the drugs have film coating designed to prevent health care personnel or patients from coming into direct contact with the drug, as well as to mask the unpleasant taste. Before a tablet is crushed or a capsule is opened, it is crucial to understand the pharmacokinetics of the drug and to find stability data available in the literature. Although some oral anticancer drugs can be crushed, (eg thioguanine tablet), the formulation should be prepared at least under a Class 1 biologic safety cabinet or bench top hood with High-Efficiency Particulate Air (HEPA) filters as required by the National Institute for Occupational Safety and Health (NIOSH).

When preparing an oral liquid from a soft gelatin capsule that contains liquid content (e.g., tretinoin or isotretinoin), one may place the capsule and warm fluid (water or milk) inside an oral syringe to allow the capsule to dissolve. The suspension can be administered orally or through a nasogastric tube. This preparation have to be administered immediately due to lack of stability data. However, some oral anticancer drugs may have impaired pharmacokinetic profile when administered together with products that contain milk, calcium, magnesium, or other polyvalent ions. Hence, care must be taken before deciding what to mix the medicine with. Wearing double gloves, non-permeable gowns as well as thorough hand washing should be considered when administering an oral anticancer liquid formulation to minimize risk of skin exposure in case of splashing and contamination of the hands.

In a nutshell, adequate information on the safe handling of cytotoxic oral chemotherapy must be disseminated among other healthcare professionals as well as caregivers who will be administering and preparing the oral anticancer drugs at home. This can be achieved by providing both oral instructions as well as patient-friendly written educational materials (e.g., leaflets or pamphlets) in lay language provided to patients and caregivers. Information provided should include the active ingredient of the drug and its indication, preparation method, dosing and schedule instructions, administration technique, storage conditions, proper disposal of contaminated medicine cups, adverse effects, and symptoms management.

**Examples of Hazardous Oral Anticancer Drugs by Classification** by Barton, 2011; Occupational Safety and Health Administration, 1999; Prostate Cancer Research Institute, 2011 Prostate Cancer Research Institute, 2011

**Chemotherapy:** Busulfan, capecitabine, chlorambucil, cyclophosphamide, etoposide, lomustine, methotrexate, procarbazine, temozolamide

**Targeted Agents:** erlotinib, everolimus, gefitinib, imatinib, lenalidomide, nilotinib, sunitinib, thalidomide

**Sample of cytotoxic labels available in PPUKM**



### Reference:

- 1) [http://www.medscape.com/viewarticle/736921\\_9](http://www.medscape.com/viewarticle/736921_9)
- 2) HSE Safe handling of cytotoxic drug
- 3) Masha, S.H. Extemp compounding of oral liquid dosage formulations and alternative drug delivery methods for anticancer drugs. 2011. Pharmacotherapy 164-192
- 4) Barton, 2011; Occupational Safety and Health Administration, 1999; Prostate Cancer Research Institute, 2011



10%

Of  
chemotherapy  
is given orally

## Tips For Safe Handling of Oral Cytotoxic Drugs

### Control Of Exposure

Use totally enclosed systems as the first choice for controlling exposure to carcinogens. Personal protective equipments (PPEs) should be worn at all times if there is no closed system hood. The room must have adequate ventilation systems and appropriate organizational measures.

### Drug Preparation

The preparation should be under the direction of a suitably trained and experienced pharmacist/nurse. The work area should be clearly designated for drug preparation. Enclosed systems should be used. Task such as dividing or crushing tablets should be restricted to a controlled environment. Once prepared, a drug should be clearly labeled as cytotoxic and packaged to minimize the risk of spillage or leakage when transported to the area where it will be administered.

### Drug Administration

The administration should be carried out **away** from areas where food and drink may be consumed. When handling oral preparations, direct contact with the skin should be avoided. If continually exposed without proper precautions, nurses/pharmacists or caregivers may increase their risks of contact dermatitis, liver damage, spontaneous abortion, or respiratory tissue damage (OSHA, 1999; Wilkes & Barton-Burke, 2011). Skin, eyes, and mucosa are sites of possible irritation from surface- or direct-contact contamination, inhalation, and ingestion.

### Waste Disposal

When handling waste, all staffs should wear suitable protection PPE. Suitable containers, clearly labeled and reserved solely for the use of cytotoxic drug waste should be used. Sharp containers should be used for the safe disposal of needles. Spill kits should be made available in all wards in case leakage or spillage occur during administration.



### Protective Personal Equipment (PPE)

Protective Personal Equipment (PPEs) should be used whenever there are risk to health and safety that cannot be adequately controlled. Double gloves should be used at all times during compounding. Eye and face protection is relevant when cytotoxic drugs are being handled outside an enclosed system. Double face mask can be used. Respiratory protective equipment should be used if exposure to powders or aerosols is possible. Protective clothing such as gowns and aprons can help prevent contamination of clothes and the skin.



### CASE STUDY

A 1 year old patient from pediatric oncology ward was unable to swallow all-trans retinoic acid (ATRA) capsule. The dose is 10mg once daily (one capsule/day). A query received regarding extemporaneous preparation of this medicine. Reference regarding the method of compounding this drug was referred. All PPE for personnel were worn. The soft capsule was put into sterile 50mL syringe. 20mL of milk was syringed out, the syringe capped, and was heated in a 37°C water bath in a plastic foam. After the capsule is dissolved, the milk turned yellowish colour. Subsequently, the nurse administered the medicine using syringe, slowly. Patient tolerated the preparation well. The nurses and the mother was shown the technique so that it can be freshly prepared in the wards, and at home; respectively. Written material was provided to the mother to ensure the mother adhered to the guideline of safe anticancer compounding.

#### A publication of :

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All-trans retinoic acid  
(ATRA) capsules