BC Cancer Clinical Pharmacy Guide

Parenteral Drug Delivery

Contents

Routes of Administration 2
Subcutaneous 2
Intramuscular 3
Intraocular 3
Intraperitoneal 3
Intrathecal 4
Intravesicular 4
Intravenous 5
Vesicants 5
Venous Access 6
Central Venous Access Devices (CVADs) 6
Peripheral Administration 7
Central Administration 8
Continuous Infusions 8
Stability and Compatibility 8
Y-Site Compatibility 9
Non-DEHP Equipment 10

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Routes of Administration

Parenteral cancer medications, including hormonal therapy, are administered by several routes including:

- Subcutaneous (SC)
- Intramuscular (IM)
- Intraocular (IO)
- Intraperitoneal (IP)
- Intrathecal (IT)
- Intravesical (VE)
- Intravenous (IV)

Intravenous and subcutaneous administration routes are the most frequently used for parenteral cancer drug delivery.

At BC Cancer, most cancer drugs for parenteral administration are considered hazardous drugs, and are prepared and administered in a closed system using Closed System Drug Transfer Devices (CSDTDs) to minimize exposure to them (except when incompatible).

Subcutaneous

Medications administered subcutaneously are injected into the fatty tissue layer between the skin and the muscle. Nursing practice varies by institution and may involve capping SC syringe volume at 2 to 2.5mL and more than one injection site may be required for larger volumes. However, this is not evidence based and certain drugs can be safely administered in larger volumes. For example, the rituximab monograph indicates that the rituximab SC 1400 mg dose can be administered as a single injection of 11.7 mL to one injection site. This is due to the addition of the enzyme **hyaluronidase** to the drug formulation. Recombinant human hyaluronidase (rHuPH20) acts locally to facilitate the dispersion and absorption of the subcutaneously administered drug (such as rituximab SC or daratumumab SC), allowing delivery of a larger injection volume with limited swelling or pain. The effect is transient, with hyaluronidase half-life in skin less

than 30 minutes and subcutaneous tissue expected to return to normal within 24-48 h after injection.

Because of greater ease of administration, patients may be switched from IV to SC oncology treatments or be taught to self-administer certain medications subcutaneously. *Local* injection-site and cutaneous reactions are common with SC administration. For certain drugs, administration-related *systemic* reactions may also occur, similar to infusion-related reactions following IV administration. The **first** dose of rituximab, which has a very high risk of infusion reaction, is always given by IV route to allow for easier slowing or discontinuation of the administration. If the IV dose is tolerated, subsequent rituximab doses can be switched to the SC route. With daratumumab, all doses can be given via the SC route, but they require adequate reaction prophylaxis pre- and post-medication. Refer to applicable Chemotherapy Protocols, PPPOs, and/or Cancer Drug Manual drug monographs to identify the frequency, time to onset, and nature of reactions, as well as tolerated subcutaneous injection volume for each drug where available.

Intramuscular

The onset of action is faster with intramuscular administration than subcutaneous administration. Limited volumes of fluid are tolerated; more than one injection site may be required for larger volumes. For example, the Asparaginase monograph recommends that dose volumes greater than 2 mL be administered in two injection sites if possible to reduce pain of injection, although a single site can be used if necessary.

Intraocular

Intraocular medications can be administered as injections (intravitreal injections) directly into the vitreous humor, the gel-like fluid inside of the eye. Methotrexate and rituximab are examples of medications that can be injected to treat ocular lymphoma. Certain ocular malignancies can also be treated using eye drops as topical therapy. Refer to protocols OCFU and OCMITO for more information on fluorouracil and mitomycin eye drops.

Intraperitoneal

The intraperitoneal route is used to deliver medications directly into the abdominal cavity through a catheter surgically placed in the abdominal wall. Medications are

supplied in infusion bags. Higher concentrations of medications are delivered locally to the abdominal cavity while minimizing exposure to the rest of the body. The medication may be drained out after a few hours or left inside where it is gradually absorbed. The GOOVIPPC treatment protocol is an example of an ovarian cancer treatment that includes intravenous and intraperitoneal paclitaxel and intraperitoneal carboplatin.The medication is not drained from the abdominal cavity after administration.

Intrathecal

The intrathecal route is used to bypass the blood-brain barrier to deliver drugs directly to the cerebrospinal fluid (CSF). Some protocols include medications for both intrathecal and intravenous administration. Some drugs that can be safely administered intravenously are not safe to administer intrathecally.

For example, vinca alkaloids are safely given intravenously, but can be fatal if administered by intrathecal injection. There have been numerous cases worldwide where vincristine was inadvertently given intrathecally. Vincristine is now dispensed in 50 mL minibags so that it is easier to distinguish from the intrathecal drugs which are supplied in syringes.

As outlined in ST Policy V-40 Vinca Alkaloid Preparation and Administration, the following precautions are required for vinca alkaloid dispensing:

- **Never** dispense in a syringe
- Medication or auxiliary label must include route of administration, e.g., “For intravenous route only”
- Auxiliary label with the words “Warning: Fatal if given by other routes” must be used

The additional precautions required when administering cytotoxic drugs by the intrathecal route are described in ST Procedure III-50 Administration of High Alert Medications by Intrathecal Route.

Intravesicular

Intravesicular medications are administered through a urinary catheter into the bladder in order to deliver higher concentrations of medications to the bladder while minimizing exposure to the rest of the body. Medications are supplied in syringes. After

administration, they are held in the bladder for a period of time as outlined in the BC Cancer Protocol Summary and then drained. An example of intravesicular administration is BCG for bladder cancer in the GUBCG Protocol.

Intravenous

Intravenous administration provides a faster onset of action than intramuscular administration. Larger volumes of fluids are tolerated with intravenous administration compared with intramuscular or subcutaneous administration. Vesicant or irritant drugs that may cause tissue damage when administered intramuscularly or subcutaneously can be adminstered intravenously.

Cancer drugs for intravenous administration may be prepared in:

- Syringes for IV push injection
- IV bags for intermittent or continuous infusion
- Infusion devices for continuous infusion

The pharmacist should be aware of the intravenous route chosen so that the cancer drug can be prepared appropriately for the method of administration. For example, fluorouracil may be prepared in a syringe, IV bag, or infusor. For detailed information on parenteral drug administration, refer to the BC Cancer Pharmacy – Parenteral Cancer Drugs: Administration, Complications and Safety Considerations module on the PHSA LearningHub.

Vesicants

Many cancer drugs have the potential to cause tissue necrosis if extravasation (infiltration into tissue around the vasculature) occurs. These drugs are known as vesicants. Vesicants may cause blistering, local or extensive tissue necrosis, ulceration and progressive sloughing of damaged tissue. This may occur over several weeks and require surgical excision and skin grafting. To avoid this complication, the nurse carefully selects the IV administration site for each patient.

If extravasation of a vesicant does occur, it is imperative that treatment be started immediately. An extravasation kit should be readily available in every area where cancer drugs are administered. The contents of the kit, procedures for preparing and

administering a vesicant drug and the management of extravasation, are detailed in III-20 Prevention and Management of Extravasation of Chemotherapy.

Venous Access

Administration via the intravenous route can be achieved using a peripheral site; however, a central venous access device (CVAD) is preferred in specific circumstances including:

- Cancer drug treatments with vesicants or irritants
- Frequent treatments or long-term therapy that may cause damage to veins from frequent needle access
- Cancer drugs given by continuous infusion
- Poor peripheral venous access (e.g., presence of edema or previous phlebitis)

Another term for CVAD is central venous catheter (CVC).

Central Venous Access Devices (CVADs)

There are a variety of CVADs available and depending on the needs, they may be inserted for short-term or long-term therapy. CVADs may have a single or multiple lumens. Each lumen is treated as a separate catheter. Incompatible medications can be infused simultaneously via separate lumens.

The following chart summarizes some important features of CVADs:

Table 1. Tunneled CVC, PICC, IVAD devices

CVAD	Venous Access	Duration of Use	Advantages	Disadvantages
Tunneled Central Venous Catheter [eg.,Hickman®, Broviac®]	Inserted into the subclavian vein. Tip rests in superior vena cava.	Long-term (months to years)	Can be left in place indefinitely All therapies can be administered	Surgically implanted and removed External device

CVAD	Venous Access	Duration of Use	Advantages	Disadvantages
	Tunneled subcutaneously to exit site on chest			Frequent assessments
Peripherally Inserted Central Catheter (PICC)	Inserted into a large vein just above or below the antecubital fossa Tip rests in the superior vena cava	Mid to Long-term (several days to months)	All therapies can be administered Easily removed	Not ideal for rapid infusion Frequent dressing change and assessment
Implanted Venous Access Device (IVAD) [eg.,Port-A-Cath®, BARD Power Port®]	Inserted into the subclavian vein Tip rests in superior vena cava Port implanted into subcutaneous tissue usually in the upper chest	Long-term (months to years)	Can be permanent All therapies can be administered Internal device Decreased risk of infection Unrestricted activity	Surgically implanted and removed Non-coring needle access required

Peripheral Administration

Peripheral administration of vesicants and other drugs by IV push is given through the lowest medication port (sidearm) of a primary IV line flowing freely by gravity. Vesicant drugs that are given as a peripheral infusion (e.g., vincristine) are administered by gravity through the secondary medication port of a free-flowing IV.

Vesicant drugs when given peripherally must never be administered by infusion pump because the pump may continue to deliver the vesicant drug after extravasation occurs. The peripheral administration site is observed closely for evidence of extravasation and is checked for blood return every 2-3 mL for IV push and 1-2 minutes for IV infusions.

Central Administration

At BC Cancer, both vesicant and non-vesicant cancer drugs given through a central venous access device (CVAD) may be administered by:

- IV push through the lowest medication port (sidearm) of a free-flowing IV or
- Intermittent infusion using an infusion pump

The infusion pumps used at BC Cancer are equipped with drug error reduction software (DERS) to minimize pump programming errors. The software provides a warning when dose, rate or concentration information is entered outside of the safe range for each medication in the drug library.

Continuous Infusions

Some protocols require non-vesicant drugs to be delivered continuously, over an extended period of time. This can be accomplished using portable infusion devices. These devices provide flexibility to patients, allowing them to be ambulatory while receiving medication by a continuous, regulated infusion. They are generally small and inconspicuous, in order to minimize any impact on patients' daily living activities. For example, an elastomeric infusion device is used in the GIFOLFIRI protocol in which fluorouracil (5-FU) is given intravenously by continuous infusion over 46 hours.

BC Cancer uses Baxter Infusors® (disposable elastomeric infusion devices) for all continuous infusions of 5-FU. These devices have elastomeric balloons that provide fixed infusion rates, so infusion rate programming is not required. This is one of the Institute for Safe Medication Practice (ISMP) recommendations to prevent pump infusion rate errors resulting from incorrect pump programming.

Please see **Elastomeric Infusors for fluorouracil (5-FU)** [Frequently Asked Questions - Cancer Drug Preparation and Administration] for more information about Baxter Infusors®, including checklists for rate error prevention, identifying the causes of rate errors, dose banding, and infusor selection.

Stability and Compatibility

It is the responsibility of the pharmacist to determine the stability and compatibility of the cancer drug prior to preparing the product for parenteral

administration.

The stability of the drug being administered — specifically, the chemical stability of the cancer drug — can be affected by the following factors:

- The original state of the drug: Does it need to be reconstituted?
- The diluent in which the final product will be prepared: What solution is indicated in the protocol for an infusion?
- Storage conditions: Is refrigeration required?
- The final concentration of the product: For example, the stability of etoposide decreases as the concentration increases.

To determine the stability and compatibility of a cancer drug in a given diluent or vehicle, the pharmacist can follow the recommendations in a variety of sources. The references used by BC Cancer include:

- Chemotherapy Preparation and Stability Chart [Cancer Drug Manual]
- Drug monographs from the manufacturer
- *Handbook on Injectable Drugs* by Lawrence A. Trissel
- *American Hospital Formulary Service (AHFS) Drug Information*
- *USP DI — Drug Information for the Health Care Professional*
- Information from clinical trials
- Primary literature search

Y-Site Compatibility

Cancer drugs are not usually administered concurrently by a Y-site connector, even if they are considered compatible in the references above. An exception is that leucovorin is administered concurrently with either oxaliplatin or irinotecan in some Gastrointestinal protocols.

Non-DEHP Equipment

Di(2-ethylhexyl) phthalate (DEHP) is a chemical additive found in most polyvinyl chloride (PVC) medical equipment such as intravenous bags, tubing, and administrations sets. DEHP is used to make PVC soft and flexible. Some drug solutions cause leaching of DEHP from PVC equipment into the intravenous solution. These drugs must be prepared and administered with non-DEHP equipment. It is not known what level of DEHP is 'dangerous' to humans; however, DEHP is hepatotoxic and exposure should be minimized.

There is a growing list of cytotoxic drugs that should not be used with DEHP equipment. The **Chemotherapy Preparation and Stability Chart** [Cancer Drug Manual] currently recommends non-DEHP infusion bags and tubing for blinatumomab, cabazitaxel, docetaxel, etoposide, ixabepilone, paclitaxel, paclitaxel-NAB, DPACE, EPOCHR, temsirolimus, and teniposide. BC Cancer protocols and preprinted orders also indicate when non-DEHP bags and tubing are to be used for drug administration. The terms "non-PVC" and "non-DEHP" were once used interchangeably, but they are now known to be different.