



BC Cancer Clinical Pharmacy Guide

Cancer Drug Order Assessment

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Introduction

The following steps are recommended when checking cancer drug treatment orders. The steps should be followed when the route of administration may result in systemic absorption. This includes oral, parenteral and intraperitoneal dosage forms. Systemic absorption may also result from topical administration of cancer drugs. Consideration should be given to following the checking steps for topical cancer drugs where systemic absorption may result in changes in laboratory values and/or other adverse effects. Simplified checklists of this procedure, Clinical Cancer Drug Order Review Checklist: Parenteral and Clinical Cancer Drug Order Review Checklist: Take Home Drugs, can be found in the **Appendices** section of the Clinical Pharmacy Guide. A *Final Compounded Cancer Drug Product Check* document is also located there.

Step 1 Verify Patient Identity

Use at least two identifiers to confirm that the order has been written for the correct patient:

- Name
- Identification Numbers (i.e., BC Cancer/Hospital MRN/PHN)
- Date of Birth

Patients must be positively identified when receiving outpatient medications per Provincial Pharmacy Directive III-30-05 Patient Identifiers for Outpatient Dispensing and Drug Information Services.

Step 2 Confirm Protocol Matches Clinical Indication and Eligibility for Treatment

- Ensure patient meets eligibility/exclusion criteria and does not have any contraindications to treatment.
- Ensure protocol has not changed (if beyond first cycle).
- Ensure CAP approval has been obtained for protocols that require it, extra treatment cycles, cancer drug substitutions or treatments that are not covered by an existing protocol.

BC Cancer has implemented the use of some oncology biosimilar drugs, which are not identical to the original reference product, but considered clinically equivalent. They have highly similar pharmacokinetics, pharmacodynamics, safety and clinical efficacy profiles to the reference biologic. Only the applicable biosimilar will be funded by BC Cancer per Systemic Therapy Policy [III-190 Oncology Biosimilars Utilization](#).

Step 3 Review Medical History

Check Medications

Obtain a current list of medications that the patient is taking, including prescription medications, non-prescription medications, and Complementary and Alternative Medications (CAMs).

- Check to see if any of these medications interact with the cancer drug(s) ordered.
- BC Cancer Drug Monographs [[Drug Index](#)] contain a table of potential interactions for each drug.
- Additional information may be found in standard electronic interaction databases, such as Micromedex®, Lexicomp® and NatMed® (previously Natural Medicines Database®).
- [Complementary & Alternative Therapies](#) section of the BC Cancer website can also be consulted.

Check Other Therapies

Check whether patient is receiving radiation therapy, as this can impact risk of cancer drug toxicity. Refer to Module 6 of the Clinical Pharmacy Guide for information on radiation therapy and dual modality protocols.

Check Allergies

Check for other allergies that may affect treatment delivery, such as latex allergy.

Check Childbearing Potential

Check if patients between the ages of 11 and 56 are of childbearing potential.

- Per the Provincial Pregnancy Assessment and Education Policy, these patients are assessed for reproductive potential, and educated about the potential teratogenicity of treatment.
- Documentation on the Systemic Therapy Pregnancy Assessment and Education Form or similar, and a negative serum pregnancy test, may be required prior to first treatment per local procedures.
- The Pregnancy Assessment and Education for Systemic Therapy Patients Procedure: V-220 outlines the responsibilities of the Systemic Therapy staff (prescriber, nurse and pharmacy clinician). For new take home medications, pharmacy clinicians play an important role in ensuring patients starting treatment are not pregnant and have been provided with appropriate patient education about the potential effects of treatment.
- The patient handout Preventing Pregnancy during Cancer Treatment is available to give patients while counselling on preventing pregnancy. There are links in the handout that provide more information on different contraception methods and their efficacy.

Step 4 Check Timing of Treatment

Duration of Therapy

Check that the duration of treatment falls within the recommended duration of therapy in the BC Cancer protocol. This information is located below the treatment section of the protocol or in the CAP approval.

Remember to check the total treatment duration for oral medications. For example: tamoxifen and aromatase inhibitors have specific durations of treatment depending on the protocol and treatment strategy.

Cycle Interval

When a patient first begins cancer drug treatment, the first day of treatment is considered Day 1 of Cycle 1. Timing of subsequent appointments is calculated from that date. However, if a treatment delay occurs, subsequent appointment dates would be more accurately calculated from Day 1 of each cycle. Treatment interval is specified in each protocol and should be followed as outlined in the treatment schema. It should be

checked with each cancer drug order received because treatment frequencies vary from protocol to protocol. For example, treatments are given daily for 5 consecutive days every 28 days for patients on the LYFLU protocol, while for patients on the CNCCNU protocol, treatments are given as a single dose, once every 6 weeks.

- When a cancer drug order is received, the pharmacist must check if the patient is receiving treatment for the first time or if it is a return visit. If it is the patient's first treatment, then all interval calculations are based on the first day that the patient receives the cancer drug.
- If it is a return visit, then the pharmacist should check that the protocol is the same as the previous treatment.
 - If the protocol is the same, then the interval schedule is calculated from the first day (Day 1) of the previous treatment, according to the schedule outlined in the protocol.
 - If the patient is starting on a different protocol, then the pharmacist should check that the protocol is not booked too soon after the previous treatment. The treatment date of the new protocol is considered Day 1 of Cycle 1 and will be used for calculating subsequent treatment dates.

Occasionally a treatment schedule may be modified due to circumstances such as statutory holidays, earlier compassionate scheduling for a patient, or to facilitate efficient use of treatment time in the chemotherapy unit. Consult Policy III-120 Scheduling IV Systemic Therapy Patients for a suggested guideline on scheduling patients.

Any questions or concerns regarding the treatment interval should be discussed with the prescriber before proceeding and must be documented in a pharmacy patient treatment record and the patient chart.

Step 5 Determine Patient's Body Surface Area (if applicable)

Dosage calculations for the majority of cytotoxic chemotherapeutic cancer drugs are based on the body surface area (BSA) of the patient, where the dosage is reported in milligrams, grams, or units per square meter of BSA. It is calculated for any cancer drug where the dose is based on BSA. While the dosing of some cytotoxic cancer drugs, such as docetaxel and gemcitabine, has been shown to correlate well with BSA, the dosing of

other cytotoxic drugs has not (e.g., carboplatin).

For a new patient, the baseline height and weight are documented on the *Height, Weight & BSA Record* and independently verified by two staff members, usually care aides or registered nurses. This height and weight is then used for BSA calculations. On subsequent visits, the updated weight is documented on this record for monitoring purposes and can prompt a dose recalculation as outlined below.

Methods for Determining BSA

The BSA may be calculated by a number of different methods that use formulas, slide rulers, or nomograms. A commonly used equation for BSA calculation is the Mosteller formula:

$$\text{BSA (m}^2\text{)} = \sqrt{\frac{\text{height(cm)} \times \text{weight(kg)}}{3600}}$$

Average BSA for an adult male: 1.9 m²

Average BSA for an adult female: 1.6 m²

The Mosteller formula has been adopted as the BC Cancer standard for determining BSA. The Mosteller formula has the following advantages over other BSA formulas:

- It has been validated against other BSA formulas.
- It removes the chance of mathematical error if the patient's height and weight are inadvertently switched in the calculation.
- It is much easier to remember and therefore finds more widespread use in clinical practice.
- It is applicable to children.

A [Body Surface Area Calculator](#) that uses the Mosteller formula is available on the BC Cancer website. Note: this calculator lists an unrounded answer to two decimal places.

Ideal vs. Actual Body Weight

Issues concerning the use of "ideal" versus "actual" body weight to calculate BSA have been discussed in various studies. Based on these studies, BC Cancer

has set the following recommendations.

Policy III-10 – Systemic Therapy Treatment Delivery Process excerpt:

Use actual, not ideal body weight except for the designated high dose protocols described e.g., Leukemia/Bone Marrow Transplant protocols, where corrected body weight is used. (Refer to specific protocol for details).

Capping BSA and Cancer Drug Doses

In some circumstances, prescribers may set an upper limit (i.e., “cap”) for a patient’s BSA prior to calculating the drug dose(s) or cap the dose for a specific drug. Cancer drug doses may be capped due to patient-specific factors such as age, performance status, or nutritional status. Doses are not generally capped for obesity. For example, a prescriber may choose to calculate drug dose based on the actual BSA of a young and otherwise healthy patient. However, for an older, very frail patient, capping the drug dose may be more prudent. Furthermore, in cases where more than one drug is administered in a protocol, there may be instances when the dose of one drug is capped or omitted and others are not, based on the clinical judgement of the prescriber, patient-specific considerations, and drug-specific adverse effects.

Following the first cycle of drug therapy, the prescriber may also choose to modify the dose based on the patient’s response to it; however, the dose should remain within the guidelines of the protocol. For example, a frail elderly patient whose BSA was previously capped may have their dose of cancer drug therapy increased if the prescriber has determined that the patient is responding to therapy and no toxicities were observed following the previous cycle.

Note: If it has been determined that cancer drug doses have been capped based on the prescriber’s clinical assessment of the patient (and not as part of the protocol), it is important to document this as part of the patient treatment record.

Practical Considerations

- The patient should be weighed and their BSA calculated for the **first** treatment of the cancer drug therapy protocol. Round to two decimal places. As per Policy III-10 Systemic Therapy Treatment Delivery Process, subsequent BSA recalculations need to be done only if:

- in the prescriber's opinion, it is warranted by a change in the clinical status of the patient
 - a patient's weight change results in greater than 5% variance from the prescribed dose, or if the weight change is greater than 10% from Cycle 1 of the regimen or from that used in the most recent dose calculation (see Step 6). Review with prescriber to determine if dose change and BSA re-calculation is required.
- A maximum of 5% variance in dosage calculation is permitted as per Policy [III-10 Systemic Therapy Delivery Process](#). It is recommended that all members of the health care team employ the same method to determine BSA whenever possible. This will not only ensure consistency but will also increase patient safety when calculating cancer drug therapy doses. The Mosteller formula has been adopted as the BC Cancer standard when calculating BSA.
- Note - exception to the 5% variance in dosage is when dose banding is specified within a protocol as these parameters have been considered and set by the Tumour Group.

Step 6 Check Appropriateness of Cancer Drug Dose(s)

Upon receipt of the cancer drug treatment order, the pharmacist should verify the doses written by the prescriber. Most cancer drugs require dose calculations based on BSA (mg/m^2). Cancer drug doses may also be determined by other patient-specific factors such as weight [e.g., trastuzumab (mg/kg)] or renal function [e.g., carboplatin (calculated CrCl – see **Carboplatin Dosing** in Module 3 [Renal Function Tests](#) of the Clinical Pharmacy Guide)]. Some cancer drugs use standard dosing and do not require dose calculations (e.g., erlotinib).

Policy [III-10 Systemic Therapy Treatment Delivery Process](#) permits a maximum of 5% variance in dosage calculation, unless otherwise specified by the treatment protocol. If the pharmacist's calculated doses differ from the orders by more than this 5% allowable variance, the prescriber should be contacted regarding this discrepancy and the doses reconfirmed.

If a patient's weight change results in greater than 5% variance from the prescribed dose, or if the weight change is greater than 10% from cycle 1 of the regimen or from that used in the most recent dosing calculation, discuss with the prescriber to determine if a dose change is warranted.

If the cancer drug doses are to be administered as ordered, the pharmacist should place a note clarifying this in the patient's medical record.

If, after consultation with the prescriber, it is determined that a change in dose(s) is required, the prescriber must either write a new cancer drug order or make amendments to the existing order, signing and dating the order where changes are required. Verbal orders for cancer drugs are not accepted, except for delay or cancellations. (Note: telephone orders are acceptable for hormonal therapies only.)

Practical Considerations

- BC Cancer has defined greater than 10% weight change as clinically significant. The patient should be evaluated for changes in performance status that may require adjustment of cancer drug treatment and supportive care measures.
 - For example, a patient may have a large weight gain due to ascites or peripheral edema. After discussion with the prescriber, a decision may be made to keep BSA/dose the same, and arrange for paracentesis supportive care for ascites if applicable.
 - Alternatively, a patient may have a large weight loss that warrants discussion with the prescriber, due to reasons such as disease progression, cachexia, or unmanaged pain. In these cases, the prescriber may: recalculate the BSA and decrease the dose, discontinue or change the treatment, refer the patient for nutritional support or pain management as applicable, etc.
- Note - any weight change resulting in a 5% dose variance should be flagged for discussion with the prescriber, even if the weight change is less than 10%. For weight-based dosing regimens, even a small weight change of between 5% and 10% may result in dose variance of greater than 5%. See [Case study 9](#) for an example.
- BC Cancer has implemented the use of dose banded infusors for protocols utilizing 46-hour fluorouracil infusions. Dose banding involves rounding a calculated dose up or down to a predetermined standard dose within defined ranges, or bands. Dose banding is optional for facilities outside BC Cancer. Refer to III-140 Management of Dose Banded Cancer Drug Treatments [Policy](#) and [Procedure](#) for further information about dose banding, including the requirement for a pharmacist to initial and date the dose band selected on the pre-printed order.

Check Maximum Cumulative Doses (if applicable)

Some cytotoxic agents, such as bleomycin and the anthracyclines, have a suggested maximum lifetime dose or a dose threshold above which increased monitoring is recommended due to toxicities associated with accumulated doses.

In the case of bleomycin, pulmonary toxicity may be exhibited by the onset of symptoms such as a dry hacking cough, shortness of breath, fever and fatigue. These can occur during active bleomycin therapy or after treatment has been completed. Progression of symptoms may continue for months, even after discontinuation of therapy. Patients who are most at risk include elderly patients, patients with emphysema, patients with renal impairment, patients receiving concomitant chest radiation or other cancer medications (e.g., cisplatin, cyclophosphamide, methotrexate, etc.) and those with previous bleomycin treatments within the last 6 months. Although the incidence of toxicity is low when the accumulated dose is less than 400 units, a cumulative dose of greater than 450 units is a risk factor for developing pulmonary toxicity, and no dose is considered safe. Bolus doses can also carry an increased risk, due to the peak concentrations of bleomycin that can be seen. The treatment for pulmonary toxicity is non-specific. Thus, the most effective control is to set a maximum cumulative dose (400 units for adults) and also to stop treatment at the first sign of toxicity.

Cardiac toxicity is a well-documented side effect of anthracyclines. Risk increases with cumulative doses, especially in patients with known risk factors such as thoracic radiation therapy and exposure to other potentially cardiotoxic agents. The pharmacist must consider the total cumulative dose the patient has received in their lifetime. When the anthracycline doses have reached monitoring thresholds, a cardiac assessment and/or consultation with an oncologist should be considered before continuing treatment. See the **Appendices** section of the Clinical Pharmacy Guide, located below the modules, for a table of [Guidelines for Anthracycline Monitoring Thresholds](#). Treatment may continue beyond these thresholds in selected patients at the discretion of the treating prescriber. Addition of the cardioprotectant dexrazoxane may be considered and cardiac monitoring may be increased. The protocol or drug monograph may also suggest a maximum cumulative dose for a drug. However, maximum tolerated anthracycline doses are variable and depend on patient specific characteristics and risk factors. For example, one patient may start to exhibit symptomatic heart failure at the monitoring threshold dose, while another patient may tolerate double that dose.

Refer to the Pharmacy FAQ [Documentation for Cumulative Doses of Anthracyclines and Bleomycin](#) for more information on why and how to do the documentation on a patient chart.

Check Biosimilar Drug Selection (if applicable)

The Systemic Therapy Policy [III-190 Oncology Biosimilars Utilization](#) outlines the decision making process when choosing a biosimilar. The International Nonproprietary Name (e.g., bevacizumab) will be used to order biologic treatment. Pharmacy will select the appropriate brand, either reference or biosimilar (e.g., Avastin® or Zirabev®), and document the brand name used on the original order and drug label.

Check for Concurrent Radiation Therapy (if applicable)

In case of concurrent radiation therapy (RT), it is also important to note the start and end date of RT as chemotherapy may have to be given on specific days during RT. For example, in the [GICART](#) protocol, capecitabine is given twice daily on days with RT (Monday to Friday) whereas mitomycin is given on days 1 and 29 only. Find information on radiation therapy in **Module 6** of the [Clinical Pharmacy Guide](#).

Step 7 Review Laboratory Values

Before the first cycle of cancer drug treatment, baseline lab tests are required. Each protocol summary identifies the required lab tests that are needed for both baseline and subsequent monitoring. Monitoring lab tests in oncology patients can serve a number of functions.

Screen for Pre-existing Disease

Patients must meet the eligibility criteria for a cancer drug therapy protocol before they can start treatment. The eligibility criteria are used to help ensure that the patient receives the correct treatment for their cancer and that they have suitable baseline health and organ function to tolerate the cancer drug.

Monitor for Cancer Drug-Induced Toxicity

Lab tests are used to monitor adverse effects common to cancer drugs such as:

- Hematological toxicity
- Renal toxicity
- Liver toxicity

See *Module 3*, for detailed parameters on monitoring laboratory tests in cancer patients.

Determine the Need for Dose Modifications

Adverse effects of cancer drugs may be increased in the presence of organ dysfunction via two different mechanisms.

- Organ dysfunction can lead to reduced clearance of a drug. The resulting higher drug level can lead to increased toxicity. For example:
 - Capecitabine is excreted by the kidneys and may accumulate in the presence of renal dysfunction.
 - Docetaxel is hepatically cleared and may accumulate in the presence of hepatic dysfunction.
- Cancer drugs that cause toxicity to an organ that is already damaged can lead to further damage. For example:
 - Cisplatin may cause nephrotoxicity that could further damage already diseased kidneys.
 - Imatinib may cause hepatotoxicity that could further damage a diseased liver.

Monitor Treatment Progress

Changes in lab test results can sometimes reflect a treatment response. For example, liver function tests (LFTs) may show improvement when liver cancer is responding to treatment. Conversely, worsening LFTs may occur when liver cancer is progressing. Renal function tests may give similar clues for renal cancer. Lactate Dehydrogenase (LDH) is a non-specific test that is elevated in many cancers. Increasing LDH levels may suggest progression and decreasing levels may suggest improvement in disease. Other lab tests used to monitor progression of cancer, called tumour markers, are beyond the scope of this guide.

Timing of Laboratory Tests

The results of baseline lab tests must come from samples taken within 4 weeks of the start of Day 1 of Cycle 1 of cancer drug treatment. For all other subsequent cycles of cancer drugs, lab test results should be obtained within a reasonable amount of time from the scheduled appointment: the closer in time to the treatment date that the samples are taken, the better.

The BC Cancer Chemotherapy Protocols and Provincial Pre-printed Orders (PPPOs) that are available on the BC Cancer website specify when samples should be taken prior to the treatment date. The PPPO's were created from the protocols as a tool for the prescriber ordering cancer drugs. They can be found under each specific protocol on the BC Cancer website.

For those protocols where no PPPO or Cerner PowerPlan is available, a suggested guide to follow is:

Cycle less than 3 weeks:	Lab work acceptable within 24 hours pretreatment
Cycle of 3 weeks or longer:	Lab work acceptable within 96 hours pretreatment

For cycles of 3 weeks or longer, and a sample taken 72 or 96 hours prior to treatment which results in counts low enough to necessitate a treatment reduction or delay, a repeat blood test should be taken closer to (or on) the scheduled treatment day.

Practical Considerations

- When reviewing lab results, the pharmacist should first refer to the BC Cancer protocol to determine which lab values should be assessed. Upon review of lab values and the specific BC Cancer protocol, the pharmacist should then determine if the cancer drug is to proceed at full dose or if a dose reduction is required.
- Prescribers can include an order stating, "Proceed with treatment based on blood work from (XXXX date)", to specify use of older lab results. Note – this order is intended to avoid needing a separate communication order due to the lab date being outside of the required timeframe. It does **not** authorize using lab results that fall outside of protocol parameters. Any lab results that do not meet protocol

parameters will still need clarification with the prescriber.

- If a lab result does not meet protocol parameters (e.g., ANC 1.3 when 1.5 is required), the pharmacist should check the order to see if proceeding with treatment as ordered despite this result was clearly indicated. If not, the pharmacist must contact the prescriber to clarify the plan – whether to repeat labs, delay treatment and/or adjust doses, or proceed as prescribed based on clinical judgement. A clear communication order detailing the lab result and plan will be needed per site standards.

Step 8 Verify Appropriate Method of Drug Delivery

Cancer drugs can be administered in a variety of ways. The most common routes of administration are the oral, intravenous and subcutaneous routes.

Oral Administration

Consideration should be given to a patient's ability to swallow, especially in the case of large tablets or capsules. For example, a patient who has difficulty swallowing may tolerate intravenous fluorouracil better than oral capecitabine.

Patients that require medications to be given by feeding tube should not be given oral drugs unsuitable for administration by this route. Crushing or compounding enteric-coated or sustained-release dosage forms damages the integrity of the dosage form and can affect the drug's absorption and effectiveness.

Medications that are considered to be cytotoxic or hazardous ideally should only be crushed or compounded in a containment cabinet such as a Biological Safety Cabinet. If patients or caregivers crush them at home, they risk exposure to the cytotoxic or hazardous drug because of powder generated by crushing. Some cancer medications can be dissolved if patients are unable to swallow, using different methods and solutions depending on the evidence. For example, the Cancer Drug Manual capecitabine monograph includes directions on how to dissolve these tablets in water for patients who cannot swallow them whole. The BC Cancer patient handout Handling Cancer Drugs and Body Fluids in the Home provides patients with direction on what precautions to take when handling cancer medication.

Please see [Medications by NG Tube](#) found under **Cancer Drug Preparation and Administration** in the Pharmacy [Frequently Asked Questions](#) for more information on administering medications by feeding tube.

Parenteral Administration

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

Drugs for intravenous administration may be given by intravenous (IV) push, intermittent infusion, or continuous infusion. Selecting the correct method and rate of administration helps to ensure patient comfort and adequate absorption of cancer drugs. IV drugs may be prepared in syringes, infusion bags, or specialty infusion devices such as disposable elastomeric infusors. Module 4 [Parenteral Drug Delivery](#) has information on selecting the correct route of administration and method for preparing intravenous drugs.

Subcutaneous administration is a convenient and rapid route of administration. Major advantages of providing treatment by this route are less time in the chemotherapy chair and, depending on the medication, the possibility of administration at home (e.g., subcutaneous cytarabine). Examples of drugs that were given IV routinely in the past, but are now being administered more commonly subcutaneously include bortezomib, daratumumab and rituximab.

Step 9 Monitor for Potential Cancer Drug Toxicity

Cancer drug toxicities that require monitoring are outlined in the chemotherapy protocols, protocol-specific patient handouts, and drug-specific patient handouts. The handouts can be used as guides to counsel patients about adverse effects. The patient should be assessed for adverse effects at each clinic visit. The protocol and patient handout can be used as an aid for assessing adverse effects. They provide recommended interventions based on the severity of adverse effect. Nursing [Symptom Management Guidelines](#) are also available on the BC Cancer website.

Step 10 Verify Protocol-Related Supportive Care Provided

Medications

Supportive medications are ordered with cancer drugs in the form of parenteral and/or oral therapies that are administered either at the treatment facility or as take-home medications. Ensure that there are orders written for any take home medications required by the protocol for prevention or management of adverse effects. It is important to refer to the protocol rather than the PPPO because not all take-home medications may be indicated on the PPPO. Some of the medications used for managing adverse effects include antinauseants, antibiotics, and growth factors. These medications are generally used to treat adverse effects rather than prevent them, although some may be used for both (i.e., antinauseants). See Module 5 Supportive Care Medication for more information about these medications.

Step 11 Counsel Patients

Patients receiving take home medications only, or take home medications as a part of their treatment protocol, must be counselled by a Pharmacist at each dispense. Patient education handouts should be provided as deemed necessary. See the Cancer Drug Manual Drug Index for BC Cancer drug-specific patient handouts. See the Chemotherapy Protocols for protocol-specific (if available) patient handouts. See the Symptom & Side Effect Management Resource Guide for links to various other supportive care handouts.