Clinical Pharmacy Guide: Chemotherapy Assessment and Review 4th Edition

Chemotherapy Order Assessment and Review

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Introduction

The following steps are recommended when checking chemotherapy 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 chemotherapy. Consideration should be given to following the checking steps for topical chemotherapy where systemic absorption may result in changes in laboratory values or other adverse effects. A simplified checklist of this procedure can be found in the *Clinical Chemotherapy Assessment and Review Checklist* located in Appendices section, located below the modules. A *Final Compounded Chemotherapy 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 Agency/Hospital/PHN)
- Date of Birth

Patients must be positively identified when receiving outpatient medications per *III-30-05 Patient Identifiers for Outpatient Dispensing* [Safe Handling Manual – Module 2, Directives].

**Step 2: Confirm Protocol Matches Clinical Indication and Eligibility for Treatment**

- Patient meets eligibility 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 or for treatments that are not covered by an existing protocol.
Step 3: Review Medical History for Potential Interactions and Allergies

Obtain a current list of medications that the patient is taking, including prescription drugs, non-prescription medications, and Complementary and Alternative Medications (CAMs). Check to see if any of these medications interact with the chemotherapy ordered. The BC Cancer Agency 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® and Lexicomp®. The Complementary and Alternative Medications (CAMs) section of the BC Cancer Agency Website can also be consulted.

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

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 Agency protocols. This information is located below the treatment section of the protocol or in the CAP approval.

Remember to check the total 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 chemotherapy, 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. This treatment interval is specified in each protocol and should be followed as outlined in the treatment schema. It should be checked with each chemotherapy 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; for patients on the CNCCNU protocol, treatments are given as a single dose, once every 6 weeks.

When a chemotherapy 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 chemotherapy.
- 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 Patients over Statutory Holidays [Systemic Therapy - Policies & Procedures] for a suggested guideline for scheduling patients over statutory holidays.

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

**Step 5: Determine Patient’s Body Surface Area (if applicable)**

Dosage calculations for the majority of cytotoxic chemotherapeutic agents 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. BSA is calculated for any chemotherapy where the dose is based on BSA. While the dosing of some cytotoxic chemotherapy 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). (See information on CARBOplatin dosing in Module 3 – Renal Function Tests).
Methods for Determining BSA

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

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

Average BSA for an adult male: 1.9 m$^2$
Average BSA for an adult female: 1.6 m$^2$

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

- 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 will find 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 Agency website.

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, the BC Cancer Agency has set the following recommendations.

**Policy III-10 – Systemic Therapy Delivery Process** [Systemic Therapy - Policies & Procedures] (excerpt):

Body Surface Area calculations are based on actual body weight for all medical oncology protocols. **Exception:** BSA calculations for acute leukemia protocols and for peripheral blood stem cell or bone marrow transplants supported high dose protocols are based on ideal weight when specified in the protocol.
Capping BSA and Chemotherapy Doses

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

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

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

Practical Considerations

- The patient should be weighed and his/her BSA calculated for the first treatment of the chemotherapy protocol. As per Policy III-10 Systemic Therapy Delivery Process [Systemic Therapy - Policies & Procedures], subsequent BSA recalculation will be done only if, in the physician’s opinion, it is warranted by a change in the clinical status of the patient.
- A maximum of 5% variance in dosage calculation is permitted (as per III-10 Systemic Therapy Delivery Process [Systemic Therapy - Policies & Procedures]). 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 chemotherapy doses. The Mosteller formula has been adopted as the BC Cancer Agency standard when calculating BSA.
- When selecting the method of BSA determination, it is important to
consider the potential limitations of each method, especially when dealing with patients whose body type may be outside the normal range (e.g., obese patients).

- A slide rule is not recommended as the first choice when determining a patient's BSA due to the following limitations:
  - The method is subjective (results may be rounded up or down)
  - Commercially available slide rules employ a number of different BSA formulas. These may lead to conflicting results if more than one type is used in the same institution.
- However, if it is determined that a slide rule is an acceptable method of BSA determination within your institution, only one type or brand should be used, to ensure consistency. The pharmacist should confirm that the slide rule is based on a known and accepted BSA formula and should establish guidelines which address the "rounding" of BSA values. This will help to reduce the limitations of slide rules mentioned above.

Step 6: Check Appropriateness of Chemotherapy Dose(s)

Upon receipt of the chemotherapy order, the pharmacist should verify the doses written by the physician. Most chemotherapy requires dose calculations based on BSA. Chemotherapy doses may also be determined by other patient-specific factors such as weight (e.g., trastuzumab) or renal function (e.g., CARBOplatin). Some chemotherapy does not require dose calculations (e.g., erlotinib). The BC Cancer Agency 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 the BC Cancer Agency. Refer to III-140 Dose Banded Chemotherapy Treatments [Systemic Therapy - Policies & Procedures] for further information about dose banding.

Policy III-10 Systemic Therapy Delivery Process [Systemic Therapy - Policies & Procedures] permits a maximum of 5% variance in dosage calculation. If the pharmacist's calculated doses differ from the physician's orders by more than this 5% allowable variance, the physician should be contacted regarding this discrepancy and the doses reconfirmed.

If the chemotherapy doses are to be administered as ordered, the pharmacist should place a note clarifying this in the patient's chart.

If, after consultation with the physician, it is determined that a change in dose(s) is required, the physician must either write a new chemotherapy order or make
amendments to the existing order, signing and dating the order in which the changes are required. Verbal orders are not accepted.

Check Maximum Cumulative Doses (if applicable)

Some cytotoxic agents, such as bleomycin and the anthracyclines, have a suggested maximum lifetime dose 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, and those with previous bleomycin treatments within 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 his/her lifetime. When the maximum cumulative dose is reached, a cardiac assessment and/or consultation with an oncologist should be considered before continuing treatment. See the Appendices section, located below the modules, for a table of Guidelines for Anthracycline Monitoring Threshold.

Step 7: Review Laboratory Values

Before the first cycle of chemotherapy 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 serves the following functions:
A. Screen for Preexisting Disease

Patients must meet the eligibility criteria for a chemotherapy 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 chemotherapy.

B. Monitor for Chemotherapy-Induced Toxicity

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

- Hematological toxicity
- Renal toxicity
- Liver toxicity

See Module 3, located below this module, for detailed parameters for monitoring laboratory tests in chemotherapy patients.

C. Determine the Need for Dose Modifications

Adverse effects of chemotherapy 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:
  - Gemcitabine is eliminated 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.
- Chemotherapy that causes organ toxicity to an organ that is already damaged can lead to further damage. For example:
  - CIPLatin may cause nephrotoxicity that could further damage already diseased kidneys.
  - Imatinib may cause hepatotoxicity that could further damage a diseased liver.

D. 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 suggest improvement in disease. Other lab tests used to monitor progression of cancer, called tumor 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 chemotherapy. For all other subsequent cycles of chemotherapy, 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 Agency Chemotherapy Protocols and Preprinted Orders (PPOs) that are available on the BC Cancer Agency website specify when samples should be taken prior to the treatment date. The PPO’s were created from the protocols as a tool for the physician ordering chemotherapy. They can be found under each specific protocol on the BC Cancer Agency website.

For those protocols where no PPO 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, 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.

When reviewing lab results, the pharmacist should first refer to the BC Cancer Agency protocol to determine which lab values should be assessed. Upon review of lab values and the specific BC Cancer Agency protocol, the pharmacist should then determine if chemotherapy is to proceed at full dose or if a dose reduction is required.
Step 8: Verify Appropriate Method of Drug Delivery

Chemotherapy drugs can be administered in a variety of ways. The most common routes of administration are the oral or intravenous 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 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. Please see Medications by NG Tube for more information on medications by feeding tube.

Intravenous Administration

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 chemotherapy. IV drugs may be prepared in syringes, infusion bags, or specialty infusion devices such as disposable elastomeric infusors. See Module 4 - Parenteral Drug Delivery for more information on selecting the correct route of administration and method for preparing the parenteral drugs.

Step 9: Monitor for Potential Chemotherapy Toxicity

Chemotherapy 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 on each clinic visit. The protocol can be used as an aid for assessing adverse effects. It provides
recommended interventions based on the severity of adverse effect. *Symptom Management Guidelines* [Symptom Management] are also available on the BC Cancer Agency website.

Step 10: Verify Protocol-Related Supportive Care Provided

Medications

Supportive medications are ordered with chemotherapy 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 chemotherapy protocol for management of adverse effects. It is important to refer to the protocol rather than the PPO because not all take home medication may be indicated on the PPO. 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 Medications* for more information about these medications.