



Example Case Studies

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Example Case Studies

The following case studies demonstrate a systematic approach to the clinical review and assessment of cancer drug orders using *Appendix A: Clinical Cancer Drug Order Review Checklist*. Summaries of all BC Cancer treatment protocols and preprinted orders can be found on the BC Cancer website (www.bccancer.bc.ca) under **Chemotherapy Protocols**.

Example Case Study 1a: BRAJFEC

Patient D.N. (BC Cancer ID #20-45678) is a 48-year-old female in good health, recently diagnosed with breast cancer. The pathology report indicates: invasive lobular carcinoma, high risk, Grade 3, tumor size 2.5 cm, no lymphovascular invasion (0/11 lymph nodes involved), estrogen and progesterone receptor positive (3+/3+), HER2 negative. D.N. has had a mastectomy and is scheduled for cancer treatment.

She arrives in preparation for treatment to start on May 27. She had baseline blood tests performed at an outside lab 2 weeks ago, as follows:

Lab results - May 12

WBC	5.3	Bilirubin	12	LDH	409
ANC	4	Creatinine	55	GGT	29
Hgb	120	Alk Phos	93		
Platelets	320	AST	35		

Pharmacy received a **written** order on a BRAJFEC preprinted order sheet:

Epirubicin 160 mg IV push
Fluorouracil 800 mg IV push
Cyclophosphamide 800 mg IV in 100 to 250mL NS over 20 to 60 minutes

BSA calculated by the ordering physician is 1.65 m² (see height and weight given in Step 1 on the following page).



Step 1: Verify Patient Identity

Two identifiers were used to confirm that the order was written for the correct patient: name (D.N.) and BC Cancer ID number (20-45678). The BC Cancer ID number verifies that D.N. is registered with BC Cancer. If a BC Cancer ID number is not available, the pharmacist should check with the ordering prescriber or the BC Cancer Registry (604-877-6000 x 674610) to determine whether it has been issued. A BC Cancer ID number is required before BC Cancer benefit drugs are dispensed.

Date of birth, allergy status and pregnancy status should be confirmed at this time.

The current height and weight are also necessary for calculation of BSA and cancer treatment dose. The following height and weight were documented in the patient chart on May 26:

Height: 5'5" (165.1 cm)

Weight: 130 lb (59.1 kg)

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

BRAJFEC is a BC Cancer protocol currently in use as adjuvant therapy for breast cancer patients. A current version of this protocol can be found on the BC Cancer website. Before proceeding, always check that the version you are using is the most current. The revision dates are found in the footer, and on the last page of the protocol. It is possible that the protocols themselves may be changed during the course of a patient's treatment. Changes to protocols are announced monthly in the [Systemic Therapy Update](#) newsletter.

The "AJ" in the protocol name indicates that this is an adjuvant treatment, used in combination with surgery or radiation. This protocol has a curative intent.



Determine diagnosis

This information should be available in the chart. If a chart is not available, you may wish to contact the ordering prescriber to confirm that the protocol chosen is consistent with the diagnosis.

In this example, D.N. is diagnosed with breast cancer, with no axillary lymph node involvement.

Does the diagnosis match the eligibility requirements for the protocol?

To be eligible for this treatment, patients must be less than or equal to 60 years of age or a fit patient greater than 60 years of age, with one or more axillary lymph node metastasis(es). Patients may also have high risk, node negative disease to qualify for this protocol.

D.N. is less than 60 years old (48) with high risk disease, and no lymph node involvement. She is in good health and does not have any significant heart disease (an exclusion factor for this protocol). Therefore, the treatment protocol is appropriate for the diagnosis.

The title of the protocol and the “BR” at the beginning of the protocol code indicate that this treatment is for breast cancer so you can proceed with checking the rest of the order. If a lung protocol had been ordered, further investigation would be required (i.e., the prescriber would have to be contacted because the wrong protocol had been ordered, or perhaps the order had been written for the wrong patient).

Benefit status requirements

Is the protocol ordered Class I or Restricted Funding (R)? Protocols with a restricted funding designation require CAP approval through the BC Cancer Compassionate Access Program **prior** to initiation of therapy. Protocols and preprinted orders indicate when CAP approval is required. The ***Benefit Drug List*** [Systemic Therapy - Reimbursement & Forms] also indicates the designation for each drug and protocol. Protocol codes are required at the time of drug order entry.



Because D.N. is a registered BC Cancer patient and is a resident of British Columbia, medications for treatment of her cancer are benefits of the BC Cancer Systemic Therapy Program. The cancer drugs to be administered in this protocol (epirubicin, fluorouracil and cyclophosphamide) are all Class I drugs and the cancer drug protocol does not require any extra documentation regarding benefit status.

Step 3: Review Medical History

D.N. is not currently taking any medications or complementary/alternative medicines. Her past medical history is unremarkable. She does not have any known allergies. She will need to have a negative pregnancy test prior to start of her cancer drug treatment (see Assessment of Patient Pregnancy Status: Female Sex Patients Policy).

Step 4: Check Timing of Treatment

D.N. has had no previous treatment for breast cancer. Her first treatment date will be May 27, which will be Day 1 of Cycle 1.

Step 5: Determine Patient's Body Surface Area

Calculate the patient's body surface area, using the Mosteller formula:

$$\begin{aligned} \text{BSA (m}^2\text{)} &= \sqrt{\frac{\text{height(cm)} \cdot \text{weight(kg)}}{3600}} \\ &= \sqrt{\frac{165.1\text{cm} \cdot 59.1\text{kg}}{3600}} \\ &= 1.65 \text{ m}^2 \end{aligned}$$

Ensure that the body weight and height are the most recent results.



Step 6: Check Appropriateness of Cancer Drug Dose(s)

Calculation of doses for Cycle 1:

$$\text{Epirubicin: } 100 \text{ mg/m}^2 \times 1.65 \text{ m}^2 = 165 \text{ mg IV}$$

$$\text{Fluorouracil: } 500 \text{ mg/m}^2 \times 1.65 \text{ m}^2 = 825 \text{ mg IV}$$

$$\text{Cyclophosphamide: } 500 \text{ mg/m}^2 \times 1.65 \text{ m}^2 = 825 \text{ mg IV}$$

These calculated doses are within 5% of the doses ordered by the prescriber so the prescriber's orders are acceptable and can be processed as written. If there was a variance of greater than 5%, the prescriber must be contacted and the discrepancy resolved.

Doses administered must be documented on the patient chart as well as on the pharmacy record.

The maximum cumulative dose for epirubicin is 720 – 1000 mg/m² according to the BC Cancer epirubicin monograph. The BRAJFEC protocol, however, specifies a maximum of 720 mg/m², so this value will be used. For D.N., this would be 720 mg/m² x 1.65 m² = 1188 mg. If the patient received the full six cycles of treatment at full dose, the total epirubicin administered would be 990 mg, which is within the maximum cumulative dose guideline. She has not received any prior cancer drug treatment.

Step 7: Review Laboratory Values

Lab tests are performed routinely throughout treatment, depending on the protocol. In this example, there are baseline tests (i.e., prior to the initiation of treatment), tests before each treatment and tests done if clinically indicated.

D.N. has lab results dated May 12. These baseline tests have been ordered, as outlined in the protocol. The lab work is acceptable because it was drawn within 4 weeks of starting treatment.

Comparison of lab tests to protocol

D.N.'s lab results are within normal limits so treatment can proceed as ordered.



Step 8: Verify Appropriate Method of Drug Delivery

Prepare and administer as per protocol, following sterile technique and safe handling procedures for hazardous drugs. As indicated in the BRAJFEC protocol, epirubicin and fluorouracil are dispensed in a syringe and given as IV push. Cyclophosphamide for IV infusion is dispensed in a 100 mL Normal Saline minibag for doses less than or equal to 1000 mg.

Step 9: Monitor for Potential Cancer Drug Toxicity

Epirubicin is a vesicant, so the pharmacy and nursing staff should review Policy ***III-20 Chemotherapy Extravasation*** [Systemic Therapy - Policies & Procedures] prior to administration.

Step 10: Verify Protocol-Related Supportive Care Provided

Antiemetics

The protocol specifies an antiemetic regimen for highly emetogenic chemotherapy (SCNAUSEA). The patient should have been given prescriptions for NK₁ and 5-HT₃ antagonists (either Akynzeo® or aprepitant plus ondansetron), dexamethasone, and either olanzapine, prochlorperazine or metoclopramide. These are not supplied by BC Cancer and should be filled at a community retail pharmacy.

Filgrastim (G-CSF)

If the patient develops febrile neutropenia while on this protocol, there is an option for the patient to start filgrastim (G-CSF). If the prescriber chooses that option, a completed Filgrastim Special Authority Request Form [Systemic Therapy - Reimbursement & Forms] must be submitted to Pharmacare for outpatients. Please note that for outpatient use, the cost of filgrastim is not reimbursed by BC Cancer. Filgrastim (G-CSF) usage Forms are no longer required for inpatients. Instead, the indication for filgrastim is filled in at the time of OSCAR billing for CON hospitals.



Resources

Information for Patients

Information for the patient on the above medications can be found on the BC Cancer website under:

- [BRAJFEC Patient Handout](#)
- Cancer Drug Manual [[Drug Index](#)]
 - Cyclophosphamide
 - Epirubicin
 - Fluorouracil
- **Nausea and Vomiting** [[Pharmacy Symptom and Side Effect Management Resource Guide](#)]
 - SCNAUSEA for antiemetics (Akynzeo®, aprepitant, ondansetron, dexamethasone),
 - How to control nausea

The pharmacist is encouraged to review this information with the patient.

Information for Health Professionals

Information for health professionals on the above medications can also be found on the BC Cancer website:

- [BRAJFEC Patient Handout and Protocol](#)
- Cancer Drug Manual [[Drug Index](#)]
- **Chemotherapy Preparation and Stability Chart – Drugs A to K** [[Cancer Drug Manual](#)]
- [SCNAUSEA](#)



Subsequent Doses

Cycle 2: First occurrence of low counts, no febrile neutropenia

D.N. returns on June 17 for her second cycle of BRAJFEC. She complains of some mild fatigue but no episodes of fever. Her weight remains at 59 kg. Subsequent BSA recalculations will be done only if, in the prescriber's opinion, it is warranted by a change in the clinical status of the patient, or if there was a weight change significant enough that it results in a dose variance of greater than 5%, or if there has been a weight change of greater than 10% from cycle 1 of this regimen.

BRAJFEC orders written on June 14 (during the oncologist appointment) for administration on June 17:

Epirubicin 160 mg IV push
Fluorouracil 800 mg IV push
Cyclophosphamide 800 mg IV in 100 to 250 mL NS over 20 to 60 minutes

Due to scheduling, patients may be seen several days prior to their cancer drug administration date, with blood work ordered either prior to or on the day of treatment.

In this case, the prescriber ordered bloodwork for the day of treatment. Generally, the patients are asked to go to the laboratory at least one to two hours prior to their treatment time to allow time for the lab to process and report the results.

<u>Lab results – June 17</u>			
WBC	2	Bilirubin	12
ANC	1.3	Creatinine	55
Hgb	115		
Platelets	80		



This is Cycle 2 of the same protocol that the patient had last time, so begin the clinical check by considering the timing of the treatment (time interval between cycle 1 and cycle 2).

BRAJFEC protocol indicates that this treatment is to be given every 21 days. June 17 is 3 weeks (21 days) from Day 1 of Cycle 1, so the timing of the appointment is appropriate.

Lab work was drawn that morning so timing of lab results is acceptable. However, D.N.'s ANC is low (less than 1.5) and her platelets are low (less than 100). A review of the protocol indicates that the treatment should be delayed by one week. This necessitates a call to the ordering prescriber for further discussion.

Results

The prescriber writes orders to delay treatment for one week and D.N. is rescheduled to begin Cycle 2 on June 24. Orders for lab work and future appointments are adjusted accordingly. Documentation of this change is recorded on the patient's chart and the pharmacy treatment record. Include a reason for the change in the documentation, as this may influence future treatment decisions.

BRAJFEC orders for administration June 24:

Epirubicin	160 mg IV push
Fluorouracil	800 mg IV push
Cyclophosphamide	800 mg IV in 100 to 250 mL NS over 20 to 60 minutes

Timing of appointment is appropriate (delay of one week from previously scheduled date).

- Lab work is within acceptable parameters, i.e., ANC has recovered to greater than or equal to 1.5 and platelets to greater than or equal to 100.
- Doses are within 5% of calculated doses for this protocol.
- According to the *Dose Modifications* Section of the protocol, D.N. can receive 100% of the previous cycle's dose.



Doses can be prepared and administered to patient as ordered; treatment documented in patient's chart and pharmacy preparation record.

Cycle 3: Second occurrence of low counts, no febrile neutropenia

D.N. returns on July 15 for Cycle 3 and again, her counts are low. A new order is written to delay her treatment by one week.

<u>Lab results – July 15</u>			
WBC	2.1	Bilirubin	12
ANC	0.95	Creatinine	55
Hgb	115		
Platelets	83		

D.N. returns on July 22. No episodes of fever; reports moderate fatigue. Timing of appointment is appropriate as ordered. No new labs have been done since July 15. The prescriber is contacted to order bloodwork for July 22.

Lab results and BRAJFEC protocol orders for July 22 are:

<u>Lab results – July 22</u>			
WBC	3.9	Bilirubin	12
ANC	1.6	Creatinine	55
Hgb	115		
Platelets	103		

Since this delay was after the second occurrence of low counts, the prescriber has ordered 75% of the previous cycle dose per the protocol's *Dose*

Modification section:

Epirubicin	120 mg IV push
Fluorouracil	600 mg IV push



Cyclophosphamide 600 mg IV in 100 to 250 mL NS over 20 to 60 minutes

All written doses are acceptable, so medication may be prepared and administered as ordered and documentation completed as in previous cycles.

Cycle 4

D.N. returns for Cycle 4 on August 12 and lab tests are ordered that morning.

BRAJFEC protocol orders for August 12 are:

Epirubicin	120 mg IV push
Fluorouracil	600 mg IV push
Cyclophosphamide	600 mg IV in 100 to 250 mL NS over 20 to 60 minutes

The treatment interval and lab results are appropriate and bloodwork is within acceptable limits. The patient had a 75% dose reduction in the previous cycle and will continue further cycles at this dose.

Doses are prepared and administered as ordered. Documentation is completed.

Cycles 5 and 6

D.N. does not experience any other treatment delays for the remaining two cycles of this protocol.

Note: if the prescriber were to order a 7th cycle, prior approval from the **Compassionate Access Program** [[Systemic Therapy](#)] would be required as the protocol indicates a total of 6 cycles only under the *Treatment* section. Approval must be granted before the patient is eligible to receive further treatment.

Example Case Study 1b: BRAVDOC

Four years later, D.N., now 52 years old, returns complaining of bone pain and shortness of breath. A diagnosis of metastatic disease with pulmonary and osseous involvement is confirmed by CT and bone scan. She is scheduled to receive cancer drug treatment with the BRAVDOC protocol on May 22.



<u>Lab work – May 8</u> (2 weeks prior to first cycle of treatment)			
WBC	7	Bilirubin	10
ANC	3.9	Alk Phos	69
Hgb	128	ALT	24
Platelets	216	AST	30

Written orders received on a BC Cancer preprinted order.

Treatment plan: Docetaxel 155 mg IV every 21days, as indicated in the BRAVDOC protocol.

Step 1: Verify Patient Identity

D.N. is still a B.C. resident and retains her previously assigned BC Cancer ID number (20-45678). Patient-specific information: height 165 cm, weight 115 lbs (52.3 kg), as of May 8. Her ECOG performance status is 1. Confirm allergy status (any new allergies since last treatment) as well as pregnancy status again.

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

BRAVDOC is a BC Cancer protocol used for treatment of advanced breast cancer. The current version of this protocol can be found on the BC Cancer website. Once again, ensure that you are using the most current version.

The “AV” in the protocol name indicates that this is treatment for advanced, metastatic cancer.

Determine diagnosis

D.N. was treated with 6 cycles of BRAJFEC four years ago, for primary treatment of breast cancer. Diagnosis for metastatic disease has been confirmed by a bone scan (osseous involvement) and CT scan (pulmonary involvement).



Does the diagnosis match the eligibility requirements for the protocol?

In the eligibility section of the BRAVDOC protocol, there is a list of approved indications for the use of this protocol. D.N. is eligible for this treatment based on a diagnosis of metastatic breast cancer, ECOG status of 1, and a life expectancy greater than 3 months.

Benefit status requirements

The first 8 cycles of the BRAVDOC protocol has a Class I indication; however further cycles would require approval from the **Compassionate Access Program** [Systemic Therapy] prior to the patient receiving cycle 9.

Step 3: Review Medical History

D.N. does not take other medications or complementary/alternative medicines. She does not have any known allergies. She will need to have a negative pregnancy test prior to start of her cancer drug treatment.

Step 4: Check Timing of Treatment

Previous treatment was four years ago. This is her first cycle of treatment for relapse. Her first treatment date will be May 22.

Step 5: Determine Patient's Body Surface Area

Calculate body surface area using the Mosteller formula:

$$\begin{aligned} \text{BSA (m}^2\text{)} &= \sqrt{\frac{\text{height(cm)} \cdot \text{weight(kg)}}{3600}} \\ &= \sqrt{\frac{165\text{cm} \cdot 52.3\text{kg}}{3600}} \end{aligned}$$



$$= 1.55 \text{ m}^2$$

Step 6: Check Appropriateness of Cancer Drug Dose(s)

Dose calculation for Cycle 1:

Using 100 mg/m^2 , as indicated in the BRAVDOC protocol, the docetaxel dose is calculated to be 155 mg, as prescribed. There is no variance in the dose, therefore proceed with checking the lab work.

Dose administered should be documented on the pharmacy treatment record.

Docetaxel does not require monitoring for cumulative dosing.

Step 7: Review Laboratory Values

Lab work for current treatment is from 2 weeks ago. The lab work is acceptable because it was drawn within 4 weeks of starting treatment. All baseline tests have been ordered.

Comparison of lab tests to protocol

All lab values fall within normal range so treatment can proceed as ordered.

Step 8: Verify Appropriate Method of Drug Delivery

The protocol states that if the dose is between 75 – 185 mg, a 250 mL non-DEHP bag is used.

Step 9: Monitor for Potential Cancer Drug Toxicity

The duration of infusion for docetaxel is designated as 1 hour; however, there are precautions, due to infusion-related reactions. For docetaxel, a physician must remain on site for 30 minutes following the start of the infusion for every treatment. Refer to Policy ***III-60 Drug Reaction Management – Physician Coverage During Delivery of Selected Systemic Therapy Drugs*** [[Systemic Therapy - Policies & Procedures](#)] for more information. Although this is not directly a pharmacy consideration, pharmacists should be aware of these



precautions. Treatment appointments must be scheduled during a time when a physician is present in the facility.

Docetaxel is an irritant and can cause pain and local tissue necrosis if extravasated, as indicated under *Precautions* section in the protocol and policy ***III-20 Chemotherapy Extravasation*** [Systemic Therapy - Policies & Procedures] Prevention and Management of Extravasation of Chemotherapy.

Docetaxel-induced onycholysis (nail changes) and cutaneous toxicity of the hands may be prevented by wearing frozen gloves starting 15 minutes before docetaxel infusion and continuing for 15 minutes following the docetaxel infusion. Frozen gloves should be replaced after 45 minutes of wearing to ensure that the hands remain cold during the entire docetaxel infusion.

Step 10: Verify Protocol-Related Supportive Care Provided

Dexamethasone is given to reduce fluid retention and to reduce the severity of the infusion-related reactions as well as cutaneous toxicity associated with docetaxel administration.

As specified in the protocol, the dexamethasone dose is 8 mg PO BID for 3 days, starting one day prior to each docetaxel administration. Patient must receive a minimum of 3 doses prior to treatment. Pharmacy staff may wish to have confirmation that the patient has taken their premedications appropriately, prior to preparing the cancer drug treatment.

Supportive care medications are not reimbursed by BC Cancer, and should be obtained from a community retail pharmacy. Additional antiemetics are not usually required with this protocol.

Resources

Information on the BRAVDOC protocol and on docetaxel can be found on the BC Cancer website under:

- [BRAVDOC Patient Handout and Chemotherapy Protocol](#)
- [Docetaxel Drug Monograph](#)

Subsequent Doses

D.N. continues treatment and is now at her third cycle. She presents 21 days following her 2nd cycle, on July 3, with lab work taken the same day.

<u>Lab results – July 3</u>			
WBC	2.5	Hgb	116
ANC	0.93	Platelets	103

Treatment is delayed for 1 week due to low ANC, with lab work reordered, including liver enzymes.

D.N. returns 1 week later, July 10, with the following lab work:

<u>Lab results – July 10</u>			
WBC	3.3	Alk Phos	257
ANC	1.4	ALT	123
Hgb	118	AST	88
Platelets	140	Bilirubin	20

Her weight has decreased to 50 kg; however, recalculation of BSA is not required, so the BSA remains (1.55 m²) as previously calculated by the prescriber.

A dose reduction of 75% is ordered, at 116 mg, due to continued low ANC, and an elevation of hepatic enzymes.

D.N. continues treatment without delay or any further dose reductions. She receives a total of 8 cycles, as indicated in the treatment protocol.

Note: if the prescriber were to order a 9th cycle, this would require approval from the **Compassionate Access Program** [[Systemic Therapy](#)]. Approval must be granted *prior* to the patient receiving cycle 9.

Example Case Study 2: Oral Cancer Drug Treatment with LUVERL

Patient B.B. (BC Cancer ID #19-12345) is a 69-year-old female non-smoker, who has recently been diagnosed with metastatic lung adenocarcinoma. She arrives on June 21 in pharmacy with a prescription for erlotinib.

She had baseline blood tests performed at an outside lab 2 weeks ago, as follows:

<u>Lab results - June 7</u>					
WBC	4.4	Bilirubin	4	GGT	16
ANC	2.8	Creatinine	63	LDH	231
Hgb	131	Alk Phos	135	Albumin	39
Platelets	312	AST	25	CRP	1

Pharmacy has received a written order on a BC Cancer preprinted order for the LUVERL protocol requesting the following:

Erlotinib 150 mg PO daily for 28 days

Step 1: Verify Patient Identity

Has the patient been registered with BC Cancer? B.B has a BC Cancer ID number (19-12345) and is therefore a registered patient with BC Cancer.

Date of birth and allergy status should be confirmed at this time.

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

LUVERL is a BC Cancer protocol currently in use for treatment of advanced Non-Small Cell lung cancer (NSCLC). The most current version of this protocol is found on the BC Cancer website. Before proceeding, ensure that you are referring to the most current version of the protocol and the preprinted order.



“AV” in the protocol name indicates that this is treatment for advanced, metastatic cancer. This information should be available in the chart. If a chart is not available, you may wish to contact the ordering prescriber to confirm that those written orders are consistent with the indication on the protocol.

In this example, B.B. is diagnosed with metastatic lung adenocarcinoma which is a non-small cell lung cancer (NSCLC).

The protocol eligibility section indicates that patients must have progressive disease on or after first- or second-line therapy for advanced NSCLC. B.B.’s medication history indicates that she was previously on carboplatin and gemcitabine (LUAVPG). Her disease progressed (worsened) after 4 cycles.

Is erlotinib Class I, or does it require CAP approval? The LUAVERL protocol indicates that erlotinib for second or third line treatment of metastatic NSCLC is Class I. This information can also be confirmed using the BC Cancer [Benefit Drug List](#).

Erlotinib is being used as a second line agent for B.B., so it is considered Class I. Therefore, this protocol does not require any extra documentation regarding benefit status. If erlotinib had been prescribed for first line therapy, approval would have been required from the BC Cancer Compassionate Access Program (CAP) before the patient started treatment.

Because B.B. is a registered patient with BC Cancer and is a resident of British Columbia, erlotinib, for treatment of her cancer is eligible for reimbursement through the BC Cancer Systemic Therapy Program.

Step 3: Review Medical History

According to B.B.’s PharmaNet profile, she is currently taking levothyroxine, allopurinol, simvastatin, dexamethasone, ramipril and oxazepam. According to the drug interactions section of the erlotinib monograph, dexamethasone is a CYP3A4 inducer and may increase the metabolism of erlotinib (reduce therapeutic effect of erlotinib). A call to the ordering prescriber is required. She does not have any known allergies. She is not required to do a pregnancy test prior to start of her cancer drug therapy.



Results

The ordering prescriber discontinues dexamethasone and since B.B. had only been taking dexamethasone short term for cough, dose tapering is not required.

B.B. is counselled to avoid grapefruit and grapefruit juice because it can increase the serum erlotinib concentration by inhibiting CYP3A4 enzymes in the liver.

Step 4: Check Timing of Treatment

B.B. received her last treatment with LUAVPG on May 3. Her first dose of erlotinib will be on June 21, which will be Day 1 of Cycle 1 for this new treatment. The planned schedule is appropriate.

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

A BSA calculation is not necessary since erlotinib dosing is not based on BSA.

Step 6: Check Appropriateness of Cancer Drug Dose(s)

The dose written for erlotinib is 150 mg daily, which is the correct starting dose according to the protocol.

Step 7: Review Laboratory Values

Lab tests are performed at various times throughout treatment, depending on the protocol. In this example, there are baseline tests (i.e., prior to the initiation of treatment), tests two weeks after initiation of therapy and tests before each subsequent visit. B.B. has lab results dated June 7. These baseline tests have been ordered, as outlined in the protocol. The lab work is acceptable because it was drawn within 4 weeks of starting treatment.

All of B.B.'s lab results are within normal limits so treatment can proceed as ordered.



Step 8: Verify Appropriate Method of Drug Delivery

B.B. has no problems swallowing tablets, so erlotinib oral tablets are a suitable dosage form.

Step 9: Monitor for Cancer Drug Toxicity

The pharmacist used the BC Cancer patient handout for erlotinib to counsel B.B. regarding administration instructions, precautions and common side effects, including nausea/vomiting, diarrhea, skin rash, sore mouth and fatigue.

Step 10: Verify Protocol-Related Supportive Care Provided

The erlotinib monograph indicates that the emetogenic classification is rare. No antiemetic prescription is required. However, the ordering prescriber may prescribe them if they feel the patient is at risk.

B.B. is quite anxious about nausea and vomiting because she had a lot of trouble with it during her previous cancer drug regimen and she also reports a history of motion sickness. Since there was no prescription for an antiemetic, the pharmacist contacts the prescriber and a prescription for prochlorperazine 10 mg every 4 to 6 hours as needed is provided to the patient's local community pharmacy.

Resources

Information for the patient on the above medication can be found on the BC Cancer website under:

- [Erlotinib Patient Handout](#)
- [LUAVERL Patient Handout](#)
- [Nausea and Vomiting \[Pharmacy Symptom & Side Effect Management Resource Guide\]](#)

The pharmacist is encouraged to review this information with the patient.



The information for health professionals on the above medication can also be found on the BC Cancer website:

- [LUAVERL Chemotherapy Protocol](#)
- [Erlotinib Drug Monograph](#)
- [Nausea and Vomiting \[Pharmacy Symptom & Side Effect Management Resource Guide\]](#)

Subsequent Doses

Cycle 2

B.B. returns on July 19 with a prescription for erlotinib 100 mg daily for 28 days. Her bloodwork was drawn that morning. You notice that she has a maculopapular rash on her face. She did not have any other problems related to her first cycle of treatment.

Her weight remains at 59 kg.

<u>Lab results – Jul 18</u>	
Bilirubin	3
Alk Phos	124
AST	28
LDH	223

As this is a continuation of the previous treatment, reviewing the patient’s cancer drug order can begin with timing of the treatment. This appointment has been scheduled 28 days from Day 1 of cycle 1 so the timing is appropriate.

When checking the dose for cycle 2, the pharmacist notes that the dose has been reduced to 100 mg daily. The prescriber’s dictation reveals that the dose was reduced because the patient developed a maculopapular rash during cycle 1. B.B. started minocycline mid cycle, but the rash progressed so she wants to try a reduced dose. The protocol indicates that rash may require treatment interruption and/or dose reduction. The dose reduction to 100 mg daily is consistent with the protocol recommendations for rash management.



Lab work is acceptable and within normal limits as specified in the protocol.

Cycle 3

B.B. returned for consideration of cycle 3 on Aug 16. Her rash has improved considerably and her LFTs are normal.

<u>Lab results – Aug 15</u>	
Bilirubin	5
Alk Phos	119
AST	27
LDH	241

B.B. is tolerating erlotinib well and her treatment is continued at the reduced dose of 100 mg daily for 28 days.

Cycle 4

B.B. returned to clinic on Sep 13 for consideration of Cycle 4. A CT scan from the week prior showed evidence of tumor progression. Erlotinib was discontinued and further treatment with docetaxel was considered.

Example Case Study 3: GIFOLFOX

The following example demonstrates that deviation from the protocol can occur.

A.C. (20-99999) is a 43-year-old female, diagnosed with carcinoma of the sigmoid colon, previously treated with surgery and post-op chemotherapy (12 cycles of GIAJFL) completed in August of the previous year. She returns to clinic, now diagnosed with metastatic disease (hepatic involvement) and is scheduled for treatment with GIFOLFOX on March 12. Baseline blood tests were performed at an outside lab 3 weeks ago. A.C. is not taking any other medications.

Lab results - February 18					
WBC	13.7	Creatinine	60	Electrolytes	WNL*
ANC	10.23	Bilirubin	20	Ca, Mg	WNL
Hgb	124	AST	40		
Platelets	495	Alk Phos	203	(* Within Normal Limits)	

Step 1: Verify Patient Identity

Pharmacy has received a written order for the following:

Oxaliplatin 130 mg IV in 500 mL D5W over 2 hours
 Leucovorin 600 mg IV in 250 mL D5W over 2 hours
 Fluorouracil 600 mg IV bolus, after Leucovorin, THEN
 Fluorouracil 3600 mg by continuous IV infusion over 46 hours

A.C.'s name, DOB and BC Cancer ID number were checked on the written order, as A.C. is returning for treatment. Her allergy status and pregnancy status should be checked again prior to start of new cancer drug treatment.

Patient-specific information: height 150 cm, weight 55 kg, as written in the chart on March 11.

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

GIFOLFOX is a BC Cancer protocol currently in use for second line palliative combination treatment of metastatic colorectal cancer. Before proceeding, ensure that the protocol version you are using is the most current. This protocol has numerous eligibility criteria and cautions. The cautions do not apply to this patient and all other criteria are met. Therefore, A.C. is eligible for this protocol, based on her diagnosis.

Step 3: Review Medical History

A.C. is not taking any other medications. She does not have any known allergies. She will need to have a negative pregnancy test prior to start of her cancer drug treatment.

Step 4: Check Timing of Treatment

A.C. has received treatment in the past, which was completed 6 months prior. This is her first cycle of treatment for relapse. Her first treatment date will be March 12.

Step 5: Determine Patient's Body Surface Area

Calculate the patient's body surface area:

$$\begin{aligned} \text{BSA (m}^2\text{)} &= \sqrt{\frac{\text{height(cm)} \times \text{weight(kg)}}{3600}} \\ &= \sqrt{\frac{150\text{cm} \times 55\text{kg}}{3600}} \\ &= 1.51 \text{ m}^2 \end{aligned}$$

Step 6: Check Appropriateness of Cancer Drug Dose(s)

Calculation of doses for Cycle 1:

$$\begin{aligned} \text{Oxaliplatin: } &85 \text{ mg/m}^2 \times 1.51 \text{ m}^2 = 128 \text{ mg} \\ \text{Leucovorin: } &400 \text{ mg/m}^2 \times 1.51 \text{ m}^2 = 604 \text{ mg} \\ \text{Fluorouracil bolus: } &400 \text{ mg/m}^2 \times 1.51 \text{ m}^2 = 604 \text{ mg} \\ \text{Fluorouracil infusion: } &2400 \text{ mg/m}^2 \times 1.51 \text{ m}^2 = 3624 \text{ mg} \end{aligned}$$

These calculated doses are within 5% of the doses ordered by the prescriber so are acceptable, as per Policy ***III-10 Systemic Therapy Treatment Delivery Process*** [[Systemic Therapy - Policies & Procedures](#)]. If there was a variance of greater than 5%, the prescriber must be contacted and the discrepancy



resolved. The order will be processed as written by the prescriber. Note: If dose banding is used, the infusional fluorouracil will be dispensed in a Baxter LV5 Infusor® containing 3600 mg of fluorouracil.

Doses administered should be documented on the medication order, as well as on the pharmacy treatment record.

The patient is not receiving a drug with a maximum cumulative dose.

Step 7: Review of Laboratory Values

Lab work for current treatment is from 3 weeks ago. In accordance with BC Cancer Policy ***III-10 Systemic Therapy Treatment Delivery Process*** [Systemic Therapy - Policies & Procedures], the lab work is acceptable because it was drawn within 4 weeks of starting treatment.

Step 8: Verify Appropriate Method of Drug Delivery

Prepare and administer as per protocol, following sterile technique and safe handling procedures for hazardous drugs. As per protocol, oxaliplatin and leucovorin are administered in D5W and may be given concurrently by using a Y-site connector placed immediately before the injection site. Oxaliplatin and leucovorin cannot be combined in the same bag, and oxaliplatin is not compatible with NS, as per the ***Chemotherapy Preparation and Stability Chart*** [Cancer Drug Manual]. The first fluorouracil is given as IV push, and the second dose is given as a 46-hour infusion. The GIFOLFOX preprinted orders indicate that BC Cancer uses Baxter LV5 infusors™ for this protocol.

Step 9: Monitor for Potential Cancer Drug Toxicity

Leucovorin

As part of the protocol, leucovorin plays a supportive role. Read the *Protectants* section of the supportive care module [Clinical Pharmacy Guide – Modules – Module 5] for more information.

Step 10: Verify Protocol-Related Supportive Care Provided

Anti-emetics

GIFOLFOX has an older high/moderate rating of emetogenic potential, which is now classified as “Moderately Emetogenic Chemotherapy (MEC)” as per the updated BC Cancer Supportive Care Protocol SCNAUSEA. Ondansetron and dexamethasone are indicated as premedication, and the patient should have been given a prescription for these drugs to be filled at a community retail pharmacy. Prochlorperazine, metoclopramide, and olanzapine may also be prescribed for this patient. Read the *Antiemetics* section of the supportive care module [Clinical Pharmacy Guide - Modules – Module 5] for more information. Supportive care medications are not reimbursed by BC Cancer, and should be obtained from a community retail pharmacy.

Loperamide

Both oxaliplatin and fluorouracil have the potential to cause diarrhea. When used in combination, this potential increases. Loperamide may be an option for this patient. Supportive care medications are not reimbursed by BC Cancer, and should be obtained from a community retail pharmacy. See the BC Cancer funding [Drug Funding] section for more information.

Resources

Information for Patients

- GIFOLFOX Patient Handout
- Fluorouracil INFUSOR™ Patient Handout (Your Infusor – A Guide for Patients) [Drug Index]
- Drug Index – Patient Handouts:
 - Oxaliplatin
 - Leucovorin
 - Fluorouracil
 - Ondansetron
 - Metoclopramide
 - Prochlorperazine



- Dexamethasone
- Nausea and Vomiting [[Pharmacy Symptom & Side Effect Management Resource Guide](#)]

The pharmacist is encouraged to review this information with the patient.

Information for health professionals for this protocol can also be found on the BC Cancer website:

- [GIFOLFOX](#) Chemotherapy Protocols
- Drug Monographs [[Drug Index](#)]
- ***Chemotherapy Preparation and Stability Chart*** [[Cancer Drug Manual](#)]

Subsequent Doses

Cycle 3: April 9

A.C. returns for her third cycle of treatment. Her previous treatment was on March 26. She has been troubled with diarrhea and mucositis. Since the patient has been heavily pretreated with 5-FU, the prescriber has decided to reduce the 5-FU dose by one dose level. She is experiencing grade 2 level peripheral neuropathy and pharyngeal dysesthesia as well. According to the protocol dose modifications, the dose of oxaliplatin should be decreased by one dose level. However, based on patient-specific factors and clinical experience, the prescriber decides to continue at the present oxaliplatin dose. The pharmacist contacts the prescriber to confirm this deviation in protocol and documents this information on the pharmacy treatment record and the patient chart.

<u>Lab results – April 8</u>					
WBC	7.7	Bilirubin	8	Electrolytes	WNL
ANC	3.44	AST	41	Ca, Mg	WNL
Hgb	126	Alk Phos	69		
Platelets	185	Creatinine	70		

Her weight is 51.8 kg, and her doses still fall within 5% of the doses ordered despite her weight change. As per Policy **III-10 Systemic Therapy Treatment Delivery Process** [Systemic Therapy - Policies & Procedures], the prescriber has chosen to keep using the same (1.51 m^2) as previously calculated. Pharmacy receives the following orders:

Oxaliplatin 130 mg IV in 500 mL D5W over 2 hours
 Leucovorin 600 mg IV in 250 mL D5W over 2 hours
 Fluorouracil 480 mg IV bolus
 Fluorouracil 3000 mg continuous IV infusion over 46 hours

Calculated doses are as follows:

Oxaliplatin: $1.51 \text{ m}^2 \times 85 \text{ mg/m}^2 = 128 \text{ mg}$
 Leucovorin: $1.51 \text{ m}^2 \times 400 \text{ mg/m}^2 = 604 \text{ mg}$
 Fluorouracil: $1.51 \text{ m}^2 \times 320 \text{ mg/m}^2 = 483 \text{ mg}$
 Fluorouracil infusion: $1.51 \text{ m}^2 \times 2000 \text{ mg/m}^2 = 3020 \text{ mg}$

These calculated doses are within 5% of ordered doses, therefore are acceptable. Doses can be prepared as ordered by the prescriber and administered to patient. If dose banding is used the infusional fluorouracil will be dispensed in a Baxter LV5 Infusor® containing 3200 mg of fluorouracil.

Cycle 5: May 21

A.C. returns for consideration of her 5th cycle of treatment. Her previous treatment was on April 23, and one week following this treatment she was hospitalized for severe abdominal pain, diarrhea, nausea and vomiting, with mild dehydration. She remained in hospital for over one week. Her treatment for May 7 was cancelled as a result. On May 21, her neurotoxicity is at grade 3 and, according to the protocol, oxaliplatin should be discontinued. Again, based on clinical experience and patient-specific factors, the prescriber makes the decision to continue oxaliplatin treatment, but at one dose level lower than before. The prescriber also feels that her hospitalization was due to 5-FU toxicity, and therefore, decreases the dose of 5-FU by another dose level. The pharmacist contacts the prescriber to confirm these deviations in protocol and documents this information on the pharmacy treatment record.

<u>Lab results – May 20</u>					
WBC	15.5	Creatinine	50	Electrolytes	WNL
ANC	9.3	Bilirubin	12	Ca, Mg	WNL
Hgb	116	AST	42		
Platelets	330	Alk Phos	72		

Pharmacy receives the following orders:

- Oxaliplatin 98 mg IV in 250 mL D5W over 2 hours
- Leucovorin 600 mg IV in 250 mL D5W over 2 hours
- Fluorouracil 300 mg IV bolus
- Fluorouracil 2400 mg continuous IV infusion over 46 hours

Calculated doses are as follows:

- Oxaliplatin: $1.51 \text{ m}^2 \times 65 \text{ mg/m}^2 = 98.2 \text{ mg}$
- Leucovorin: $1.51 \text{ m}^2 \times 400 \text{ mg/m}^2 = 604 \text{ mg}$
- Fluorouracil: $1.51 \text{ m}^2 \times 200 \text{ mg/m}^2 = 302 \text{ mg}$
- Fluorouracil infusion: $1.51 \text{ m}^2 \times 1600 \text{ mg/m}^2 = 2416 \text{ mg}$

All calculated doses are within 5% of written orders; therefore drugs can be prepared and administered as ordered. As the infusional dose of 5-FU is less than 3000 mg, BC Cancer Pharmacy will mix the dose as prescribed and a premixed banded dose is not used as per protocol.

Cycle 6: June 3

A.C. returns for consideration of her 6th cycle. She is nauseous, dehydrated and feeling “rotten”. A CT scan of the liver reveals significant disease progression compared with previous CT scan of March. A.C. does not feel she has the strength to face further treatment and agrees to a palliative care consultation. Cancer drug treatment is discontinued.