Change BC Cancer Protocol Summary for Palliative Treatment of Metastatic or Locally Advanced Gastric or Gastroesophageal Junction (GEJ) Adenocarcinoma using Oxaliplatin, Fluorouracil, Leucovorin and Zolbetuximab

Protocol Code:	*GIGAVFFOXZ*
Tumour Group:	*Gastrointestinal*
Contact Physician:	*GI Systemic Therapy*

ELIGIBILITY:

Patients must have:

- Previously untreated locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma, and
- Tumour that is HER2-negative and Claudin (CLDN) 18.2 positive, defined as greater than or equal to 75% of tumour cells demonstrating moderate to strong CLDN 18.2 immunohistochemical staining as determined by IHC

Patients should have:

- Good performance status
- Adequate marrow reserve, renal and liver function

Note:

- Patients currently receiving first line treatment with immunotherapy plus chemotherapy may switch to GIGAVFFOXZ upon confirmation of CLDN 18.2 status, if they have not progressed on treatment.
- Patients discontinuing first line treatment with immunotherapy plus chemotherapy due to toxicity may switch to zolbetuximab and chemotherapy provided all eligibility criteria are met.
- Patients who received adjuvant treatment with immunotherapy are eligible for treatment with zolbetuximab, provided that progression occurred more than 6 months after treatment completion

EXCLUSIONS:

Patients must not have:

- HER2-positive tumour
- Progression on or within 6 months of adjuvant immunotherapy treatment
- Uncontrolled CNS metastases
- Congenital long QT syndrome
- Severe pre-existing peripheral neuropathy

CAUTIONS:

- Active, known or suspected autoimmune disease
- Patients with long term immunosuppressive therapy or systemic corticosteroids (requiring more than 10 mg predniSONE/day or equivalent)
- Patients with recent myocardial infarction, uncontrolled angina, hypertension, cardiac arrhythmias, congestive heart failure or other serious medical illness
- Patients with baseline greater than 3 loose BM per day (in patients without colostomy or ileostomy)
- Patients with symptomatic peripheral neuropathy

TESTS:

- Baseline: CBC & Diff, creatinine, ALT, alkaline phosphatase, total bilirubin, albumin, sodium, potassium, *DPYD* test (not required if previously tested, or tolerated fluorouracil or capecitabine)
- Baseline if clinically indicated: CEA, CA 19-9, GGT, magnesium, random glucose, ECG
- Prior to each cycle: CBC & Diff, creatinine, total bilirubin, ALT
- If clinically indicated: CEA, CA 19-9, alkaline phosphatase, albumin, GGT, sodium, potassium, magnesium, random glucose, ECG
- For patients on warfarin, weekly INR during fluorouracil therapy until stable warfarin dose established, then INR prior to each cycle

PREMEDICATIONS:

- Antiemetic protocol for highly emetogenic chemotherapy (see SCNAUSEA)
- Antiemetics may be de-escalated after Cycle 3, at provider discretion
- If prior infusion reaction to zolbetuximab: diphenhydrAMINE 50 mg PO/IV 30 minutes prior to treatment
- If Grade 1 or 2 oxaliplatin hypersensitivity reactions:
  - 45 minutes prior to oxaliplatin:
    - dexamethasone 20 mg IV in 50 mL NS over 15 minutes
  - 30 minutes prior to oxaliplatin:
    - diphenhydrAMINE 50 mg IV in NS 50 mL over 15 minutes and famotidine 20 mg IV in NS 100 mL over 15 minutes (Y-site compatible)
- **Counsel patients to avoid cold drinks and exposure to cold air, especially for 3-5 days following oxaliplatin administration.**
- **Cryotherapy (ice chips) should NOT be used as may exacerbate oxaliplatin-induced pharyngo-laryngeal dysesthesias.**

SUPPORTIVE CARE:

- In patients with an intact stomach, consider starting an H2 blocker or PPI one week before treatment initiation for mucosal protection and prevention of dyspepsia which can mimic nausea
- metoclopramide 10mg PO/IV every 4 to 6 hours as needed during zolbetuximab infusion for nausea or vomiting

TREATMENT:

Cycle #1: any baseline nausea and/or vomiting should be resolved to less than or equal to Grade 1 before starting the first treatment

Drug	Dose	BC Cancer Administration Guidelines
zolbetuximab	800 mg/m^2 on Day 1	IV in 250 to 500 mL NS using 0.2 micron in-line filter Start at 75 **mg/m^2/hour** for 60 minutes. If no reaction after 60 minutes, increase to 150 mg/m^2/hour for 60 minutes, then increase to 300mg/m^2/hour for the remainder of the infusion unless toxicity occurs. See Appendix.1 for titration rate titration table. Vital signs pre- and post-infusion, at each increment change and as clinically indicated. To be under constant visual observation during all increment changes. Observe for 2 hours post-infusion.
oxaliplatin*	85 mg/m^2 on Day 2	IV in 250 to 500 mL D5W over 2 hours**
leucovorin†	400 mg/m^2 on Day 2	IV in 250 mL D5W over 2 hours**
fluorouracil†	400 mg/m^2 on Day 2	IV push
fluorouracil‡	2400 mg/m^2 on Day 2	IV over 46 h in D5W to a total volume of 230 mL by continuous infusion at 5 mL/h via Baxter LV5 INFUSOR***

Cycle 2 onwards (to start 14 days after Cycle 1):

Drug	Dose	BC Cancer Administration Guidelines
zolbetuximab	400 mg/m^2 on Day 1	IV in 100 to 500 mL NS using 0.2 micron in-line filter Start at 75 **mg/m^2/hour** for 60 minutes. If no reaction after 60 minutes, increase to 150 mg/m^2/hour for 60 minutes, then increase to 300mg/m^2/hour for the remainder of the infusion unless toxicity occurs. See Appendix.1 for titration rate titration table. Vital signs pre- and post-infusion, at each increment change and as clinically indicated. If no reaction or Grade 1 reaction during previous infusion, observe for 1 hour post-infusion. If Grade 2 reaction during previous infusion, observe for 2 hours post-infusion. Vital signs and observation may be discontinued after 3 treatments with no infusion-related reactions.
oxaliplatin*	85 mg/m^2 on Day 2	IV in 250 to 500 mL D5W over 2 hours**
leucovorin†	400 mg/m^2 on Day 2	IV in 250 mL D5W over 2 hours**
fluorouracil†	400 mg/m^2 on Day 2	IV push
fluorouracil‡	2400 mg/m^2 on Day 2	IV over 46 h in D5W to a total volume of 230 mL by continuous infusion at 5 mL/h via Baxter LV5 INFUSOR***

- Repeat every 14 days until disease progression or unacceptable toxicity.

* Oxaliplatin is not compatible with normal saline. Do not piggyback or flush lines with normal saline.

** Oxaliplatin and leucovorin may be infused over the same two-hour period by using a Y- site connector placed immediately before the injection site. Oxaliplatin and leucovorin should not be combined in the same infusion bag.

† fluorouracil IV push is optional in the advanced setting:

fluorouracil IV push	leucovorin administration options
fluorouracil IV push given	• leucovorin given as IV infusion OR • leucovorin given as 20 mg/m^2 IV push
fluorouracil IV push omitted	• leucovorin omitted OR • leucovorin given as IV infusion OR • leucovorin given as 20 mg/m^2 IV push

‡ Select dose per Dose Banding Table (Appendix.2).

*** *Alternative administration:*
- Inpatients: 1200 mg/m^2/day in 1000 mL D5W by continuous infusion daily over 23 h for 2 days

Patients with PICC lines should have a weekly assessment of the PICC site for evidence of infection or thrombosis.

DOSE MODIFICATIONS (A, B & C):

Fluorouracil Dosing Based on DPYD Activity Score (DPYD-AS)
Refer to "Fluorouracil and Capecitabine Dosing Based on DPYD Activity Score (DPYD-AS)" on www.bccancer.bc.ca/health-professionals/clinical-resources/cancer-drug-manual.

1. **For zolbetuximab:**
   No specific dose modifications for zolbetuximab. Toxicity is managed by treatment delay or other measures.

   A. Infusion-related reactions and hypersensitivity reactions to zolbetuximab :

Severity*	Management
Grade 2	▪ Interrupt the infusion and manage symptoms per SCDRUGRX ▪ After resolution of symptoms to less than or equal to Grade 1, resume at a reduced infusion rate for the remaining infusion** ▪ Premedicate with antihistamine prior to subsequent infusions
Anaphylactic reactions OR Suspected anaphylaxis OR Grade 3 or 4	▪ Immediately stop the infusion and manage symptoms per SCDRUGRX ▪ Permanently discontinue

*Toxicity grade per NCI-CTCAE v5.0.
**Rechallenge infusion rate should be guided by the providers clinical judgment and symptoms severity. It is suggested to restart the infusion at 50% of the infusion rate

at which the reaction occurred, then gradually increase in 25% increments every 30–60 minutes.

B. Nausea and vomiting due to zolbetuximab:

Severity*	Management
Grade 1	▪ If nausea alone, consider administering metoclopromide 10 mg PO/IV every 4 to 6 hours as needed. ▪ May consider stopping infusion for 30 to 60 minutes and restarting at the same rate once symptoms resolve
Grade 2 or 3	▪ Interrupt the infusion and manage symptoms until resolution of symptoms to less than or equal to Grade 1 ▪ Resume at a reduced infusion rate for the remaining infusion**
Grade 4	▪ Permanently discontinue

*Toxicity grade per NCI-CTCAE v5.0.
**Rechallenge infusion rate should be guided by the providers clinical judgment and symptoms severity. It is suggested to restart the infusion at 50% of the infusion rate at which the reaction occurred, then gradually increase in 25% increments every 30–60 minutes.

2. **For oxaliplatin and fluorouracil :**

A. Dose Modifications for NEUROLOGIC Toxicity
B. Dose Modifications for HEMATOLOGIC Toxicity
C. Dose Modifications for NON-HEMATOLOGIC, NON-NEUROLOGIC Toxicity

Table 1 - Dose Reduction Levels for All Toxicity

Agent	Starting Dose	Dose Level -1	Dose Level -2*
oxaliplatin	85 mg/m^2	65 mg/m^2	50 mg/m^2
leucovorin	No dose modifications. ▪ If fluorouracil push is omitted, leucovorin may also be omitted or given as 20 mg/m^2 IV push ▪ If oxaliplatin is omitted, leucovorin may be given as 20 mg/m^2 IV push		
fluorouracil push	400 mg/m^2	320 mg/m^2	200 mg/m^2
fluorouracil infusion	2400 mg/m^2	2000 mg/m^2	1600 mg/m^2

* For any additional dose reductions, use 20% less than previous level or consider discontinuing this regimen.

** The recommended starting doses are based on the modified FOLFOX6 regimen which is widely accepted but has not been studied in comparison to the original FOLFOX6 regimen. Patients may start with oxaliplatin 100 mg/m^2 as per FOLFOX6 at the discretion of their physician.

Table 2 - Oxaliplatin Neurotoxicity Definitions

Grade 1	Paresthesias / dysesthesias of short duration that resolve; do not interfere with function
Grade 2	Paresthesias / dysesthesias interfering with function, but not activities of daily living (ADL)
Grade 3	Paresthesias / dysesthesias with pain or with functional impairment which interfere with ADL
Grade 4	Persistent paresthesias / dysesthesias that are disabling or life-threatening
Pharyngo-laryngeal dysesthesias (investigator discretion used for grading): Grade 0 = none; Grade 1 = mild; Grade 2 = moderate; Grade 3 = severe	

Neuropathy may be partially or wholly reversible after discontinuation of therapy; patients with good recovery from Grade 3 (not Grade 4) neuropathy may be considered for re-challenge with oxaliplatin, with starting dose one level below that which they were receiving when neuropathy developed.

A. Dose Modifications for oxaliplatin NEUROLOGIC Toxicity

Toxicity Grade	**Duration of Toxicity**		**Persistent (present at start of next cycle)**
	1 to 7 days	**Greater than 7 days**	
Grade 1	Maintain dose level	Maintain dose level	Maintain dose level
Grade 2	Maintain dose level	Maintain dose level	Decrease 1 dose level
Grade 3	1st time: ↓ 1 dose level 2nd time: ↓ 1 dose level	1st time: ↓ 1 dose level 2nd time: ↓ 1 dose level	Discontinue
Grade 4	Discontinue therapy	Discontinue therapy	Discontinue therapy
Pharyngo-laryngeal (see precautions)	Maintain dose level	N/A	N/A

B. Dose Modifications for HEMATOLOGIC Toxicity

Prior to a Cycle (Day 1)	Toxicity		Dose Level For Subsequent Cycles	
	Grade	**ANC (x 10^9/L)**	**oxaliplatin**	**fluorouracil**
▪ If ANC less than 1.2 on Day 1of cycle, hold treatment. Perform weekly CBC, maximum of 2 times. ▪ If ANC is greater than or equal to 1.2 within 2 weeks, proceed with treatment at the dose level noted across from the **lowest ANC** result of the delayed week(s). ▪ If ANC remains less than 1.2 after 2 weeks, discontinue treatment.	1	Greater than or equal to 1.2	Maintain dose level	Maintain dose level
	2	1.0 to less than 1.2	Maintain dose level	Maintain dose level
	3	0.5 to less than 1.0	↓ 1 dose level	Maintain dose level
	4	Less than 0.5	↓ 1 dose level	omit IV push and ↓ 1 infusion dose level

Prior to a Cycle (Day 1)	Toxicity		Dose Level For Subsequent Cycles	
	Grade	**Platelets (x 10^9/L)**	**oxaliplatin**	**fluorouracil**
▪ If platelets less than 75 on Day 1 of cycle, hold treatment. Perform weekly CBC, maximum of 2 times. ▪ If platelets greater than or equal to 75 within 2 weeks, proceed with treatment at the dose level noted across from the **lowest platelets** result of the delayed week(s). ▪ If platelets remain less than 75 after 2 weeks, discontinue treatment.	1	Greater than or equal to 75	Maintain dose level	Maintain dose level
	2	50 to less than 75	Maintain dose level	Maintain dose level
	3	10 to less than 50	↓ 1 dose level	Maintain dose level
	4	Less than 10	↓ 2 dose levels	Maintain dose level

Dose Modifications for NON-HEMATOLOGIC, NON-NEUROLOGIC Toxicity

Prior to a Cycle (Day 1)	Toxicity		Dose Level For Subsequent Cycles
	Grade	**Diarrhea**	
▪ If diarrhea greater than or equal to Grade 2 on Day 1 of cycle, hold treatment. Perform weekly checks, maximum 2 times. ▪ If diarrhea is less than Grade 2 within 2 weeks, proceed with treatment at the dose level noted across from the **highest** Grade experienced. ▪ If diarrhea remains greater than or equal to Grade 2 after 2 weeks, discontinue treatment.	1	Increase of 2 to 3 stools/day, or mild increase in loose watery colostomy output	Maintain dose level
	2	Increase of 4 to 6 stools, or nocturnal stools or mild increase in loose watery colostomy output	Maintain dose level
	3	Increase of 7 to 9 stools/day or incontinence, malabsorption; or severe increase in loose watery colostomy output	↓ 1 dose level of IV push and infusional fluorouracil
	4	Increase of 10 or more stools/day or grossly bloody colostomy output or loose watery colostomy output requiring parenteral support; dehydration	↓ 1 dose level of oxaliplatin, IV push and infusional fluorouracil
	Grade	**Stomatitis**	
▪ If stomatitis greater than or equal to Grade 2 on Day 1 of cycle, hold treatment. Perform weekly checks, maximum 2 times. ▪ If stomatitis is less than Grade 2 within 2 weeks, proceed with treatment at the dose level noted across from the **highest** Grade experienced. ▪ If stomatitis remains greater than or equal to Grade 2 after 2 weeks, discontinue treatment.	1	Painless ulcers, erythema or mild soreness	Maintain dose level
	2	Painful erythema, edema, or ulcers but can eat	Maintain dose level
	3	Painful erythema, edema, ulcers, and cannot eat	↓ 1 dose level of IV push and infusional fluorouracil
	4	As above but mucosal necrosis and/or requires enteral support, dehydration	↓ 1 dose level of oxaliplatin, IV push and infusional fluorouracil

PRECAUTIONS:

1. **Nausea and Vomiting:** Severe nausea and vomiting despite antiemetic prophylaxis is a frequent side effect of zolbetuximab. Symptoms are most common during the first two zolbetuximab treatments. During the first zolbetuximab treatment, nausea and/or vomiting typically occur within 1 hour. Patients with a prior gastrectomy are less likely to experience severe nausea and vomiting. Management of nausea and vomiting includes adequate antiemetic prophylaxis, interruption of infusion until symptoms improve to Grade 1 or less and resuming treatment with a reduced infusion rate. Zolbetuximab should be permanently discontinued if Grade 4 vomiting occurs. Consideration may be given to de-escalation of antiemetic prophylaxis after Cycle 3.
2. **Infusion-related reactions (IRRs) and hypersensitivity reactions:** have been reported with zolbetuximab. IRR signs and symptoms include nausea, vomiting, abdominal pain, salivary hypersecretion, pyrexia, chest discomfort, chills, back pain, cough, and hypertension. Hypersensitivity reactions, including anaphylactic reactions, have also been reported. To minimize reactions, start each infusion at the recommended initial rate and increase the rate as tolerated. For patients who have experienced grade 2 IRRs or hypersensitivity reactions, premedication with antihistamines is recommended prior to subsequent infusions. Permanently discontinue zolbetuximab in the event of Grade 3 or 4 reactions, or if anaphylaxis is suspected. For management of infusion-related reactions, see BC Cancer Protocol SCDRUGRX.
3. **Platinum hypersensitivity** can cause dyspnea, bronchospasm, itching and hypoxia. Appropriate treatment includes supplemental oxygen, steroids, epinephrine and bronchodilators. Vasopressors may be required (see table below). For Grade 1 or 2 acute hypersensitivity reactions no dose modification of oxaliplatin is required and the patient can continue treatment with standard hypersensitivity premedication. See Premedications.

   Reducing infusion rates (e.g., from the usual 2 hours to 4-6 hours) should also be considered since some patients may develop more severe reactions when rechallenged, despite premedications.

   The practice of rechallenging after severe life-threatening reactions is usually discouraged, although desensitization protocols have been successful in some patients. The benefit of continued treatment must be weighed against the risk of severe reactions recurring. The product monograph for oxaliplatin lists rechallenging patients with a history of severe HSR as a contraindication. Various desensitization protocols using different dilutions and premedications have been reported. Refer to SCOXRX: BC Cancer Inpatient Protocol Summary for Oxaliplatin Desensitization for more information.

2. **Pharyngo-laryngeal dysesthesia** is an unusual dysesthesia characterized by an uncomfortable persistent sensation in the area of the laryngopharynx without any objective evidence of respiratory distress (i.e. absence of hypoxia, laryngospasm or bronchospasm). This may be exacerbated by exposure to cold air or foods/fluids. If this occurs during infusion, stop infusion immediately and observe patient. Rapid resolution is typical, within minutes to a few hours. Check oxygen saturation; if normal, an anxiolytic agent may be given. The infusion can then be restarted at a slower rate at the physician's discretion. In subsequent cycles, the duration of infusion should be prolonged (see Dose Modifications above in the Neurological Toxicity table).

Clinical Symptoms	**Pharyngo-laryngeal Dysesthesia**	**Platinum Hypersensitivity**
Dyspnea	Present	Present
Bronchospasm	Absent	Present
Laryngospasm	Absent	Present
Anxiety	Present	Present
O_2 saturation	Normal	Decreased
Difficulty swallowing	Present (loss of sensation)	Absent
Pruritus	Absent	Present
Cold induced symptoms	Yes	No
Blood Pressure	Normal or Increased	Normal or Decreased
Treatment	Anxiolytics; observation in a controlled clinical setting until symptoms abate or at physician's discretion	Oxygen, steroids, epinephrine, bronchodilators; Fluids and vasopressors if appropriate

3. **QT prolongation and torsades de pointes** are reported with oxaliplatin. Use caution in patients with history of QT prolongation or cardiac disease and those receiving concurrent therapy with other QT prolonging medications. Correct electrolyte disturbances prior to treatment and monitor periodically. Baseline and periodic ECG monitoring is suggested in patients with cardiac disease, arrhythmias, concurrent drugs known to cause QT prolongation, and electrolyte abnormalities. In case of QT prolongation, oxaliplatin treatment should be discontinued. QT effect of oxaliplatin with single dose ondansetron 8 mg prechemo has not been formally studied. However, single dose ondansetron 8 mg po would be considered a lower risk for QT prolongation than multiple or higher doses of ondansetron, as long as patient does not have other contributing factors as listed above.
4. **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated aggressively.
5. Oxaliplatin therapy should be interrupted if symptoms indicative of **pulmonary fibrosis** develop – nonproductive cough, dyspnea, crackles, rales, hypoxia, tachypnea or radiological pulmonary infiltrates. If pulmonary fibrosis is confirmed oxaliplatin should be discontinued.
6. **Extravasation**: Oxaliplatin causes irritation if extravasated. Refer to BC Cancer Extravasation Guidelines.

7. **Venous Occlusive Disease** is a rare but serious complications that has been reported in patients (0.02%) receiving oxaliplatin in combination with fluorouracil. This condition can lead to hepatomegaly, splenomegaly, portal hypertension and/or esophageal varices. Patients should be instructed to report any jaundice, ascites or hematemesis immediately.
8. Oxaliplatin therapy should be interrupted if **Hemolytic Uremic Syndrome (HUS)** is suspected: hematocrit is less than 25%, platelets less than 100,000 and creatinine greater than or equal to 135 micromol/L. If HUS is confirmed, oxaliplatin should be permanently discontinued.
9. **Myocardial** ischemia and angina occurs rarely in patients receiving fluorouracil or capecitabine. Development of cardiac symptoms including signs suggestive of ischemia or of cardiac arrhythmia is an indication to discontinue treatment. If there is development of cardiac symptoms patients should have urgent cardiac assessment. Generally re-challenge with either fluorouracil or capecitabine is not recommended as symptoms potentially have a high likelihood of recurrence which can be severe or even fatal. Seeking opinion from cardiologists and oncologists with expert knowledge about fluorouracil / capecitabine toxicity is strongly advised under these circumstances. The toxicity should also be noted in the patient's allergy profile.
10. **Diarrhea:** Patients should report mild diarrhea that persists over 24 hours or moderate diarrhea (4 stools or more per day above normal, or a moderate increase in ostomy output). Mild diarrhea can be treated with loperamide (eg. IMODIUM®) following the manufacturer's directions or per the BC Cancer Guidelines for Management of Chemotherapy-Induced Diarrhea. Note that diarrhea may result in increased INR and the risk of bleeding in patients on warfarin.
1. **Dihydropyrimidine dehydrogenase (DPD) deficiency** may result in severe and unexpected toxicity – stomatitis, diarrhea, neutropenia, neurotoxicity – secondary to reduced drug metabolism. This deficiency is thought to be present in about 3% of the population. Fluorouracil should be permanently discontinued in patients exhibiting exaggerated or prolonged neutropenia, mucositis, and diarrhea.
11. **Possible drug interaction with fluorouracil and warfarin** has been reported and may occur at any time. For patients on warfarin, weekly INR during fluorouracil therapy is recommended until a stable warfarin dose is established. Thereafter, INR prior to each cycle. Consultation to cardiology/internal medicine should be considered if difficulty in establishing a stable warfarin dose is encountered. Upon discontinuation of fluorouracil, repeat INR weekly for one month.
12. **Possible drug interaction with fluorouracil and phenytoin and fosphenytoin** has been reported and may occur at any time. Close monitoring is recommended. Fluorouracil may increase the serum concentration of these two agents.

Call the GI Systemic Therapy physician at your regional cancer centre or the GI Systemic Therapy Chair with any problems or questions regarding this treatment program.

References:

1. Shitara K, Lordick F, Bang YJ et al. Zolbetuximab Plus mFOLFOX6 in Patients with CLDN18.2-positive, HER2-negative, Untreated, Locally Advanced Unresectable or Metastatic Gastric or Gastro-oesophageal Junction Adenocarcinoma (SPOTLIGHT): a Multicentre, Randomised, Double-blind, Phase 3 Trial. Lancet. 2023 May 20;401(10389):1655-1668.
2. Shah MA, Shitara K, Ajani JA, et al. Zolbetuximab plus CAPOX in CLDN18.2-positive Gastric or Gastroesophageal Junction Adenocarcinoma: the Randomized, Phase 3 GLOW trial. Nat Med. Aug 2023;29(8):2133-2141.
3. Zolbetuximab (Vyloy) CDA-AMC Canada's Drug Agency Reimbursement Recommendation. Canadian Journal of Health Technologies. Feb 2025; 5(2): 1-30.

Appendix.1 Zolbetuximab Rate Titration Table

Below infusion rates are standardized and take into account volume of drug added to infusion bag, infusion bag overfill, and maximum infusion bag volume. The standardized infusion rates are within the allowable +/- 5% variance per Systemic Therapy Policy III-10.

Cycle 1: Loading Dose 800 mg/m^2

	DILUENT BAG 250 mL	DILUENT BAG 500 mL
75 mg/m^2/hour x 60 min	30 mL/hour	55 mL/hour
150 mg/m^2/hour x 60 min	60 mL/hour	110 mL/hour
300 mg/m^2/hour for the remainder of infusion	120 mL/hour	220 mL/hour

Cycle 2 onwards: Maintenance Dose 400 mg/m^2

	DILUENT BAG 100 mL	DILUENT BAG 250 mL
75 mg/m^2/hour x 60 min	25 mL/hour	60 mL/hour
150 mg/m^2/hour x 60 min	50 mL/hour	120 mL/hour
300 mg/m^2/hour for the remainder of infusion	100 mL/hour	240 mL/hour

Appendix. 2 Fluorouracil Dose Banding Table

Ordered Dose (mg)		Rounded dose (mg) for INFUSOR
From:	**To:**	
Less than 3000		**Pharmacy prepares specific dose**
3000	3400	**3200 mg**
3401	3800	**3600 mg**
3801	4200	**4000 mg**
4201	4600	**4400 mg**
4601	5000	**4800 mg**
5001	5500	**5250 mg**
More than 5500		**Pharmacy prepares specific dose**