BC CANCER
Provincial Health Services Authority

Systemic Therapy Update

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For Health Professionals Who Care For Cancer Patients

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EDITOR'S CHOICE

NEW PROGRAMS

Effective 01 November 2018, the BC Cancer Provincial Systemic Therapy Program has approved the following treatment program:

Gastrointestinal:

Capecitabine and Bevacizumab for Metastatic Colorectal Cancer (GIAVCAPB) – The BC Cancer Gastrointestinal Tumour Group has introduced this new regimen for the first-line treatment of metastatic colorectal cancer in patients who are not suitable for combination chemotherapy with irinotecan or oxaliplatin. In an open-label, phase III randomized trial, the addition of bevacizumab to capecitabine significantly improved progression free survival from 5.1 to 9.1 months (HR 0.53, p<0.0001) and overall response rate from 10.0% to 19.3% (p=0.04).[1] There was also a trend towards longer overall survival from 16.8 to 20.7 months (p=0.18). This regimen was well tolerated with a safety profile consistent with that previously reported for bevacizumab in the metastatic colorectal cancer setting.

References:
1. Cunningham D, Lang I, Marcuello E, et al. Bevacizumab plus capectiabine versus capecitabine alone in elderly patients with previously untreated metastatic colorectal cancer (AVEX): an open-label, randomised phase 3 trial. Lancet Oncol 2013;14(11):1077-1085.

Revised Programs

Effective 01 November 2018, the BC Cancer Provincial Systemic Therapy Program has revised the following treatment programs:

Lymphoma:

1600 mg Subcutaneous Rituximab Option Added to ULYCLLFBR and ULYIDELAR – The 1600 mg subcutaneous (SC) rituximab formulation is now available to be administered as a fixed-dose in patients receiving rituximab (500 mg/m^2) with either bendamustine or idelalisib for chronic lymphocytic leukemia or small lymphocytic lymphoma. Similar to other lymphoma treatments that utilize SC rituximab, only patients who have previously tolerated an intravenous (IV) dose of rituximab are eligible to receive the SC formulation for subsequent treatment cycles. Please note that other rituximab-containing protocols (that use rituximab 375 mg/m^2) will continue to use the 1400 mg fixed-dose SC formulation. Caution should be exercised to ensure that the product with the correct drug concentration and administration route is selected. Please see the *Drug Update* announcement below for more information about the new 1600 mg SC rituximab formulation. This formulation has also been added to the Benefit Drug List.

Drug Update

BC PharmaCare Approves Filgrastim for Primary Prophylaxis of Febrile Neutropenia

Effective immediately, BC PharmaCare Special Authority has expanded the drug coverage of filgrastim (GRASTOFIL®) to include the primary prophylaxis of febrile neutropenia in cancer patients receiving potentially curative myelosuppressive chemotherapy regimens, where the risk of febrile neutropenia is estimated to be 20% or higher. While current BC Cancer chemotherapy protocols do not specify the risk of febrile neutropenia, physicians should exercise their clinical judgement with consideration of the patient, the disease, and the chosen drug regimen when assessing a patient's risk of febrile neutropenia and the need for primary prophylaxis.

The Special Authority Request Form for filgrastim (GRASTOFIL®) has been updated to include the new eligibility criterion, and can be found on the BC PharmaCare Special Authority website.

New 1600 mg Subcutaneous Rituximab Formulation Available

Effective immediately, the Provincial Systemic Therapy Program is making available the new 1600 mg subcutaneous (SC) rituximab formulation for patients receiving lymphoma treatment protocols that use rituximab 500 mg/m^2 dosing – ULYCLLFBR and ULYIDELAR. Similar to other lymphoma treatment protocols that have instituted SC rituximab, it is expected that patients who have tolerated a dose of rituximab intravenous (IV) infusion will have subsequent doses administered by SC injection.

SC Rituximab Administration:

The 1600 mg SC injection is administered as a fixed-dose to reduce the potential for dosing errors. It is injected into the abdomen by a trained nurse over approximately 7 minutes. The SC formulation contains the enzyme hyaluronidase, which temporarily degrades the extracellular matrix under the skin. This

allows the absorption of 13.4 mL (1600 mg) of rituximab. **Hence, it is NOT necessary to divide the dose into multiple syringes.** Following the SC injection, patients should be monitored for at least 15 minutes. Local reactions such as redness, tenderness and swelling at the site of injection can be managed with cool compresses.

Safety:

With the availability of this new formulation, BC Cancer now carries the following 3 rituximab formulations.

Rituximab IV *(for weight-based dosing)*	Rituximab 1400 mg SC *(for 375 mg/m^2 dosing)*	Rituximab 1600 mg SC *(for 500 mg/m^2 dosing)*
		

As illustrated in the images above, the 3 drug vials look and sound alike. Risk mitigation strategies should be instituted by Pharmacy to reduce the risk of product selection errors. Such strategies may include:

- Store medications in separate locations/bins with proper labelling.
- Avoid gathering different IV and SC (different doses) vials in one batch/bin.
- Avoid having both IV and SC (different doses) vials in the same biological safety cabinet at the same time.
- Handle one drug per patient in the hood at a given time.
- Review with pharmacy professional practice leader and pharmacy team members to determine best risk mitigation strategies for your centre.

FLUOROURACIL 96-HOUR INFUSION PROTOCOLS AND PRE-PRINTED ORDERS REVISED

Effective immediately, all BC Cancer Chemotherapy Protocols that contain fluorouracil (5-FU) to be given as a continuous infusion over 96 hours have been revised (GIEFUPRT, GIFUART, GIFUPART, HNAVFUP, HNLACAFRT, HNNAVFUP, HNSAVFUP). Previously, the continuous infusion was delivered over 96 hours using a **Baxter LV2 infusor**. Moving forward, all infusional 5-FU regimens should be given by equally dividing the total 5-FU dose into two **Baxter LV5 infusors**, with each infusor running over 48 hours. Patients must be scheduled for a return chemotherapy appointment at 48 hours for removal of the first infusor, and replacement with the second infusor.

The change was prompted by a new minimum volume needed to maintain a consistent infusion rate with the Baxter LV2 infusors. This meant that the Baxter LV2 infusors could no longer be used to deliver a continuous 96-hour infusion for 5-FU doses specified in the affected protocols.

BENEFIT DRUG LIST

NEW PROGRAMS

Effective 01 November 2018, the following treatment program has been added to the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Palliative Therapy of Metastatic Colorectal Cancer using Capecitabine and Bevacizumab	GIAVCAPB	Class I

REVISED PROGRAMS

Effective 01 November 2018, the following treatment programs have been revised on the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Treatment of Previously Untreated Chronic Lymphocytic Leukemia (CLL) with Bendamustine and Rituximab	ULYCLLFBR	Restricted *(SC formulation added)*
Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL) using Idelalisib and Rituximab	ULYIDELAR	Restricted *(SC formulation added)*

DELETED PROGRAMS

Effective 01 November 2018, the following treatment programs have been deleted from the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code
Treatment of Hodgkin's Disease using Cyclophosphamide, Vincristine, Prednisone	LYCCOP
Palliative Therapy for Metastatic Melanoma using Lomustine (CCNU)	SMCCNU
Intralesional BCG	SMILBCG
Therapy for Malignant Melanoma using Tamoxifen	SMTAM

CANCER DRUG MANUAL

REVISED MONOGRAPHS AND PATIENT HANDOUTS

Highlights of key changes and/or updates to the Monographs, Patient Handouts and Chemotherapy Preparation and Stability Chart (CPSC) are listed below:

Atezolizumab Monograph:
- *Uses:* updated Health Canada-approved indications
- *Side Effects:* added immune-mediated nephritis and myocarditis

Gemcitabine Monograph and **CPSC:**
- *Parenteral Administration table:* clarified instructions for intravesical administration
- *Supply and Storage:* updated available brands
- *Chemotherapy Preparation and Stability Chart:* added Pfizer brand

Ibrutinib Monograph:
- *Cautions:* added Hepatitis B reactivation and ventricular tachyarrhythmias
- *Side Effects table:* added Hepatitis B reactivation, ventricular tachyarrhythmias and progressive multifocal leukoencephalopathy

Obinutuzumab Monograph:
- *Solution Preparation and Compatibility:* clarified instructions for preparation of infusion bags for split-dose regimens
- *Parenteral Administration table:* updated intermittent infusion guidelines to include recommended infusion rate and rate increments used for follicular lymphoma
- *Dosing:* added dosing for follicular lymphoma

Rituximab Monograph and **CPSC:**
- *Cautions:* added warning about non-interchangeability of 1600 mg SC formulation with other dosage forms
- *Parenteral Administration table:* added administration instructions for 1600 mg SC formulation
- *Dosing:* added dosing for chronic lymphocytic leukemia

Zoledronic Acid CPSC:
- Added MDA brand

List of Revised Protocols, Pre-Printed Orders and Patient Handouts

BC Cancer Protocol Summaries, Provincial Pre-Printed Orders (PPPOs) and Patient Handouts are revised periodically. New, revised or deleted protocols, PPPOs and patient handouts for this month are listed below. Protocol codes for treatment requiring BC Cancer Compassionate Access Program approval are prefixed with the letter "U".

NEW Protocols, PPPOs and Patient Handouts (Affected Documents are Checked)

CODE	Protocol	PPPO	Patient Handout	Protocol Title
GIAVCAPB	☑	☑	☑	Palliative Therapy of Metastatic Colorectal Cancer using Capecitabine and Bevacizumab

Revised Protocols, PPPOs and Patient Handouts (Affected Documents are Checked)

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAVCAP	☑	☑	☐	*Eligibility and lab tests clarified*	Therapy of Metastatic Breast Cancer using Capecitabine
GICIRB	☑	☐	☑	*Eligibility, Tests and Precautions clarified; Side Effects, Special Notes, and Instructions for Patients updated in Patient Handout*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Irinotecan, Bevacizumab and Capecitabine
GICOXB	☑	☐	☑	*Eligibility, Tests and Precautions clarified; Side Effects, Special Notes, and Instructions for Patients updated in Patient Handout*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Oxaliplatin, Bevacizumab and Capecitabine
GIEFUPRT	☑	☑	☑	*Institution name, Eligibility, Exclusion, Tests, Treatment, and Contact Physician revised*	Combined Modality Therapy for Locally Advanced Esophageal Cancer using Cisplatin, Infusional Fluorouracil and Radiation Therapy
GIFFIRB	☑	☐	☑	*Eligibility clarified; Side Effects, Special Notes, and Instructions for Patients updated in Patient Handout*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Irinotecan, Fluorouracil, Leucovorin and Bevacizumab
GIFFOXB	☑	☐	☑	*Eligibility clarified; Side Effects, Special Notes, and Instructions for Patients updated in Patient Handout*	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Oxaliplatin, Fluorouracil, Leucovorin and Bevacizumab

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
GIFUART	☑	☑	☑	*Institution name, Eligibility, Exclusion, Tests, Treatment, and Contact Physician revised*	Curative Combined Modality Therapy for Carcinoma of the Anal Canal using Mitomycin, Infusional Fluorouracil and Radiation Therapy
GIFUPART	☑	☑	☑	*Institution name, Eligibility, Exclusion, Tests, Treatment, and Contact Physician revised*	Curative Combined Modality Therapy for Carcinoma of the Anal Canal using Cisplatin, Infusional Fluorouracil and Radiation Therapy
UGIYTT	☑	☐	☐	*Eligibility updated*	Yttrium-90 for Transarterial Radioembolisation (TARE)
HLHETCSPA	☑	☑	☐	*Tests, Diagnostic Criteria, Treatment and References updated*	Treatment of Hemophagocytic Lymphohistiocytosis with Etoposide, Dexamethasone and Cyclosporine
HNAVFUP	☑	☑	☑	*Institution name, Tests, and Treatment revised*	Advanced Squamous Cell Carcinoma of the Head and Neck Cancer using Fluorouracil and Platinum
HNLACAFRT	☑	☑	☑	*Institution name, Tests, and Treatment revised*	Combined Chemotherapy (Carboplatin and Fluorouracil) and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck
HNNAVFUP	☑	☑	☑	*Institution name, Tests, and Treatment revised*	Advanced Nasopharyngeal Cancer of the Head and Neck using Platinum and Fluorouracil
HNSAVFUP	☑	☑	☑	*Institution name, Tests, and Treatment revised*	Treatment of Advanced Head and Neck Cancer using Cisplatin and Fluorouracil
ULUAVOSI	☑	☐	☐	*Eligibility clarified*	Treatment of EGFR T790M Mutation-Positive Advanced Non-Small Cell Lung Cancer (NSCLC) with Osimertinib
ULYCLLFBR	☑	☑	☐	*SC Rituximab option added*	Treatment of Previously Untreated Chronic Lymphocytic Leukemia (CLL) with Bendamustine and Rituximab
ULYIDELAR	☑	☑	☐	*SC Rituximab option added*	Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL) Using Idelalisib and Rituximab
LYRITUX	☑	☐	☐	*Eligibility revised*	Treatment of Lymphoma with Single-Agent Rituximab
MYBORMTN	☑	☑	☐	*VZV prophylaxis clarified*	Maintenance Therapy of Multiple Myeloma using Bortezomib for Patients with the High-Risk Chromosome Abnormality

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Changes**	**Protocol Title**
MYBORPRE	☑	☑	☐	*VZV prophylaxis clarified*	Treatment of Multiple Myeloma using Bortezomib, Dexamethasone with or without Cyclophosphamide as Induction Pre-Stem Cell Transplant
MYBORREL	☑	☑	☐	*Treatment and VZV prophylaxis clarified*	Treatment of Relapsed Multiple Myeloma using Bortezomib, Dexamethasone with or without Cyclophosphamide
UMYCARDEX	☑	☑	☐	*VZV prophylaxis clarified*	Therapy of Multiple Myeloma using Carfilzomib and Dexamethasone with or without Cyclophosphamide
UMYCARLD	☑	☑	☐	*VZV prophylaxis clarified*	Therapy of Multiple Myeloma using Carfilzomib, Lenalidomide with Dexamethasone
MYMPBOR	☑	☑	☐	*VZV prophylaxis clarified*	Treatment of Multiple Myeloma using Melphalan, Prednisone and Weekly Bortezomib with the Option of Substituting Cyclophosphamide for Melphalan
SMAVTMZ	☑	☑	☐	*Institutional name and hepatic dosing updated*	Palliative Therapy for Malignant Melanoma with Brain Metastases using Temozolomide

DELETED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)				
CODE	**Protocol**	**PPPO**	**Patient Handout**	**Protocol Title**
LYCCOP	☑	☐	☐	Treatment of Hodgkin's Disease using Cyclophosphamide, Vincristine, Prednisone
SMCCNU	☑	☑	☑	Palliative Therapy for Metastatic Melanoma using Lomustine (CCNU)
SMILBCG	☑	☐	☐	Intralesional BCG
SMTAM	☑	☑	☑	Therapy for Malignant Melanoma using Tamoxifen

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