

Systemic Therapy Update

September 2019 + Vol. 22 + No. 9

For Health Professionals Who Care For Cancer Patients

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EDITOR'S CHOICE

New Programs

Effective 01 September 2019, the BC Cancer Provincial Systemic Therapy Program has approved the following treatment program:

Lymphoma:

Venetoclax for Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma (ULYVENETO) – The BC Cancer Lymphoma Tumour Group is introducing venetoclax monotherapy for patients with or without chromosome 17p deletion, who have progressed on or are intolerant to B-cell receptor pathway inhibitors (e.g. ibrutinib, idelalisib). A BC Cancer Compassionate Access Program (CAP) approval is required.

Venetoclax is a novel, oral small-molecule B-cell lymphoma 2 (BCL-2) inhibitor that restores apoptosis in BCL-2-dependent cancer cells. It is primarily eliminated hepatically, and is a substrate of CYP 3A4 (major) and P-glycoprotein. Specific recommendations on how to manage drug interactions during and after the ramp-up phase are outlined in the Protocol. Notable adverse effects include myelosuppression (14% to 43%)¹ and tumour lysis syndrome (TLS) (3% to 6%)². To significantly reduce the risk of TLS, the dose of venetoclax must be increased gradually. As such, venetoclax is initiated in a 5-week "ramp-up" schedule to slowly achieve the recommended dose of 400 mg per day. A "Starting Pack" is available from the manufacturer to facilitate the dispensing of the first 4 weeks of venetoclax during the ramp-up phase.

EDITOR'S CHOICE

Week	Dose			
1	20 mg PO once daily (2 x 10 mg)			
2	50 mg PO once daily (1 x 50 mg)			
3	100 mg PO once daily (1 x 100 mg)			
4	200 mg PO once daily (2 x 100 mg)			
5 and onward	400 mg PO once daily (4 x 100 mg)			

Patients are required to undergo intensive blood work and monitoring as outlined in the Protocol. Three PPPOs have also been created to facilitate treatment for the following scenarios:

- Patients with high TLS risk during the ramp-up phase
- Patients with low-moderate TLS risk during the ramp-up phase
- Treatment in the post-ramp-up phase (week 6 and onward)

BC Cancer Pharmacy and Nursing have established clear monitoring and communication procedures to assist in the monitoring of TLS. A number of education sessions and resources have also been developed to support the Pharmacy and Nursing staff in this role. For more information about tumour lysis syndrome, please see the Education Corner section below.

References:

- 1. Jones J, Choi MY, Mato AR, et al. Venetoclax (VEN) monotherapy for patients with chronic lymphocytic leukemia (CLL) who relapsed after or were refractory to ibrutinib or idelalisib. Blood (ASH Annual Meeting Abstracts) 2016;128:637.
- 2. Venetoclax. Created 01 August 2018 . BC Cancer Drug Manual[®]. Badry, Nadine (editor). BC Cancer. Vancouver, British Columbia. Available at: <u>http://www.bccancer.bc.ca/</u>. (Accessed 16 August 2019).

DRUG UPDATES

DRUG SHORTAGES

The following outlines updates of drug supply shortages in BC. Further details about the shortages and their recommended treatment alternatives can be found in the associated briefing notes and/or email communications previously circulated to BC Cancer and the Communities Oncology Network (CON).

Resolved Drug Shortages:

- Leucovorin injectable
- Hydrocortisone injectable

Fludarabine Injectable:

(Adapted from BC Cancer Briefing Note Update 23Aug2019)

Supply interruptions of fludarabine injectable are expected to last until December 2019. Fludarabine is an option in some lymphoma protocols, stem cell transplant (SCT) conditioning regimens and pediatric protocols. It is recommended that conservation strategies be reinstituted to ensure current supplies are available for high priority patients, and that fludarabine tablets be used where possible.

DRUG **U**PDATES

Raltitrexed Injectable:

(Adapted from BC Cancer Briefing Note 29Aug2019)

There is a shortage of raltitrexed injectable with no current anticipated supply return date. Raltitrexed is used in the adjuvant and advanced settings for patients with colon and colorectal cancers, respectively. BC Cancer recommends reserving existing supplies for current patients and that no new patients are started on treatment. Please see associated briefing note for specific recommendations on supply conservation strategies and alternative treatment options.

MEDICAL PATIENT ASSISTANCE PROGRAMS UPDATE

The listing of oncology medical patient assistance programs offered by pharmaceutical companies has been updated and can be found at: <u>www.bccancer.bc.ca/mpap</u>.*

*Located on the BC Cancer Systemic Therapy website under Health Professionals > Systemic Therapy > Reimbursement & Forms

EDUCATION CORNER

TUMOUR LYSIS SYNDROME

Tumour lysis syndrome (TLS) is an oncologic emergency caused by massive tumour cell lysis, resulting in the release of its intracellular contents (e.g. potassium, phosphate and nucleic acids). This can lead to hyperuricemia and electrolyte abnormalities including hyperkalemia, hyperphosphatemia, secondary hypocalcemia, as well as acute kidney injury. Severity can range from asymptomatic biochemical derangements to multi-organ dysfunction (e.g. renal failure, cardiac arrhythmias, seizures), and death.¹ Symptoms attributed to electrolyte abnormalities include nausea, vomiting, diarrhea, muscle cramps, tetany, syncope, arrhythmias and seizures.¹ TLS may occur as early as 6 hours after treatment initiation or following dose increases. Patients should be carefully monitored by routine blood work and clinical assessments.

Risk Factors

Cancer patients who are at highest risk for TLS include those with:²

- High tumour burden
- Tumours with high proliferation rates
- Tumours that are highly sensitive to radiation therapy, cytotoxic chemotherapy or other cancer therapies (e.g. venetoclax, imatinib, bortezomib, corticosteroids, etc.)
- Underlying renal dysfunction
- Underlying electrolyte abnormalities

EDUCATION CORNER

Definitions of Tumour Lysis Syndrome¹

Laboratory TLS	Clinical TLS
 Presence of two or more abnormal serum values within 3 days before or 7 days after initiation of therapy, in the setting of adequate hydration and use of an antihyperuricemic agent: Potassium Phosphorus Calcium Uric acid 	 Laboratory TLS <u>Plus</u> Any 1 or more of the following: ↑ serum creatinine of 26.5 umol/L or single value ≥ 1.5 times the upper limit of normal Cardiac arrhythmias/sudden death Seizures

Prevention and Monitoring

The best prevention for TLS includes identifying high-risk patients, implementing prophylactic measures, and close laboratory and clinical monitoring.^{1,2} This includes:

- Aggressive hydration
- Prophylaxis with antihyperuricemic agents (e.g. allopurinol, rasburicase)
- Correcting any underlying electrolyte abnormalities
- Avoiding nephrotoxic drugs if possible (e.g. non-steroidal anti-inflammatories, contrast dyes).²
- Promptly managing any electrolytes abnormalities and/or clinical symptoms detected during treatment and holding the offending drug until these have been resolved
- Consider inpatient hospitalization for high-risk patients to allow for close monitoring and urgent management as needed

For details about the prevention of TLS specific to patients on venetoclax, please see the ULYVENETO Chemotherapy Protocol.

References:

- 1. Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. Br J Haematol 2004;127:3–11.
- 2. Hochberg J and Cairo MS. Tumor lysis syndrome: current perspective. Haematologica 2008; 93: 9-13.

BC CANCER SUMMIT EARLY BIRD REGISTRATION CLOSES SEPTEMBER 20, 2019

Early Bird Registration for the 2019 BC Cancer Summit closes on **September 20, 2019**. We encourage attendees to consider submitting a poster abstract to share and showcase the fantastic research or projects you are undertaking to improve cancer care.

Date:	November 21-23, 2019
Location:	Sheraton Wall Centre, Downtown Vancouver, BC
Theme:	Person-Centered Care
Abstract Submission Deadline:	September 20 @ 5 PM PST

For details about the conference program and registration details, please visit the Summit website at <u>www.bccancersummit.ca</u>.

BENEFIT DRUG LIST

New Programs

Effective 01 September 2019, the following treatment programs have been added to the BC Cancer <u>Benefit Drug List</u>:

Protocol Title	Protocol Code	Benefit Status
Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma using Venetoclax	ULYVENETO	Restricted
Treatment of Pediatric Patients with Philadelphia Chromosome-Negative (Ph-) Relapsed or Refractory Pre-B-Cell Acute Lymphoblastic Leukemia using Blinatumomab	Pediatric	Restricted
Treatment of Pediatric Patients with Acute Myeloid Leukemia Receiving Anthracycline on the COG Protocol AAML1031 using Dexrazoxane	Pediatric	Class I

CANCER DRUG MANUAL

New Monographs and Patient Handouts

The following drug is <u>NOT</u> a BC Cancer Benefit Drug and requires application to the BC Cancer Compassionate Access Program (CAP). The corresponding Monograph is made available for reference only. All BC Cancer drug monographs and patient handouts can be accessed from the Cancer Drug Manual <u>Drug Index</u>.

The **Dinutuximab Monograph** has been developed with expert review provided by Dr. Rebecca Deyell (pediatric hematologist/oncologist) and Dr. Jennifer Kendrick (clinical pharmacy specialist) of Children's and Women's Health Centre of British Columbia. Dinutuximab is a human-murine monoclonal antibody used in combination with other agents to treat neuroblastoma in children. The usual dose of dinutuximab is 17.5 mg/m² IV given over 10 to 20 hours, once daily for four consecutive days.

As there are no current adult indications for dinutuximab, a Patient Handout will not be made available at this time. Cancer Drug Manual patient handouts are designed for use by adult ambulatory patients.

Highlights from this document include:

- Hypersensitivity reactions have been reported
 - When used as a single agent (7% patients)
 - Potentially life-threatening reactions when used in combination therapy (up to 26% patients)
 - Patients should receive prehydration and premedications including an antihistamine, antipyretic, and analgesic with each infusion

CANCER DRUG MANUAL

- Continuous opioid infusions and co-analgesics should be pre-emptively started prior to dinutuximab to manage severe neuropathic pain
- Severe capillary leak syndrome, serum sickness, and neurologic ocular disorders have been reported

REVISED MONOGRAPHS AND PATIENT HANDOUTS

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

Afatinib Monograph:

- Cautions added gastrointestinal perforation
- Side Effects added gastrointestinal perforation, Stevens Johnson syndrome, and toxic epidermal necrolysis
- Dosing updated renal dosing

Cemiplimab Interim Monograph and Chemotherapy Preparation and Stability Chart:

- Common Trade Name(s) updated as now marketed in Canada
- Supply and Storage added Canadian manufacturer
- Parenteral Administration table revised recommended filter for administration
- Chemotherapy Preparation and Stability Chart updated manufacturer, and preparation and stability instructions per Canadian brand

Gemcitabine Chemotherapy Preparation and Stability Chart:

Brands – updated

Venetoclax Monograph and Patient Handout:

- Side Effects updated creatinine clearance limits in paragraph on hyperuricemia and tumour lysis syndrome
- Drug Interactions azithromycin, digoxin, and ritonavir interactions added to table; updated theoretical P-glycoprotein interactions
- Supply and Storage added information pertaining to available packaging (starting packs, blister cards, etc.)
- Dosing added new protocol and updated references
- Patient Handout updated instructions for missed doses to align with the protocol's Patient Handout

Vinorelbine Chemotherapy Preparation and Stability Chart:

Brands – updated

DELETED MONOGRAPHS AND PATIENT HANDOUTS

The **Ofatumumab Interim Monograph** has been deleted and the drug removed from the **Chemotherapy Preparation and Stability Chart,** as ofatumumab is no longer available in Canada.

SYSTEMIC THERAPY UPDATE EDITORIAL BOARD

MEMBERSHIP UPDATES

The Systemic Therapy Update Editorial Board would like to bid farewell to Ava Hatcher (Senior Practice Lead, Nursing, BC Cancer Centre for the North) as she steps down from the Board. The Board would like to thank Ava for her tremendous contributions to the ST Update over the past several years, and for the invaluable insight she has brought. We wish Ava the very best in her future endeavours.

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	РРРО	Patient Handout	Protocol Title		
ULYVENETO	\checkmark	\checkmark	\checkmark	atment of Relapsed/Refractory Chronic Lymphocytic Leukemia or all Lymphocytic Lymphoma using Venetoclax		
UMYCARDEX			\checkmark	Therapy of Multiple Myeloma using Carfilzomib and Dexamethasone With or Without Cyclophosphamide		
UMYCARLD			\checkmark	Therapy of Multiple Myeloma using Carfilzomib, Lenalidomide with Dexamethasone		

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)						
CODE	Protocol	РРРО	Patient Handout	Changes Protocol Title		
CNCARV	V	V		Logo updated, AST removed, LFT parameters added Carboplatin and Etoposide in the Treatmen Recurrent Ependymoma		
CNOCTLAR	V	V		Logo updated, typo corrected, brand name capitalized	Treatment of Growth Hormone Secreting Pituitary Adenoma using Octreotide	
CNTEMOZ			V	Logo updated, typo corrected	Therapy for Malignant Brain Tumours using Temozolomide	

Revised Protocols, PPPOs and Patient Handouts (Affected Documents are Checked)						
CODE	Protocol	РРРО	Patient Handout	Changes	Protocol Title	
GIAVCAP	Ø		Ø	Tumour markers and Side effects management information updated	Palliative Therapy of Advanced Colorectal Cancer using Capecitabine	
GIAVCAPB	V			Eligibility and Dose Modifications updated	Palliative Therapy of Metastatic Colorectal Cancer using Capecitabine and Bevacizumab	
GICIRB	V			Eligibility updated	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Irinotecan, Bevacizumab and Capecitabine	
GICOXB	V		V	Oxaliplatin diluent volume clarified; Side effects management information updated	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Oxaliplatin, Bevacizumab and Capecitabine	
GIEFFOXRT	Ø		V	Eligibility and Oxaliplatin diluent volume clarified; Side effects management information updated	Combined Modality Therapy for Locally Advanced Esophageal Cancer using Oxaliplatin, Fluorouracil, Leucovorin, and Radiation Therapy	
GIGAVCC			V	Tumour markers updated, Side effects management information updated	Palliative Therapy of Metastatic or Locally Advanced Anal Squamous Cell Carcinoma using Cisplatin and Capecitabine	
GIPAJGCAP	V	V	V	Institutional name, Eligibility, Tests, Systemic Therapy Chair contact info, and Side effects management information updated	Adjuvant Chemotherapy for Resected Pancreatic Adenocarcinoma using Capecitabine and Gemcitabine	
GIRAJFFOX		\checkmark		Institutional name updated	Adjuvant Combination Chemotherapy for Stage III Rectal Cancer using Oxaliplatin, Fluorouracil and Leucovorin	
GIRCAP	V	V	V	Institutional name, Tests, Dose Modifications, Systemic Therapy Chair contact info, Tumour markers, and Side effects management information updated	Adjuvant Therapy for Stage II and III Rectal Cancer Previously Treated with Preoperative Radiation Therapy using Capecitabine	

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED) CODE Patient Chempose Patient						
CODE	Protocol	PPPO	Handout	Changes	Protocol Title	
GIRCRT			V	Institutional name and Side effects management information updated	Combined Modality Adjuvant Therapy for High Risk Rectal Carcinoma using Capecitabine and Radiation Therapy	
UGOOVBEVG	V			Exclusions clarified	Treatment of Platinum-Resistant Epithelial Ovarian Cancer with Bevacizumab and Gemcitabine	
UGOOVBEVLD	V			Exclusions clarified	Treatment of Platinum-Resistant Epithelial Ovarian Cancer with Bevacizumab and Doxorubicin Pegylated Liposomal (CAELYX)	
UGOOVBEVP	V			Exclusions clarified	Treatment of Platinum-Resistant Epithelial Ovarian Cancer with Bevacizumab and Paclitaxel	
UGOOVBEVV	V			Exclusions clarified	Treatment of Platinum-Resistant Epithelial Ovarian Cancer with Bevacizumab and Vinorelbine	
UGOOVCATB	V			Exclusions clarified	Primary Treatment of Invasive Epithelial Ovaria Fallopian Tube or Primary Peritoneal Cancer w High-Risk of Relapse using Bevacizumab, Carboplatin and Paclitaxel	
UGUAVIPNI	V	V		lpilimumab diluent volume clarified	Treatment of Metastatic or Advanced Renal Cel Carcinoma using Ipilimumab and Nivolumab	
GUBGEM	V	\checkmark		Dosing administration guidelines updated	Intravesical Therapy for Non-Muscle Invasive Bladder Cancer using Gemcitabine	
UHNLADCF	V	V		Prehydration and fluorouracil dose adjustment clarified; Institutional name updated	Treatment of Locally Advanced Squamous Cell Carcinoma of the Head and Neck with Docetaxel, Cisplatin and Infusional Fluorouracil	
LKATOATRA	V			Dose Modifications revised	First-Line Induction and Consolidation Therapy of Acute Promyelocytic Leukemia using Arsenic Trioxide and Tretinoin (All-Trans Retinoic Acid)	
LKATOP	V			Dose Modifications revised	First-Line Induction and Consolidation Therapy of Acute Promyelocytic Leukemia using Arsenic Trioxide, Tretinoin (All-Trans Retinoic Acid) and Daunorubicin	
LKATOR	V			Dose Modifications revised	Induction and Consolidation Therapy of Relapsed Acute Promyelocytic Leukemia using Arsenic Trioxide and Tretinoin (All-Trans Retinoic Acid)	

REVISED PROTOCOLS, PPPOS AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)						
CODE	Protocol	РРРО	Patient Handout	Changes	Protocol Title	
ULKBLIN	V			Eligibility, Tests, Treatment, Dose Modifications and Precautions updated	Treatment of Philadelphia Chromosome-Negative Refractory or Relapsed Pre-B-Cell Acute Lymphoblastic Leukemia with Blinatumomab	
LUOTCAV	V	V	V	Institutional name and Tests updated Treatment of Thymoma/Thymic Carcinoma Cyclophosphamide, Doxorubicin and Vincrist (CAV)		
LUOTPAC	V	\checkmark	V	Institutional name and Tests updated	Treatment of Thymoma with Platinum, Doxorubicin and Cyclophosphamide	
LUOTPERT	V	V	V	Institutional name and Tests updated	Treatment of Thymoma using Cisplatin and Etoposide with Radiation Therapy	
LUPUPE	V	\checkmark	V	Institutional name and Tests updated	Treatment of Cancer of Unknown Primary Involving the Thorax with Cisplatin and Etoposide	
ULYOBBEND		V		Default acetaminophen premedication dose revised	Treatment of Rituximab-Refractory Follicular Lymphoma (FL) with Obinutuzumab in Combination with Bendamustine	
ULYOBCHLOR		V		Default acetaminophen premedication dose revised	Previously Untreated Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma with Obinutuzumab and Chlorambucil	
UMYCARLD	V			Eligibility clarified	Therapy of Multiple Myeloma using Carfilzomib, Lenalidomide with Dexamethasone	
MYMPBOR		Ø		Clarified ANC and platelet parameters for cyclophosphamide	Treatment of Multiple Myeloma using Melphalan, Prednisone and Weekly Bortezomib with the Option of Substituting Cyclophosphamide for Melphalan	
SAIME		V		Diluent and Labs updated	Etoposide, Ifosfamide-Mesna (SAIME) for Use in Sarcomas	

WEBSITE RESOURCES AND CONTACT INFORMATION

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To update contact information of any CON sites, ple	ase contact:		bulletin@bccancer.bc.ca
Oncology Drug Information	604-877-6275		druginfo@bccancer.bc.ca
Nurse Educators	604-877-6000 x 672638		nursinged@bccancer.bc.ca
Library/Cancer Information	604-675-8003 Toll Free 888-675-8001 x 8003		requests@bccancer.bc.ca
Pharmacy Professional Practice	604-877-6000 x 672247		mlin@bccancer.bc.ca
Provincial Professional Practice Nursing			BCCancerPPNAdmin@ehcnet.phsa.ca
OSCAR	888-355-0355	604-708-2051	oscar@bccancer.bc.ca
Compassionate Access Program (CAP)	604-877-6277	604-708-2026	cap bcca@bccancer.bc.ca
Pharmacy Oncology Certification	250-712-3900 x 686820		rxchemocert@bccancer.bc.ca
BC Cancer-Abbotsford	604-851-4710 Toll Free 877-547-3777		
BC Cancer-Prince George (Centre for the North)	250-645-7300 Toll Free 888-775-7300		
BC Cancer-Surrey	604-930-2098 Toll Free 800-523-2885		
BC Cancer-Kelowna	250-712-3900 Toll Free 888-563-7773		
BC Cancer-Vancouver	604-877-6000 Toll Free 800-663-3333		
BC Cancer-Victoria	250-519-5500 Toll Free 800-670-3322		

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