

# **Systemic Therapy Update**

Volume 22 Issue 12 December 2019

## For Health Professionals Who Care for Cancer Patients

### **Inside This Issue:**

#### **Editor's Choice**

<u>New Programs</u>: Nivolumab for Relapsed or Refractory Hodgkin Lymphoma (ULYNIV, ULYNIV4); Systemic Therapy Update – Revision Table Formatting

#### **Drug Update**

Biosimilar Trastuzumab Coming Soon; Patient Assistance Programs

#### **Drug Shortages**

<u>New</u>: Erwinia asparaginase; <u>Updated</u>: Raltitrexed; Resolved: Fludarabine Injectable

#### **Cancer Drug Manual**

<u>New</u>: Pralatrexate; <u>Revised</u>: Daratumumab, Doxorubicin Pegylated Liposomal, Gemcitabine; Retired: Porfimer

#### **Benefit Drug List**

New: ULYNIV, ULYNIV4; Revised: ULYBV; Deleted: Porfimer

#### New and Revised Protocols, PPPOs and Patient Handouts

New: ULYNIV, ULYNIV4

Revised: BMTMM301, UBRAJPAM, BRAJZOL2, BRAJZOL5, GIAJCAP, GIAVPANI, GIFIRINOX, GIPAJFIROX, GOBEP, GOCXCRT, UGUAVIPNI, GUBMITO, GUVEIP, HNLAALTPRT, HNLACAFRT, HNLACETRT, HNLAPRT, HNNLAPRT, UHNOTLEN, ULYAJBV, LYASPMEDEX, ULYBV, LYCODOXMR, LYHDMRP, LYHDMTXP, LYHDMTXR, LYSMILE. UMYCARLD, UMYLDF, UMYLDREL, UMYLENMTN, UMYPOMDEX, SAAJAP, SAAVAP, USAAVGR, USMAVDT, USMAVFIPI, USMAVIPI, USMAVIPNI, USMAVNIV, USMAVNIV4, USMAVTRA

#### **Resources and Contact Information**

## Editor's Choice

### **New Programs**

Effective 01 December 2019, the BC Cancer Provincial Systemic Therapy Program has approved the following new treatment programs. The full details of these programs can be found on the BC Cancer website in the Chemotherapy Protocols section.

#### Lymphoma

Nivolumab for Relapsed or Refractory Hodgkin Lymphoma (ULYNIV, ULYNIV4) – The BC Cancer Lymphoma Tumour Group is introducing nivolumab for classical Hodgkin lymphoma (cHL) that has relapsed or progressed after autologous stem cell transplantation (ASCT) and brentuximab vedotin (BV). Most patients who relapse after ASCT are treated with BV, the majority of whom will relapse again. Nivolumab fills an unmet need in this small, heavily pretreated patient population for which there was previously no standard treatment. Nivolumab is administered every two weeks (ULYNIV) or every four weeks (ULYNIV4). A BC Cancer Compassionate Access Program (CAP) approval is required.

Approval of nivolumab in cHL is predominantly based on the single-arm, phase II CHECKMATE-205 trial.<sup>2</sup> An objective response rate was achieved in 68% (95% CI 56-78) of patients after failure of ASCT and BV, with a median duration of response of 16 months (95% CI 8-20). The overall survival rate was 89.2% after a minimum follow-up of 20 months. Among patients who had no response to prior BV treatment, 72% achieved an objective response with nivolumab. In general, adverse effects were as expected for checkpoint inhibitors, with the most common drug-related adverse events including fatigue, infusion-

## Editor's Choice

related reactions, and rash. The most frequent grade 3 or higher events were neutropenia and increased lipase concentrations. Patient input indicates that a majority of patients felt that nivolumab was able to manage their disease symptoms as well as improve their health and well-being.<sup>1</sup>

#### References

- Pan-Canadian Oncology Drug Review (pCODR) Expert Review Committee (pERC). Final recommendation for nivolumab (Opdivo®) for classical Hodgkin lymphoma (cHL). 03 May 2018.
- Younes A, Santoro A, Shipp M, et al. Nivolumab for classical Hodgkin's lymphoma after failure of both autologous stem-cell transplantation and brentuximab vedotin: a multicentre, multicohort, single-arm phase 2 trial. Lancet Oncol 2016;17:1283-1294.
   Available from: <a href="https://doi.org/10.1016/S1470-2045(16)30167-X">https://doi.org/10.1016/S1470-2045(16)30167-X</a>

## Systemic Therapy Update - Revision Table Formatting

Revisions to BC Cancer Protocol Summaries, Provincial Pre-Printed Orders (PPPOs) and Patient Handouts are presented in a table at the end of each monthly issue of the BC Cancer Systemic Therapy Program Update. Many of these document revisions are also incorporated into the cancer treatment PowerPlans in the Computerized Physician Order Entry (CPOE) system within the Clinical and Systems Transformation (CST) project. The table has now been formatted to identify revisions specific to each document. Please see the *Revised Protocols, PPPOs and Patient Handouts* table at the end of the newsletter.

## **Drug Update**

## **Biosimilar Trastuzumab Coming in February 2020**

Effective 01 February 2020, the BC Cancer Provincial Systemic Therapy Program will implement the use of biosimilar trastuzumab in all BC Cancer trastuzumab-containing protocols. All three biosimilars, Herzuma®, Ogivri® and Trazimera®, are eligible for reimbursement. BC Cancer regional centres will stock Herzuma® as the designated biosimilar.

The following outlines key funding details:

- Patients starting on trastuzumab on or after February 1<sup>st</sup> will be funded for biosimilar trastuzumab only. Requests for the use of Herceptin® on or after February 1<sup>st</sup> will require submission through the BC Cancer Compassionate Access Program (CAP).
- Patients who started treatment with the reference biologic, Herceptin®, prior to February 1<sup>st</sup>, may continue to receive it for the duration of treatment. Clinicians may choose to switch patients currently receiving trastuzumab to the biosimilar, after discussion with the patient.
- All patients on combination pertuzumab and trastuzumab in the advanced setting (i.e., BRAVPTRAD and BRAVPTRAT) will continue to receive the reference biologic, Herceptin®, regardless of start date.
- Patients who have had a treatment interruption may continue to receive their initial brand of trastuzumab if resuming the same protocol.

More information and resource materials on biosimilar drugs are available on the BC Cancer website, located in the <u>Biosimilar Drugs</u> section.

## **Drug Update**

## **Manufacturer Patient Assistance Programs**

The listing of patient assistance programs offered by pharmaceutical manufacturers has been updated and can be accessed directly at <a href="www.bccancer.bc.ca/mpap">www.bccancer.bc.ca/mpap</a>. It can also be found on the BC Cancer website under Health Professionals > Systemic Therapy > <a href="Reimbursement & Forms">Reimbursement & Forms</a>.

## **Drug Shortages**

The following are updates of drug supply shortages in BC. Details about new, ongoing and resolved drug shortages and their recommended treatment alternatives can be found in the briefing notes and/or email communications previously circulated to BC Cancer and the Community Oncology Network (CON).

## **New Shortages**

### Erwinia asparaginase

(Adapted from BC Cancer Briefing Notes 09Nov2019 and 22Nov2019)

There is a worldwide shortage of Erwinia asparaginase (Erwinase®). Although the manufacturer anticipates supply to be available by early December, this is an estimate, and the manufacturer recommends that no new patients be started at this time. Erwinia asparaginase is funded by BC Cancer for use in leukemia and lymphoma patients who are allergic to asparaginase (Kidrolase®). It is recommended that BC Cancer and CON centres implement conservation strategies. Pegaspargase (Oncaspar®) may be used in patients who have experienced an allergic reaction with asparaginase (Kidrolase®) or Erwinia asparaginase (Erwinase®); consider using pegaspargase as a therapeutic alternative if Erwinia asparaginase is not available.

## **Updated Shortages**

#### Raltitrexed

(Adapted from BC Cancer Briefing Note Update 25Nov2019)

It is anticipated that the Canadian inventory of raltitrexed will be depleted by January 2020, with no confirmed supply return date. BC Cancer recommends reserving existing supplies for current patients, and prioritizing adjuvant treatments over metastatic treatments. No new patients should be started on raltitrexed at this time.

## **Resolved Shortages**

#### Fludarabine Injectable

(Adapted from BC Cancer email communication 15Nov2019)

Fludarabine injectable supply is now available.

# Cancer Drug Manual

## **New Monographs and Patient Handouts**

The following drug is <u>NOT</u> a BC Cancer Benefit Drug. The corresponding Interim Monograph and Patient Handout are 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 **Pralatrexate Monograph and Patient Handout** have been developed with expert review provided by Dr. Kerry Savage, medical oncologist, and Louisa Pang, pharmacist, of the BC Cancer Lymphoma Tumour Group. Pralatrexate, a methotrexate analogue, is a folate antagonist with a high affinity for cells expressing reduced folate carrier type 1. Pralatrexate is indicated for the treatment of relapsed or refractory peripheral T-cell lymphoma. The usual dose is 30 mg/m² IV weekly for six weeks out of a sevenweek cycle.

Highlights of these documents include:

- Severe, grade 3 or 4 mucositis is reported in up to 21% of patients. Onset is usually within the first two weeks of treatment. To reduce the risk of mucosal inflammation, vitamin B<sub>12</sub> and folic acid supplementation must begin prior to pralatrexate therapy.
- Rare, but severe, dermatologic reactions are reported, typically occurring early in treatment. Patients
  with extensive involvement of lymphoma in the skin or subcutaneous sites may be at greater risk of
  developing severe skin reactions.

## **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:

### **Daratumumab Monograph**

Parenteral Administration: added 90-minute infusion ("rapid infusion") to table; stay tuned for implementation in daratumumab treatment protocols in the near future

### Doxorubicin Pegylated Liposomal Monograph and Patient Handout

Common Trade names: updated

Supply and Storage: updated with current brand

### **Gemcitabine Monograph**

Supply and Storage: updated with current brands

Parenteral Administration table: updated intravesical administration

Dosage Guidelines: added intravesical dosing

### **Retired Monographs and Patient Handouts**

The **Porfimer Monograph** and **Patient Handout** have been retired, as porfimer is no longer available in Canada. Porfimer has been deleted from the **Chemotherapy Preparation and Stability Chart** and the **Extravasation Hazard Table**.

# Benefit Drug List

## **New Programs**

Effective 01 December 2019, the following new treatment programs have been added to the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Treatment of Relapsed or Refractory Hodgkin Lymphoma using <b>Nivolumab</b>	ULYNIV	Restricted
Treatment of Relapsed or Refractory Hodgkin Lymphoma using 4-Weekly <b>Nivolumab</b>	ULYNIV4	Restricted

## **Revised Programs**

Effective 01 December 2019, the following treatment program has been revised on the BC Cancer Benefit Drug List:

Protocol Title	Protocol Code	Benefit Status
Treatment for Consolidation Therapy Post-Autologous Stem Cell Transplant (ASCT) for Hodgkin Lymphoma using <b>Brentuximab Vedotin</b> ( <i>Protocol Title updated</i> )	ULYBV (previously ULYAJBV)	Restricted

## **Deleted Programs**

Effective 01 December 2019, porfimer has been deleted from the BC Cancer Benefit Drug List.

# Highlights of New and Revised Protocols, PPPOs 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, with documents revisions indicated in the respective columns. Protocol codes for treatment requiring BC Cancer Compassionate Access Program approval are prefixed with the letter **U**.

New Prot	New Protocols, PPPOs and Patient Handouts (new documents checked ☑)			
Code	Protocol	PPPO	Patient Handout	Protocol Title
ULYNIV	$\overline{\checkmark}$	$\square$	$\overline{\checkmark}$	Treatment of Relapsed or Refractory Hodgkin Lymphoma using Nivolumab
ULYNIV4		$\square$	$\overline{\checkmark}$	Treatment of Relapsed or Refractory Hodgkin Lymphoma using 4-Weekly Nivolumab

Revised Protocols, PPPOs and Patient Handouts (revisions in respective columns)				
Code	Protocol	PPPO	Patient Handout	Protocol Title
BMTMM0301	Hydration updated			Conditioning Therapy for Autologous Stem Cell Transplant using High-Dose Melphalan in the Treatment of Multiple Myeloma
UBRAJPAM	Protocol Title updated (revisions in blue)			Adjuvant Therapy <del>Treatment of</del> for Breast Cancer in Postmenopausal Women using Pamidronate
BRAJZOL2	Protocol Title updated (revisions in blue)			Adjuvant Therapy Treatment of for Breast Cancer in Postmenopausal Women using 3- Monthly Zoledronic Acid
BRAJZOL5	Protocol Title updated (revisions in blue)			Adjuvant Therapy <del>Treatment of</del> for Breast Cancer in Postmenopausal Women using 6-Monthly Zoledronic Acid
GIAJCAP		Premedication and Return Appointment Orders updated		Adjuvant Therapy of Colon Cancer using Capecitabine
GIAVPANI	Tests updated (CA19-9 removed)	Tests updated (CA19-9 removed)		Palliative Third-Line Treatment of Metastatic Colorectal Cancer using Panitumumab
GIFIRINOX	Treatment updated (leucovorin infusion time)			Palliative Combination Chemotherapy for Advanced Pancreatic Adenocarcinoma using Irinotecan, Oxaliplatin, Fluorouracil and Leucovorin

Revised F	Revised Protocols, PPPOs and Patient Handouts (revisions in respective columns)			
Code	Protocol	PPPO	Patient Handout	Protocol Title
GIPAJFIROX	Treatment updated (leucovorin infusion time)			Adjuvant Chemotherapy for Resected Pancreatic Adenocarcinoma using Irinotecan, Oxaliplatin, Fluorouracil and Leucovorin
GOBEP	Eligibility revised			Therapy of Ovarian Germ Cell Cancer using Bleomycin, Etoposide and Cisplatin
GOCXCRT	Hydration updated	Hydration updated		Treatment of High-Risk Squamous Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma of the Cervix with Concurrent Cisplatin and Radiation
UGUAVIPNI	Precautions clarified, Link to SCIMMUNE added			Treatment of Metastatic or Advanced Renal Cell Carcinoma using Ipilimumab and Nivolumab
GUBMITO	Catheter insertion added, Maintenance duration clarified	Catheter insertion added, Maintenance duration clarified		Intravesical Therapy for Non-Muscle Invasive Bladder Cancer using Mitomycin
GUVEIP	Hydration updated			Consolidation/Salvage Treatment for Germ Cell Cancer using Vinblastine, Cisplatin, Ifosfamide and Mesna
HNLAALTPRT	Hydration updated	Hydration updated	Smoking cessation and Skin management updated	Locally Advanced (Alternate) Head and Neck Cancer using Cisplatin during Radiation Therapy
HNLACAFRT			Smoking cessation and Skin management updated	Combined Chemotherapy (Carboplatin and Fluorouracil) and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck
HNLACETRT			Smoking cessation and Skin management updated	Combined Cetuximab and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck
HNLAPRT	Hydration updated	Hydration updated	Smoking cessation and Skin management updated	Combined Chemotherapy (Cisplatin) and Radiation Treatment for Locally Advanced Squamous Cell Carcinoma of the Head and Neck
HNNLAPRT			Smoking cessation and Skin management updated	Treatment of Locally Advanced Nasopharyngeal Cancer with Concurrent Cisplatin and Radiation
UHNOTLEN	Dose Modification (proteinuria) clarified	Tests (albumin, urine protein) clarified		Therapy for Locally Recurrent or Metastatic, RAI-Refractory Differentiated Thyroid Cancer using Lenvatinib

Revised P	Revised Protocols, PPPOs and Patient Handouts (revisions in respective columns)			
Code	Protocol	PPPO	Patient Handout	Protocol Title
ULYAJBV	New Protocol Code ULYBV and Protocol Title (see ULYBV below)	New Protocol Code ULYBV (see below)		Treatment for Adjuvant Therapy Post- Autologous Stem Cell Transplant (ASCT) for Hodgkin Lymphoma using Brentuximab Vedotin
LYASPMEDEX	Hydration updated, Physician signature requirement clarified	Hydration updated, Physician signature requirement clarified (inpatient)		Treatment of Refractory or Relapsing Extranodal Natural Killer or T-Cell Lymphoma using Pegaspargase, Methotrexate and Dexamethasone
ULYBV	New Protocol Code (previously ULYAJBV) and Protocol Title (revisions in blue)	New Protocol Code (previously ULYAJBV)		Treatment for Consolidation Adjuvant Therapy Post-Autologous Stem Cell Transplant (ASCT) for Hodgkin Lymphoma using Brentuximab Vedotin
LYCODOXMR	Hydration updated, Physician signature requirement clarified	Hydration updated, Physician signature requirement clarified (inpatient)		Treatment of Burkitt Lymphoma and Leukemia (ALL-L3) with Cyclophosphamide, Vincristine, Doxorubicin, Methotrexate, Leucovorin (CODOX-M) and Rituximab
LYHDMRP	Hydration updated, Physician signature requirement clarified	Hydration updated, Physician signature requirement clarified (inpatient)		Treatment of Primary Intracerebral Lymphoma with High-Dose Methotrexate and Rituximab
LYHDMTXP	Hydration updated, Physician signature requirement clarified	Hydration updated, Physician signature requirement clarified (inpatient)		Treatment of Primary Intracerebral Lymphoma with High-Dose Methotrexate
LYHDMTXR	Hydration updated, Physician signature requirement clarified	Hydration updated, Physician signature requirement clarified (inpatient)		Treatment of Leptomeningeal Lymphoma or Recurrent Intracerebral Lymphoma with High- Dose Methotrexate
LYSMILE	Hydration updated, Physician signature requirement clarified	Hydration updated, Physician signature requirement clarified (inpatient)		Treatment of Natural Killer or T-Cell Lymphoma using Dexamethasone, Methotrexate, Ifosfamide, Pegaspargase and Etoposide
UMYCARLD	Pregnancy tests updated	Pregnancy tests updated, Day 8 labs clarified		Therapy of Multiple Myeloma using Carfilzomib, Lenalidomide with Dexamethasone
UMYLDF	Pregnancy tests updated	Pregnancy tests updated		Treatment of Previously Untreated Multiple Myeloma and Not Eligible for Stem Cell Transplant using Lenalidomide with Low-Dose Dexamethasone
UMYLDREL	Pregnancy tests updated	Pregnancy tests updated		Therapy of Relapsed Multiple Myeloma using Lenalidomide with Dexamethasone

Revised P	Revised Protocols, PPPOs and Patient Handouts (revisions in respective columns)				
Code	Protocol	PPPO	Patient Handout	Protocol Title	
UMYLENMTN	Pregnancy tests updated	Pregnancy tests updated		Maintenance Therapy of Multiple Myeloma using Lenalidomide	
UMYPOMDEX	Pregnancy tests updated	Pregnancy tests updated		Therapy of Multiple Myeloma using Pomalidomide with Dexamethasone	
SAAJAP	Hydration updated	Hydration updated (inpatient)		Adjuvant Therapy for Osteosarcoma using Doxorubicin and Cisplatin	
SAAVAP	Hydration updated	Hydration updated (inpatient)		Therapy of Advanced Osteosarcoma using Doxorubicin and Cisplatin	
USAAVGR	Drug storage instructions added	Treatment cycle and regimen clarified, Dispensing instructions updated		Third-Line Therapy of Advanced Gastrointestinal Stromal Cell Tumours (GIST) using Regorafenib	
USMAVDT			Fever management updated	Treatment of BRAF V600 Mutation-Positive Unresectable or Metastatic Melanoma using Dabrafenib and Trametinib	
USMAVFIPI	Ipilimumab concentration clarified			First-Line Treatment of Unresectable or Metastatic Melanoma using Ipilimumab	
USMAVIPI	Contact Physician updated, Ipilimumab concentration clarified			Treatment of Unresectable or Metastatic Melanoma using Ipilimumab	
USMAVIPNI	Contact Physician updated, Ipilimumab concentration added, Precautions clarified with link to SCIMMUNE			Treatment of Unresectable or Metastatic Melanoma using Ipilimumab and Nivolumab	
USMAVNIV			Minor wording updated	Treatment of Unresectable or Metastatic Melanoma using Nivolumab	
USMAVNIV4			Minor wording updated	Treatment of Unresectable or Metastatic Melanoma using 4-Weekly Nivolumab	
USMAVTRA			Institutional name updated in footer	Treatment of BRAF V600 Mutation-Positive Unresectable or Metastatic Melanoma using Trametinib	

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