

Multiple Myeloma

Carfilzomib for Relapsed or Refractory Multiple Myeloma (UMYCARDEX, UMYCARLD) — These BC Cancer protocols have been revised to reflect new carfilzomib dosing, and to standardize the carfilzomib infusion time and dexamethasone dosing. Carfilzomib was previously administered twice weekly, in combination with dexamethasone (UMYCARDEX) or with lenalidomide-dexamethasone (UMYCARLD). Moving forward, carfilzomib will be administered **once weekly on days 1, 8 and 15 of a 28-day cycle**. Carfilzomib will be administered over 30 minutes in both protocols. In addition, dexamethasone has been standardized to 40 mg once weekly on days 1, 8, 15 and 22, with an option to use a lower dose in older patients.

Details of the above changes are outlined below:

	UMYCARDEX		UMYCARLD	
Carfilzomib	Cycle 1	Day 1: 20 mg/m ²	Cycle 1	Day 1: 20 mg/m ²
		Days 8, 15: 70 mg/m ²		Days 8, 15: 56 mg/m ²
	Cycle 2 +	Days 1, 8, 15: 70 mg/m²	Cycles 2-18	Days 1, 8, 15: 56 mg/m²
	Infusion time	30 minutes		
no change		previously 10 minutes		
Dexamethasone	Days 1, 8, 15, 22: 40 mg			
	previously 20 mg twice weekly		no change	
Lenalidomide	-----		Days 1-21: 25 mg once daily no change	

Once-weekly high-dose (70 mg/m²) carfilzomib-dexamethasone had excellent median progression-free survival compared to twice-weekly lower-dose (27 mg/m²) carfilzomib-dexamethasone (11.2 vs. 7.6 months, HR 0.69, 95% CI 0.54-0.83).³ It is anticipated that once-weekly high-dose (70 mg/m²) carfilzomib-dexamethasone will have similar progression-free survival compared to twice-weekly high-dose (56 mg/m²) carfilzomib-dexamethasone.

When used with lenalidomide, **once-weekly high-dose (56 mg/m²) carfilzomib-lenalidomide-dexamethasone** had a high overall response rate (90.0%), comparable to that previously reported for twice-weekly dosing.⁴

The Carfilzomib Monograph, available from the [Cancer Drug Manual](#)[®], has been updated with this new dosing information.

References

1. Novartis Pharmaceuticals Canada. Zykadia[®] product monograph. Dorval, Quebec. 06 January 2020.
2. Cho BC, Obermannova R, Bearz A. Efficacy and safety of ceritinib (450 mg/d or 600 mg/d) with food versus 750 mg/d fasted in patients with ALK receptor tyrosine kinase (ALK)-positive NSCLC: primary efficacy results from the ASCENT-8 study. J Thor Oncol 2019;14:1255-1265. Available from: <https://doi.org/10.1016/j.jtho.2019.03.002>
3. Moreau P, Mateos M-V, Berenson JR, et al. Once weekly versus twice weekly carfilzomib dosing in patients with relapsed and refractory multiple myeloma (A.R.R.O.W.): interim analysis results of a randomized, phase 3 study. Lancet Oncol 2018;19:953-964. Available from: [https://doi.org/10.1016/S1470-2045\(18\)30354-1](https://doi.org/10.1016/S1470-2045(18)30354-1)
4. Biran N, Siegel D, Berdeja JG, et al. Weekly carfilzomib, lenalidomide, and dexamethasone in relapsed or refractory multiple myeloma: A phase 1b study. Am J Hematol 2019;94:794-802. doi: [10.1002/ajh.25498](https://doi.org/10.1002/ajh.25498)

All BC Cancer Drug Manual[©] documents can be accessed from the [Cancer Drug Manual[©]](#) home page on the BC Cancer website.

New Documents

Note that the following drugs are NOT BC Cancer Benefit Drugs and require application to the BC Cancer Compassionate Access Program (CAP). The corresponding Interim Monographs are made available for reference only.

The **Dacomitinib Interim Monograph** and **Patient Handout** have been developed with expert review provided by Dr. Barb Melosky (medical oncologist) and Alysha Bharmal (clinical pharmacist) of the BC Cancer Lung Tumour Group. Dacomitinib is an orally administered, second-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor. It is indicated for the treatment of EGFR mutation-positive non-small cell lung cancer. The usual dose is 45 mg PO once daily.

Highlights from these documents include:

- diarrhea is experienced in 87% of patients and may be severe; close monitoring and early intervention are essential to prevent the development of more severe diarrhea
- skin reactions are common and may be aggravated by sun exposure; sun protection during treatment is advised
- other common side effects include paronychia and stomatitis
- rare, but serious, side effects include interstitial lung disease/pneumonitis, hepatitis and keratitis

Dacomitinib has been added to the **Auxiliary Label List** (no auxiliary label required) and has been evaluated for the **BC Cancer Hazardous Drug List**.

The **Polatuzumab Vedotin Interim Monograph** has been developed. Polatuzumab vedotin is a CD79b-directed antibody-drug conjugate consisting of polatuzumab, a humanized monoclonal antibody, and monomethyl auristatin E, a small molecule anti-mitotic agent, attached by a cleavable linker. The usual dose in the treatment of non-Hodgkin lymphoma is 1.8 mg/kg IV given on day 1 of a three-week cycle.

Highlights from these documents include:

- the initial dose is administered over 90 minutes; if well tolerated, subsequent infusions may be administered over 30 minutes
- premedication with antihistamine and antipyretic is recommended prior to each infusion; most infusion-related reactions are grade 1 or 2, but severe or delayed reactions have been reported
- myelosuppression can be severe; consider prophylactic granulocyte colony stimulating factor administration as needed
- prophylaxis for opportunistic infections such as *Pneumocystis jiroveci* pneumonia and herpesvirus is recommended throughout treatment

Polatuzumab vedotin has been added to the **Chemotherapy Preparation and Stability Chart** and has been evaluated for the **BC Cancer Hazardous Drug List**.

Revised Documents

Highlights of key changes are listed below:

Bortezomib Monograph

Dosage Guidelines: updated dosing in renal failure and dialysis

Carfilzomib Monograph

Parenteral Administration: updated infusion time to include new dosing

Dosage Guidelines: added weekly dosing regimen (see *Drug Update* section above)

Ceritinib Monograph and Patient Handout

Dosage Guidelines: updated dosing (see *Drug Update* section above)

Patient Handout: revised directions to take ceritinib with food

Auxiliary Label List: 'Take with food' label added; 'Take on an empty stomach' label removed

Etoposide Monograph

Supply and Storage: updated supplier and product information for oral etoposide and etoposide phosphate

Etoposide Phosphate Interim Monograph

Supply and Storage: updated supplier and product information

Chemotherapy Preparation and Stability Chart:

Etoposide phosphate: updated supplier

Rituximab: updated stability information for final compounded solutions

Treosulfan: updated reconstitution instructions and product information

Vinblastine: clarified language for product stability for all brands; Hospira brand replaced by Pfizer

Drug Shortages

The following are updates of drug supply shortages in BC. Full details about new, updated or resolved drug shortages, including 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

Dexamethasone tablets

(Adapted from BC Cancer Briefing Note 21Feb2020)

There is currently a backorder of dexamethasone in the 2 mg and 4 mg tablet strengths, with variable supplies remaining. At BC Cancer, dexamethasone tablets are used predominantly in prophylactic antiemetic regimens (see SCNAUSEA), as hypersensitivity reaction prophylaxis (see SCDRUGRX), and as a component of cancer treatment in a number of protocols. Clinicians should continue to prescribe and/or dispense dexamethasone for all indications; multiple tablet strengths may need to be combined (0.5 mg, 0.75 mg, 2 mg, and 4 mg) to make up the appropriate dose. BC Cancer will advise on appropriate action and/or therapeutic alternatives should dexamethasone supplies become critically low.

Drug Shortages

Updated

Hydroxyurea

(Adapted from BC Cancer email communication 13Feb2020)

The hydroxyurea shortage is ongoing and supplies are expected to remain very limited until at least mid-March 2020.

Resolved

Ranitidine

(Adapted from BC Cancer email communication 11Feb2020)

Ranitidine injectable and ranitidine tablets are now available on allocation.

Community Oncology Network (CON)

2019-2020 OSCAR Billing Deadline: 03 April 2020

The 2019-2020 fiscal year will end on Tuesday 31 March 2020. To meet the deadline for external reporting to the Ministry of Health, all claims for drug reimbursement for the current fiscal year must be invoiced by **Friday 03 April 2020** via **OSCAR** (Online System for Cancer Drugs Adjudication and Reimbursement). Any claims invoiced after this date will not be eligible for reimbursement. For more information, please e-mail oscar@bccancer.bc.ca.

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 www.bccancer.bc.ca/mpap. It can also be found on the BC Cancer website under Health Professionals > Systemic Therapy > [Reimbursement & Forms](#).

Systemic Therapy Update Editorial Board

Membership Update

The Systemic Therapy Update Editorial Board would like to bid farewell to **Naren Bollipalli** (Interim Professional Practice Leader, Pharmacy, BC Cancer – Centre for the North) as he steps down from the Board. Thank you for your contributions over the past year!

The Editorial Board would also like to welcome back **Alison Pow** (Professional Practice Leader, Pharmacy, BC Cancer – Centre for the North) as she resumes her role with the Board.

Highlights of New & 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 document revisions indicated in the respective columns. Protocol codes for treatment requiring BC Cancer Compassionate Access Program approval are prefixed with the letter **U**.

NEW Protocols, PPPOs and Patient Handouts (*new documents checked*)

Code	Protocol Title	Protocol	PPPO	Handout
ULYVENETOR	Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma using Venetoclax and Rituximab	<input type="checkbox"/>	<input checked="" type="checkbox"/> New PPPO: <i>post-venetoclax ramp-up</i>	<input type="checkbox"/>

REVISED Protocols, PPPOs and Patient Handouts (*revisions in respective columns*)

Code	Protocol Title	Protocol	PPPO	Handout
BR Breast				
BRAJACT	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Doxorubicin and Cyclophosphamide followed by Paclitaxel	<i>AST replaced by ALT</i>	<i>AST replaced by ALT</i>	----
BRAJACTG	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Dose-Dense Therapy: Doxorubicin and Cyclophosphamide followed by Paclitaxel	<i>AST replaced by ALT</i>	<i>AST replaced by ALT</i>	----
BRAJACTTG	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Dose-Dense Therapy: Doxorubicin and Cyclophosphamide followed by Paclitaxel and Trastuzumab	----	<i>Minor typo corrected</i>	----
BRAJCMFPO	Adjuvant Therapy for High-Risk Breast Cancer using Cyclophosphamide (oral), Methotrexate and Fluorouracil	<i>AST replaced by ALT; Institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
BRAJFECD	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Fluorouracil, Epirubicin, Cyclophosphamide and Docetaxel	<i>Precautions updated (hepatic dysfunction)</i>	<i>AST replaced by ALT</i>	----
BRAJFECDT	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Fluorouracil, Epirubicin and Cyclophosphamide followed by Docetaxel and Trastuzumab	<i>Precautions updated (hepatic dysfunction)</i>	----	----
BRAJTDC	Neoadjuvant or Adjuvant Therapy for Breast Cancer using Trastuzumab, Docetaxel and Cyclophosphamide	<i>Precautions updated (hepatic dysfunction)</i>	----	----

REVISED Protocols, PPOs and Patient Handouts *(revisions in respective columns)*

Code	Protocol Title	Protocol	PPO	Handout
UBRAJTTW	Adjuvant Therapy for Breast Cancer using Weekly Paclitaxel and Trastuzumab	----	<i>Return Appointment Orders clarified</i>	----
BRAVABR	Palliative Therapy for Metastatic Breast Cancer using Paclitaxel-nab (Abraxane®)	----	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
BRAVCMF	Palliative Therapy for Advanced Breast Cancer using Cyclophosphamide, Methotrexate and Fluorouracil	<i>AST replaced by ALT; Institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
BRAVCMPO	Palliative Therapy for Advanced Breast Cancer using Cyclophosphamide, Methotrexate and Fluorouracil	<i>AST replaced by ALT; Institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
BRAVDOC	Palliative Therapy for Metastatic Breast Cancer using Docetaxel	<i>Precautions (hepatic dysfunction) and institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
BRAVDOC7	Palliative Therapy for Metastatic Breast Cancer using Weekly Docetaxel	<i>Precautions (hepatic dysfunction) and institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
BRAVGEMD	Palliative Therapy for Metastatic Breast Cancer using Gemcitabine and Docetaxel	<i>Precautions (hepatic dysfunction) and institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
BRAVGEMP	Palliative Therapy for Metastatic Breast Cancer using Cisplatin and Gemcitabine	<i>Carboplatin dose calculation and Precautions (renal) updated</i>	----	----
BRAVGEMT	Palliative Therapy for Metastatic Breast Cancer using Gemcitabine and Paclitaxel	<i>AST replaced by ALT; Eligibility and institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
UBRAVKAD	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab Emtansine (Kadcyla®)	----	<i>AST replaced by ALT; Observation period updated</i>	----
BRAVPTRAD	Palliative Therapy for Metastatic Breast Cancer using Pertuzumab, Trastuzumab and Docetaxel as First-Line Treatment for Advanced Breast Cancer	<i>AST replaced by ALT; Precautions (hepatic) and institutional name updated</i>	<i>Tests clarified (hematology)</i>	----
BRAVPTLAT	Palliative Therapy for Metastatic Breast Cancer using Pertuzumab, Trastuzumab and Paclitaxel as First-Line Treatment for Advanced Breast Cancer	<i>TALLman lettering corrected in Protocol Title: PACLiTaxel</i>	<i>TALLman lettering corrected: PACLiTaxel</i>	----

REVISED Protocols, PPPOs and Patient Handouts (*revisions in respective columns*)

Code	Protocol Title	Protocol	PPPO	Handout
BRAVTAX	Palliative Therapy for Metastatic Breast Cancer using Paclitaxel	<i>AST replaced by ALT; Institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----
BRAVTPCARB	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab, Paclitaxel and Carboplatin as First-Line Treatment for Advanced Breast Cancer	<i>AST replaced by ALT; Precautions updated (renal dysfunction)</i>	----	----
BRAVTRAD	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab and Docetaxel as First-Line Treatment for Advanced Breast Cancer	<i>Precautions updated (hepatic dysfunction)</i>	----	----
BRAVTRAP	Palliative Therapy for Metastatic Breast Cancer using Trastuzumab and Paclitaxel as First-Line Treatment for Advanced Breast Cancer	<i>AST replaced by ALT</i>	----	----
BRLAACD	Treatment of Locally Advanced Breast Cancer using Doxorubicin and Cyclophosphamide followed by Docetaxel	<i>Precautions (hepatic) and institutional name updated</i>	<i>AST replaced by ALT</i>	----
BRLAACDT	Treatment of Locally Advanced Breast Cancer using Doxorubicin and Cyclophosphamide followed by Docetaxel and Trastuzumab	<i>Precautions (hepatic) and institutional name updated</i>	----	----
BRLATACG	Neoadjuvant Therapy for Breast Cancer using Dose-Dense Therapy: Paclitaxel followed by Doxorubicin and Cyclophosphamide	<i>AST replaced by ALT; Institutional name updated</i>	<i>AST replaced by ALT; Institutional name and logo updated</i>	----

CN | Neuro-Oncology

CNBEV	Palliative Therapy for Recurrent Malignant Gliomas using Bevacizumab with or without Concurrent Etoposide or Lomustine	<i>Baseline Tests updated (for bevacizumab monotherapy only)</i>	----	----
CNLAN	Treatment of Growth Hormone-Secreting Pituitary Adenoma using Lanreotide (Somatuline Autogel®)	<i>Precautions clarified; Institutional name updated; Footnote corrected</i>	<i>Institutional name and logo updated</i>	----

GI | Gastrointestinal

GIFOLFOX	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer using Oxaliplatin, Fluorouracil and Leucovorin	<i>Treatment updated (oxaliplatin cut-off changed to 111 mg)</i>	----	----
GIGAJCOX	Adjuvant Chemotherapy in of Gastric Cancer Patients with D2 Resection (Node-Negative) or Ineligible for Adjuvant Chemoradiation using Oxaliplatin and Capecitabine	<i>AST replaced by ALT; Tests and Monitoring updated; Protocol Title corrected</i>	<i>AST replaced by ALT</i>	----

Revised Protocols, PPPOs and Patient Handouts (*revisions in respective columns*)

Code	Protocol Title	Protocol	PPPO	Handout
GO Gynecology				
UGOOVBEVG	Treatment of Platinum-Resistant Epithelial Ovarian Cancer with Bevacizumab and Gemcitabine	-----	<i>Blood pressure check removed (day 8 and day 15)</i>	-----
GOTDEMACO	Therapy for High-Risk Gestational Trophoblastic Neoplasia using Etoposide, Methotrexate, Leucovorin, Dactinomycin, Cyclophosphamide and Vincristine	<i>Tests added (day 8)</i>	---	-----

GU Genitourinary				
GUBMITO	Intravesical Therapy for Non-Muscle-Invasive Bladder Cancer using Mitomycin	<i>References added</i>	-----	-----
UGUCABO	Therapy for Metastatic Renal Cell Carcinoma using Cabozantinib	<i>Eligibility clarified and dispensing quantity added</i>	<i>Dispensing quantity and Dose Modification added</i>	-----

LU Lung				
ULUAVATZ	Treatment of Advanced Non-Small Cell Lung Cancer using Atezolizumab	<i>Eligibility clarified</i>	-----	-----
ULUAVCER	Treatment of ALK-Positive Advanced Non-Small Cell Lung Cancer with Ceritinib	<i>Treatment dose updated (750 mg fasting replaced by 450 mg with food). See Drug Update section above</i>		<i>Instructions revised (take with food)</i>
ULUAVNIV	Treatment of Advanced Non-Small Cell Lung Cancer using Nivolumab	<i>Exclusions updated</i>	-----	-----
ULUAVNIV4	Treatment of Advanced Non-Small Cell Lung Cancer using 4-Weekly Nivolumab	<i>Exclusions updated</i>	-----	-----
ULUAVPMB	Treatment of Advanced Non-Small Cell Lung Cancer using Pembrolizumab	<i>Exclusions updated</i>	-----	-----
ULUAVPMBF	First-Line Treatment of Advanced Non-Small Cell Lung Cancer using Pembrolizumab	<i>Exclusions updated</i>	-----	-----
ULULADUR	Treatment of Locally Advanced Non-Small Cell Lung Cancer using Durvalumab	<i>Precautions clarified (infusion reactions)</i>	-----	-----

Revised Protocols, PPPOs and Patient Handouts (revisions in respective columns)

Code	Protocol Title	Protocol	PPPO	Handout
LY Lymphoma				
LYGDP	Treatment of Lymphoma with Gemcitabine, Dexamethasone and Platinum Cisplatin	<i>Protocol Title, Tests, Premedications, Treatment, Dose Modifications, References and institutional name updated; Eligibility clarified</i>	<i>Pre-chemotherapy metrics, Tests, Premedications and Treatment updated</i>	<i>Carboplatin option added</i>
LYGDPR	Treatment of Lymphoma with Gemcitabine, Dexamethasone and Platinum Cisplatin with Rituximab	<i>Protocol Title, Tests, Premedications, Treatment, Dose Modifications and References updated; Eligibility clarified</i>	<i>Pre-chemotherapy metrics, Tests, Premedications and Treatment updated</i>	<i>Carboplatin option added</i>
ULYVENETO	Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma using Venetoclax	<i>Test clarified (uric acid)</i>	<i>Baseline Tests removed; Weight field added; Uric acid test clarified (multiple PPPOs)</i>	----
ULYVENETOR	Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma using Venetoclax and Rituximab	<i>Baseline Tests clarified</i>	<i>Baseline Tests removed; Weight field added (multiple PPPOs)</i>	----

MY Myeloma				
UMYCARDEX	Therapy of Multiple Myeloma using Carfilzomib and Dexamethasone with or without Cyclophosphamide	<i>Carfilzomib and dexamethasone dosing revised (see Drug Update section above); Baseline Tests updated with MUGA; Premedications updated with PPI/H₂-antagonist (UMYCARDEX); Precautions clarified (irradiated blood products)</i>	<i>Carfilzomib and dexamethasone dosing revised (see Drug Update section above); Baseline Tests updated with MUGA; Precautions clarified (irradiated blood products); Optional post-hydration removed</i>	<i>Carfilzomib and dexamethasone dosing revised</i>
UMYCARLD	Therapy of Multiple Myeloma using Carfilzomib, Lenalidomide with Dexamethasone			

Resources and Contact Information

Resource	Phone	Email / Toll Free / Fax
Systemic Therapy Update: www.bccancer.bc.ca/health-professionals/clinical-resources/systemic-therapy/systemic-therapy-update		
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CAP – Compassionate Access Program	604-877-6277	cap_bcca@bccancer.bc.ca fax 604-708-2026
OSCAR – Online System for Cancer Drugs Adjudication and Reimbursement	888-355-0355	oscar@bccancer.bc.ca fax 604-708-2051
Library/Cancer Information	604-675-8003	toll free 888-675-8001 x 8003 requests@bccancer.bc.ca
Library Document Delivery	604-675-8002	requests@bccancer.bc.ca
Pharmacy Professional Practice Professional Practice, Nursing Provincial Systemic Therapy Program	604-877-6000 x 672247 604-877-6000 x 672623 604-877-6000 x 672247	mclin@bccancer.bc.ca BCcancerPPNAdmin@ehcnet.phsa.ca mclin@bccancer.bc.ca
BC Cancer – Abbotsford BC Cancer – Kelowna BC Cancer – Prince George BC Cancer – Surrey BC Cancer – Vancouver BC Cancer – Victoria	604-851-4710 250-712-3900 250-645-7300 604-930-2098 604-877-6000 250-519-5500	toll free 877-547-3777 toll free 888-563-7773 toll free 855-775-7300 toll free 800-523-2885 toll free 800-663-3333 toll free 800-670-3322
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