Provincial Health Services Authority

Systemic Therapy Update

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For Health Professionals Who Care for People with Cancer

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BR BRAVPBFLV, BRAVPTRAD, BRAVPTRAT, BRAVRBFLV | **GU** GUAVIPNI, GUAVPG | **LY** LYCODOXMR | **MY** UMYDARBD, MYDARCBDF, UMYDARLD, MYDARLDF | **SC** SCNAUSEA | **SM** SMAJDT, SMAVDT

Resources and Contact Information

Editor's Choice

New Programs

BC Cancer Provincial Systemic Therapy has approved the following new treatment programs effective 01 September 2022. Full details of all treatment programs are available in the Chemotherapy Protocols section of the BC Cancer website.

Gynecologic Oncology

Methotrexate for Low-Risk Gestational Trophoblastic Cancer (GOTDLRM) — The BC Cancer Genitourinary Tumour Group is implementing single-agent methotrexate for patients with low-risk gestational trophoblastic neoplasm (GTN) with a good initial response to first-line dactinomycin (GOTDLRA) but with gradual, indolent resistance based on hCG levels. Patients with poor initial response to first-line dactinomycin or with rapid resistance, in contrast, should be treated with GOTDEMACO. In GOTDLRM, methotrexate is administered by intramuscular (IM) injection on days 1, 3, 5 and 7, with oral leucovorin taken 30 hours after each methotrexate dose.

Until now, patients in BC who develop resistance to first-line dactinomycin are switched to combination dactinomycin and methotrexate (GOTDMR). This combination is more toxic than single-agent

methotrexate, and may not provide an improved disease response due to potential resistance to dactinomycin. The most recent NCCN guideline identified patients who would be most appropriate for a switch from first-line dactinomycin to single-agent methotrexate. Amongst the various methotrexate regimens used for GTN, the regimen in GOTDLRM is preferred, given its well-established efficacy.[2]

Leukemia

Fedratinib for Symptomatic Myelofibrosis (ULKMFFED) — The BC Cancer Leukemia and BMT Tumour Group is introducing fedratinib, an oral JAK2 and FLT3 inhibitor, for patients with symptomatic myelofibrosis (MF) (primary, post-essential thrombocythemia, or post-polycythemia vera MF).[3] Myelofibrosis is a hematological malignancy characterized by progressive fibrosis of the bone marrow, leading to multi-organ extramedullary hematopoiesis that prominently involves the spleen. Patients with MF suffer from symptomatic splenomegaly, anemia, debilitating constitutional symptoms and shortened survival. The current standard of care for patients with splenomegaly or symptoms related to MF is ruxolitinib, a JAK 1/2 inhibitor (ULKMFRUX), however until now there were no treatment options for patients unable to take ruxolitinib; patients with intolerance or contraindication to ruxolitinib are eligible to receive fedratinib. Oral thiamine (vitamin B1) supplementation is necessary during fedratinib treatment to prevent thiamine deficiency-associated Wernicke's encephalopathy. BC Cancer Compassionate Access Program (CAP) approval is required.

The randomized, placebo-controlled phase III JAKARTA trial evaluated fedratinib in patients with MF who had not received previous treatment with a JAK inhibitor.[4] A significantly greater proportion of patients treated with fedratinib 400 mg achieved the primary end point of spleen response (≥35% reduction in spleen volume from baseline) (36.5% vs. 1%, between-group difference = 35.4%, 97.5% CI 24.2-46.7). Treatment with fedratinib was also associated with a statistically significant and clinically meaningful improvement in disease-related symptoms (proportion of patients who had a ≥50% reduction in the total symptom score from baseline) (39.6% vs. 8.2%, between-group difference = 31.3%, 95% CI 18.0-44.6). Common adverse events with fedratinib were anemia, gastrointestinal symptoms, and increased levels of liver transaminases, serum creatinine and pancreatic enzymes.

Lymphoma

Daratumumab, Cyclophosphamide, Bortezomib and Dexamethasone for Previously Untreated Light Chain Amyloidosis (LYDARCBDF) — The BC Cancer Lymphoma and Myeloma Tumour Group is introducing the first Health Canada-approved treatment for patients with light chain (AL) amyloidosis. AL amyloidosis is a symptomatic plasma cell dyscrasia that arises due to secretion of abnormal clonal light chains (amyloid proteins) that deposit in the tissues of vital organs, causing organs to malfunction and eventually fail. The degree to which the heart is involved has the most influence in determining long-term prognosis. Previously, the standard of care has consisted of therapies typically used for myeloma such as cyclophosphamide, bortezomib and dexamethasone (CyBorD), and there has been a need for AL amyloidosis-specific treatment that can prevent, delay or improve disease-related organ damage.[5] In LYDARCBDF, subcutaneous daratumumab is used in combination with cyclophosphamide, bortezomib, and dexamethasone (DCyBorD). Patients with previously untreated disease involving at least one organ system, and who are ineligible for stem cell transplant, are eligible for this treatment protocol. Patients who are currently on a first-line therapy that started prior to 01 September 2022 may switch to LYDARCBDF if they have not experienced progression and meet other eligibility criteria. Note that for patients transitioning therapies, the protocol code designation may change from MY (reflecting a CAP-approved myeloma protocol) to LY (for the AL amyloidosis-specific LYDARCBDF protocol).

Editor's Choice

New Programs

Supporting evidence for this treatment program comes from the ongoing, randomized, open-label, phase III ANDROMEDA trial comparing DCyBorD to CyBorD in patients with newly diagnosed AL amyloidosis.[6] At a median follow-up of 11.4 months, there was a statistically significant and clinically meaningful improvement in hematologic complete response (CR) rate in the daratumumab group (53.3% vs. 18.1%, RRR 2.9, 95% CI 2.1-4.1). The improvement in hematologic CR rate was consistent across patient subgroups of any cardiac stage and those with and without a t(11;14) translocation. The results for other response end points, including time to hematologic response and organ response (cardiac and renal), also favoured treatment with DCyBorD. The most common grade 3 or 4 adverse events were more common in the daratumumab group: lymphopenia (13.0% vs. 10.1%), pneumonia (7.8% vs. 4.3%) and cardiac failure (6.2% vs. 4.8%). Systemic administration-related reactions with subcutaneous daratumumab occurred in 7.3% of patients.

References

1 NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Gestational Trophoblastic Neoplasia. Version 1.2022 — October 06, 2021

2 Sita-Lumsden A, Short D, Lindsay I, et al. Treatment outcomes for 618 women with gestational trophoblastic tumours following a molar pregnancy at the Charing Cross Hospital, 2000-2009. *Br J Cancer* 2012;107:1810-1814. https://doi.org/10.1038/bjc.2012.462

3 CADTH Reimbursement Recommendation. Fedratinib (Inrebic®). *Canadian Journal of Health Technologies* 2021;1(6). https://www.cadth.ca/sites/default/files/attachments/2021-06/CADTH_reimbursement_recommendation_fedratinib_%28inrebic%29_comp.pdf

4 Pardanani A, Harrison C, Cortes JE, et al. Safety and efficacy of fedratinib in patients with primary or secondary myelofibrosis. *JAMA Oncol* 2015;1(5):643-651. https://doi.org/10.1001/jamaoncol.2015.1590

5 CADTH Reimbursement Recommendation. Daratumumab (Darzalex® SC). *Canadian Journal of Health Technologies* 2022;2(2). https://www.cadth.ca/sites/default/files/DRR/2022/PC0257%20Darzalex%20-%20CADTH%20Final%20Rec%20Final.pdf

6 Kastritis E, Palladini G, Minnema MC, et al. Daratumumab-based treatment for immunoglobulin light-chain amyloidosis. *N Engl J Med* 2021;385:46-58. https://doi.org/10.1056/NEJMoa2028631

Revised Programs

Skin and Melanoma

Treatment-Related Pyrexia with Dabrafenib and Trametinib

Treatment-related pyrexia is a common adverse effect seen with the combination of dabrafenib and trametinib. The dosing modification for trametinib in the management of pyrexia has been updated when it is used in combination with dabrafenib (SMAJDT, SMAVDT). Previously, only dabrafenib was held for pyrexia while trametinib could be continued. The new recommendation is to hold *both* agents for pyrexia. The Canadian guideline recommends this approach based on recent clinical trials.

Reference

Thawer A, Miller WH Jr, Gregorio N, et al. Management of pyrexia associated with the combination of dabrafenib and trametinib: Canadian Consensus Statements. *Curr Oncol* 2021;28(5):3537-3553. https://doi.org/10.3390/curroncol28050304

Drug Update

Launch of Subcutaneous Daratumumab

Effective 01 September 2022, all treatment protocols with intravenous (IV) daratumumab have been revised to include the subcutaneous (subcut) daratumumab 1800 mg fixed dose option (UMYDARBD, MYDARCBDF, UMYDARLD, MYDARLDF). The new treatment protocol, LYDARCBDF (see Editor's Choice above), includes *only* subcutaneous daratumumab.

Patients starting on daratumumab treatments can receive subcutaneous daratumumab starting from the first dose. For patients who have already started their IV daratumumab treatments, they can receive their subsequent doses administered as subcutaneous injection (EXCEPTION: patients must receive both doses of 8 mg/kg on Cycle 1 Days 1 and 2 before switching to daratumumab subcutaneous 1800 mg). The prescribers will decide if a patient can be switched to subcutaneous daratumumab. For operational considerations, patients switching from IV to subcutaneous daratumumab should complete their current cycle before making the change, rather than changing routes of administration at mid-cycle.

Treatments	Intravenous Daratumumab	Subcutaneous Daratumumab
Cycle 1	16 mg/kg on Days 1, 8, 15, 22 Or 8 mg/kg on Days 1 and 2, then 16 mg/kg on Days 8, 15, 22	1800 mg subcut on Days 1, 8, 15, 22
Cycle 2	16 mg/kg on Days 1, 8, 15, 22	1800 mg subcut on Days 1, 8, 15, 22
Cycles 3 to 6	16 mg/kg on Days 1 and 15	1800 mg subcut on Days 1 and 15
Cycle 7 and subsequent cycles	16 mg/kg on Day 1	1800 mg subcut on Day 1

Advantages

Subcutaneous daratumumab is the preferred route of administration. It has a decreased incidence of administration-related systemic reactions compared to IV administration. Subcutaneous daratumumab has a shorter administration time, allowing for shorter chair time for the patients compared to IV daratumumab, starting with their very first dose. Less frequent monitoring of vitals is required with subcutaneous administration. In addition, an observation period is only required following the first subcutaneous dose (more details below). Subcutaneous daratumumab is given as a fixed dose and it is available in a ready-to-use, single dose vial, so there is no need for weight-based calculations and further dilution, resulting in reduced preparation time, drug wastage, and potential for dosing errors.

Dosing and Administration

The IV and subcutaneous formulations are NOT interchangeable. Subcutaneous daratumumab is administered as a single injection subcutaneously into the abdomen by a systemic therapy trained nurse over approximately 5 minutes. There are no data regarding the injection of subcutaneous daratumumab at sites other than the abdomen.

The subcutaneous formulation contains the enzyme hyaluronidase to temporarily degrade the extracellular matrix under the skin. This increases the permeability of subcutaneous tissue to allow the absorption of 15 mL of daratumumab. Hence, the 15 mL dose should not be divided into multiple syringes. If a complete dose of subcutaneous daratumumab cannot be completed at a single site due to intolerance, administer the remaining dose at a second injection site on the opposite side of the abdomen.

Hyaluronidase may increase the systemic absorption of other drugs administered near the injection site for 24-48 hours. Therefore, other subcutaneous drugs should be administered at other sites whenever possible, such as when subcutaneous bortezomib and subcutaneous daratumumab are administered on the same day. Topical creams used to manage injection site discomfort, such as hydrocortisone 1%, diphenhydramine 2%, and EMLA, are unlikely to result in significant systemic toxicity because the systemic drug levels are relatively low even if fully absorbed.

Reactions, Monitoring and Observation

Premedications (antihistamines, antipyretics, corticosteroids) are the same for both subcutaneous and IV daratumumab. Because it takes longer to administer IV daratumumab (Cycle 1, Day 1), repeating premedications is sometimes necessary during intravenous infusion of daratumumab.

Serious administration-related systemic reactions are less common with subcutaneous daratumumab compared to IV daratumumab (8 - 13% vs. 35 - 48%). These usually occur with the first dose and rarely after subsequent doses. Symptoms of administration-related systemic reactions for subcutaneous daratumumab are consistent with those reported for the IV formulation. Respiratory symptoms (e.g., cough, wheeze, larynx and throat irritation, nasal congestion), chills, nausea, and vomiting may occur. Severe reactions have also been reported, including bronchospasm, laryngeal and pulmonary edema, hypertension, hypoxia, and dyspnea. Injection site reactions such as erythema, induration, and pruritus may also occur with subcutaneous daratumumab in up to 8% of patients.

Nearly all reactions would occur shortly after the subcutaneous injection. Patients should be monitored for 1 hour after administration on Cycle 1 Day 1, with physician to be on site for this observation. Observation is not required for subsequent doses, except at physician discretion. Vital signs should be checked immediately prior to the injection, at the end of the injection, and at the end of observation period for first injection (Cycle 1, Day 1), and as needed.

For patients switching from IV to subcutaneous route, patients should be observed for 30 minutes after the first subcutaneous injection. Vital signs should be checked immediately prior to the injection and at the end of the injection, and as needed.

<table>
<tr><th>Monitoring</th><th>Intravenous Daratumumab</th><th>Subcutaneous Daratumumab</th></tr>
<tr><td rowspan="2">Vitals Signs*</td><td>Cycle 1 Day 1 (and Day 2 if using Alternative regimen):
• Before the start of infusion
• During infusion: every 30 minutes x 4, then every 1 to 2 hours until the end of infusion
• 30 minutes after the end of infusion</td><td>Cycle 1 Day 1:
• Immediately prior to injection
• At the end of injection
• At the end of observation period
OR
If switching from IV to subcut daratumumab:
• Immediately prior to injection
• At the end of injection</td></tr>
<tr><td>Subsequent infusions (i.e., Cycle 1 Day 8 and beyond):
• Before start of infusion
• At the end of infusion</td><td>Subsequent injections:
• Only as needed</td></tr>
<tr><td rowspan="2">Observation Period</td><td rowspan="2">30 minutes after the end of infusion for first 3 infusions</td><td>If no previous daratumumab:
• 1 hour after administration on Cycle 1 Day 1</td></tr>
<tr><td>If switching from IV to subcut daratumumab:
• 30 minutes after administration of first subcut dose only</td></tr>
</table>

Launch of Subcutaneous Daratumumab

Medication Safety Considerations

Contributing factors to look-alike/sound-alike (LASA) error risks include:

- Same generic name and very similar brand names
- Vial concentrations look similar (20 mg/mL vs. 120 mg/mL)
- Potential dosing overlap (e.g., IV: 16 mg/kg in 112.5 kg patient = 1800 mg; subcut = 1800 mg)
- Risk of wrong route of administration (15 mL is uncommon volume for subcutaneous injection)

Strategies to mitigate LASA error risks include:

- ✓ **Physical separation**: Store the two products in distinct bins and never gather products in batch or have both products in the same IV preparation hood at the same time. Handle one drug per patient in the hood at a given time.
- ✓ **Product differentiation**: Distinguish the two products for order entry and on the drug label; create visible alerts for product selection at storage site.
- ✓ **Product checking**: Incorporate independent double-checking at appropriate steps in the compounding process to facilitate catching LASA mix-up. Use technology such as barcode scanning where available.
- ✓ **Raise awareness**: Educate all staff involved in handling both products in the medication management process. Assess local processes to determine the best risk mitigation strategies for your site.

Product Comparison

products	**intravenous daratumumab**		**subcutaneous daratumumab**
product image			
brand name	DARZALEX		DARZALEX SC
formulation	colourless to yellow solution		colourless to yellow solution; contains hyaluronidase
vial solution concentration	20 mg/mL		120 mg/mL
vial solution volume	100 mg/5 mL 400 mg/20 mL		1800 mg/15 mL
vial storage	refrigerator		refrigerator
final preparation	IV bag		syringe
administration route	IV infusion		subcutaneous injection over 5 minutes
typical dosing	16 mg/kg	*or 8 mg/kg split dosing on Cycle 1 Days 1 and 2*	1800 mg fixed dose

Medication Safety

World Patient Safety Day: 17 September 2022 – Focus on Medication Safety

Medication errors and unsafe medication practices are leading causes for preventable harm in healthcare. Globally, the estimated cost associated with medication errors is $42 billion USD per year. The ongoing COVID-19 pandemic has significantly exacerbated the risk of medication errors and associated medication-related harm due to stresses placed on the healthcare system. Hence, the World Health Organization (WHO) has chosen **Medication Safety** as the *theme* for World Patient Safety Day 2022, with the *slogan* **Medication Without Harm**. The WHO *call-to-action* is **Know. Check. Ask.**

Medication safety is particularly important in oncology practice because of the complexity of cancer treatment protocols and the risks associated with drugs with narrow therapeutic indices. Important components of medication safety include: teamwork, communication, systems thinking (e.g., understanding workflow, how processes relate), human factors (e.g., understanding how people interact with equipment and work environment), learning from medication incidents and managing risks. A patient safety culture that supports a safe environment for staff to report and follow up on errors is also essential.

At BC Cancer, many strategies are in place to enhance medication safety, starting from prescribing and extending to preparation and administration. Interdisciplinary teamwork, in collaboration with patient partners, is a key component to strengthening the medication system. Patient safety learning system (PSLS) is used to report errors, with subsequent systematic reviews conducted to prevent future errors.

Ongoing improvement opportunities exist to ensure the safe delivery of cancer treatments. As World Patient Safety Day approaches, this article is the first of a series that will share medication safety pearls and strategies.

Medication Safety Pearl #1: The World Health Organization's *call-to-action*: **KNOW. CHECK. ASK.**

KNOW your medication

CHECK you have the right

- ✓ Patient
- ✓ Medicine
- ✓ Route
- ✓ Dose
- ✓ Time
- ✓ Reason ** this additional check done at BC Cancer*
- ✓ Documentation ** this additional check done at BC Cancer*

ASK your patient if they understand

References

1 Institute for Safe Medication Practices (ISMP). Just culture and its critical link to patient safety (Part I). ISMP Medication Safety Alert! Acute Care. 2012;17(10):1-4. https://www.ismp.org/resources/just-culture-and-its-critical-link-patient-safety-part-i

2 Institute for Safe Medication Practices (ISMP). Just culture and its critical link to patient safety (Part II). ISMP Medication Safety Alert! Acute Care. 2012;17(Jul 12):1-3. https://www.ismp.org/resources/just-culture-and-its-critical-link-patient-safety-part-ii

3 Canadian Patient Safety Institute. The safety competencies: Enhancing patient safety across the health professions. 2nd edition. Edmonton, Alberta; 2020. https://www.patientsafetyinstitute.ca/en/toolsResources/safetyCompetencies/Pages/default.aspx

4 BC Cancer. Nursing Practice Reference C-252. Chemotherapeutic Agents, Administration Of: Revised 15 February 2022. SHOP

Provincial Systemic Therapy

All Systemic Therapy policies are on the Shared Health Organizations Portal (SHOP) BC Cancer page.

Policy III-60 Appendix: Drug Reaction Management – Physician Coverage

Subcutaneous daratumumab has been added to the **Appendix** to Systemic Therapy **Policy III-60: Drug Reaction Management – Physician Coverage During Delivery of Selected Systemic Therapy Drugs**.

Policy III-190: Oncology Biosimilars Utilization

The advanced breast cancer treatment protocols that use a combination of trastuzumab and pertuzumab (BRAVPTRAD, BRAVPTRAT) are no longer an exception to the biosimilars policy. Previously, the trastuzumab reference biologic, HERCEPTIN, was used for all patients receiving treatment with one of these protocols. Moving forward, only biosimilar trastuzumab will be funded for treatment starting on or after 01 September 2022. Systemic Therapy **Policy III-190: Oncology Biosimilars Utilization** is being updated.

Patients' Corner

Scalp Cooling Systems

Scalp cooling is a strategy that may be used in the prevention of chemotherapy-induced alopecia. A new patient-led approach for cold caps is under development, with implementation anticipated 01 October 2022. The new Systemic Therapy **Policy III-230: Cooling Systems and Cold Caps for Chemotherapy-Induced Alopecia** will allow patients to bring a privately purchased cold cap to their chemotherapy treatments for personal use. An educational patient handout will be available in several languages in the Coping with Cancer > Managing Symptoms & Side Effects > Hair Loss & Appearance section of the BC Cancer website. Nurses and BC Cancer staff will not be providing support on these systems in any capacity. Please contact your local chemotherapy unit leadership for specific procedures and any questions. Policy III-230 will be available on the SHOP BC Cancer page.

Cancer Drug Manual©

All documents are available in the Cancer Drug Manual© on the BC Cancer website.

Revised Documents

Abemaciclib Monograph

Cautions: added statement about dose adjustment for drug interactions
Interactions: added new recommendations for abemaciclib dose adjustment
Dosing Guidelines: added statement about dose adjustment for drug interactions

Atezolizumab Monograph and **Patient Handout**

Cautions: added statement about vaccine response

***Patient Handout**:* added statement about vaccine response to bullets

Avelumab Monograph, **Patient Handout** and **Chemotherapy Preparation and Stability Chart**

Cautions: added statement about vaccine response

***Patient Handout**:* added statement about vaccine response to bullets

***Chemotherapy Preparation and Stability Chart**:* deleted recommendation to equilibrate vial to RT prior to use as not applicable to the marketed brand

Brigatinib Monograph

Cautions: added statement about dose adjustment for drug interactions

Dosing Guidelines: added statement about dose adjustment for drug interactions

Cemiplimab Monograph and **Patient Handout**

Cautions: added statement about vaccine response

***Patient Handout**:* added statement about vaccine response to bullets

Cytarabine Chemotherapy Preparation and Stability Chart

PMS brand: added (deleted in error)

Daratumumab Monograph, **SC Patient Handout**, **IV Patient Handout** and **Chemotherapy Preparation and Stability Chart**

Common Trade Name: added brand name for subcutaneous (SC) injection

Pharmacokinetics table: updated for SC administration

Uses: updated Health Canada approved indications

Contraindications: added contraindications for hypersensitivity

Cautions: added statement about the non-interchangeability of IV and SC formulations

Side Effects: added injection site reactions and administration-related reactions to SE table; added new paragraph for administration-related reactions following SC injection

Supply and Storage: added new SC formulation

Supply and Storage (Additional information): added information related to the SC formulation (description of hyaluronidase and storage of unpunctured vials)

Solution Preparation and Compatibility (Additional information): updated IV formulation; added SC formulation

Parenteral Administration table: added information related to SC administration

Dosage Guidelines: updated IV dosing; added SC dosing; added new/updated BC Cancer protocols

***SC Patient Handout**:* created new handout for SC administration

***IV Patient Handout**:* updated header/footer, drug name, and bullets to differentiate from new SC handout

***Chemotherapy Preparation and Stability Chart**:* added new SC formulation

Durvalumab Monograph and **Patient Handout**

Cautions: added statement about vaccine response

***Patient Handout**:* added statement about vaccine response to bullets

Encorafenib Monograph
Cautions: added statement about dose adjustment for drug interactions
Dosing Guidelines: added statement about dose adjustment for drug interactions

Entrectinib Monograph
Cautions: added statement about dose adjustment for drug interactions
Dosing Guidelines: added statement about dose adjustment for drug interactions

Fedratinib Monograph
Cautions: updated recommendation for thiamine supplementation in Wernicke's encephalopathy bullet; added statement about dose adjustment for drug interactions
Side Effects: updated information related to thiamine deficiency in encephalopathy paragraph
Dosage Guidelines: bolded and italicized BC Cancer standard dosing for new protocol (ULKMFFED

Gemcitabine Chemotherapy Preparation and Stability Chart
Pfizer/Hospira brand: added information related to refrigerator storage
Sandoz brand: added information related to refrigerator storage

Methotrexate Monograph and **Patient Handout**
Uses: updated Health Canada approved indications
Special Precautions: updated carcinogenicity, mutagenicity, and fertility
Supply and Storage: updated with current Canadian brands
Parenteral Administration table: updated intramuscular administration
Dosage Guidelines: updated intramuscular administration
Dosage Guidelines (renal impairment): added recommended IM dosing adjustment
***Patient Handout (IV)**:* added intramuscular route; changed route in title

Mogamulizumab Interim Monograph
Cautions: added statement about vaccine response

Paclitaxel Chemotherapy Preparation and Stability Chart
Accord brand: updated final product stability

Pembrolizumab Monograph and **Patient Handout**
Cautions: added statement about vaccine response
***Patient Handout**:* added statement about vaccine response to bullets

Ribociclib Monograph
Cautions: added statement about dose adjustment for drug interactions
Dosing Guidelines: added statement about dose adjustment for drug interactions

Tislelizumab Interim Monograph
Cautions: added statement about vaccine response

Vinorelbine Chemotherapy Preparation and Stability Chart
Pfizer brand: deleted as no longer marketed

BC Cancer Benefit Drug List

New Programs

The following treatment programs have been added to the Benefit Drug List effective 01 September 2022:

Protocol Title	Protocol Code	Benefit Status
Therapy for Low-Risk Gestational Trophoblastic Cancer using **Methotrexate**	**GOTDLRM**	Class I
Treatment of Symptomatic Myelofibrosis with **Fedratinib**	**ULKMFFED**	Restricted
Treatment of Previously Untreated Light Chain Amyloidosis and Not-Eligible for Stem Cell Transplant using **Daratumumab**, **Cyclophosphamide**, **Bortezomib** and **Dexamethasone**	**LYDARCBDF**	Class I
Daratumumab subcutaneous injection (DARZALEX SC) has been added to the BC Cancer Benefit Drug List	*See BC Cancer Benefit Drug List – Revised Programs, immediately below, for applicable protocols*	

BC Cancer Benefit Drug List

Revised Programs

The following treatment programs have been revised on the Benefit Drug List effective 01 September 2022:

Protocol Title	Protocol Code	Benefit Status
Treatment of Relapsed and Refractory Multiple Myeloma with **Daratumumab** in Combination with **Bortezomib** and **Dexamethasone** with or without **Cyclophosphamide** ✓ **Daratumumab subcutaneous injection** added to protocol	**UMYDARBD**	Restricted
Treatment of Previously Untreated Multiple Myeloma and Not-Eligible for Stem Cell Transplant using **Daratumumab**, **Cyclophosphamide**, **Bortezomib** and **Dexamethasone** ✓ **Daratumumab subcutaneous injection** added to protocol	**MYDARCBDF**	Class I *(previously Restricted)*
Treatment of Relapsed and Refractory Multiple Myeloma with **Daratumumab** in Combination with **Lenalidomide** and **Dexamethasone** ✓ **Daratumumab subcutaneous injection** added to protocol	**UMYDARLD**	Restricted
Treatment of Previously Untreated Multiple Myeloma and Not-Eligible for Stem Cell Transplant using **Daratumumab**, **Lenalidomide** and **Dexamethasone** ✓ **Daratumumab subcutaneous injection** added to protocol	**MYDARLDF**	Class I *(previously Restricted)*

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 (CAP) approval are prefixed with the letter **U.**

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

Protocol Code	Protocol Title	Protocol	PPPO	Handout
GOTDLRM	Therapy for Low-Risk Gestational Trophoblastic Cancer using Methotrexate	☑	☑	☐
ULKMFFED	Treatment of Symptomatic Myelofibrosis with Fedratinib	☑	☑	☐
LYDARCBDF	Treatment of Previously Untreated Light Chain Amyloidosis and Not-Eligible for Stem Cell Transplant using Daratumumab, Cyclophosphamide, Bortezomib and Dexamethasone	☑	☑	☐
UMYDARBD	Treatment of Relapsed and Refractory Multiple Myeloma with Daratumumab in Combination with Bortezomib and Dexamethasone with or without Cyclophosphamide	☐	☑ **subcutaneous PPPO**	☐
MYDARCBDF	Treatment of Previously Untreated Multiple Myeloma and Not-Eligible for Stem Cell Transplant using Daratumumab, Cyclophosphamide, Bortezomib and Dexamethasone	☐	☑ **subcutaneous PPPO**	☐
UMYDARLD	Treatment of Relapsed and Refractory Multiple Myeloma with Daratumumab in Combination with Lenalidomide and Dexamethasone	☐	☑ **subcutaneous PPPO**	☐
MYDARLDF	Treatment of Previously Untreated Multiple Myeloma and Not-Eligible for Stem Cell Transplant using Daratumumab, Lenalidomide and Dexamethasone	☐	☑ **subcutaneous PPPO**	☐

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

Protocol Code	Protocol Title	Protocol	PPPO	Handout
BR | Breast				
BRAVPBFLV	Therapy of Advanced Breast Cancer using Palbociclib and Fulvestrant with or without LHRH Agonist	-----	*Mitte clarified*	-----

REVISED Protocols, PPPOs and Patient Handouts *(revisions in respective columns)*				
Protocol Code	**Protocol Title**	**Protocol**	**PPPO**	**Handout**
BRAVPTRAD	Palliative Therapy for Metastatic Breast Cancer using Pertuzumab, Trastuzumab ~~(HERCEPTIN)~~ and Docetaxel as First-Line Treatment for Advanced Breast Cancer	*Protocol title revised; trastuzumab brand name removed*	*Trastuzumab brand name removed; Pharmacy Selection Box added for trastuzumab brand*	-----
BRAVPTRAT	Palliative Therapy for Metastatic Breast Cancer using Pertuzumab, Trastuzumab ~~(HERCEPTIN)~~ and Paclitaxel as First-Line Treatment for Advanced Breast Cancer	*Protocol title revised; trastuzumab brand name removed*	*Trastuzumab brand name removed; Pharmacy Selection Box added for trastuzumab brand*	-----
BRAVRBFLV	Therapy of Advanced Breast Cancer using Ribociclib and Fulvestrant with or without LHRH Agonist	-----	*Mitte clarified*	-----
GU | Genitourinary				
GUAVIPNI	Treatment of Metastatic or Advanced Renal Cell Carcinoma using Ipilimumab and Nivolumab	*Ipilimumab infusion time revised*	*Ipilimumab infusion time revised*	*Ipilimumab infusion time revised*
GUAVPG	Palliative Therapy for Urothelial Carcinoma using Cisplatin and Gemcitabine	*Tests updated*	-----	-----
LY | Lymphoma				
LYCODOXMR	Treatment of Burkitt Lymphoma and Leukemia (ALL-L3) with Cyclophosphamide, Vincristine, Doxorubicin, Methotrexate, Leucovorin (CODOX-M) and Rituximab	-----	*Hypersensitivity banner added*	-----
MY | Myeloma				
UMYDARBD	Treatment of Relapsed and Refractory Multiple Myeloma with Daratumumab in Combination with Bortezomib and Dexamethasone with or without Cyclophosphamide	*Premedications, Treatment, Dose Modifications and Precautions updated; subcutaneous daratumumab added*	*Premedications clarified; bortezomib dosing and subcutaneous daratumumab options added* **PPPOs:** **IV Cycle 1** **IV Cycle 2+** **subcut (*new*)**	*Subcutaneous daratumumab added*

REVISED Protocols, PPPOs and Patient Handouts *(revisions in respective columns)*				
Protocol Code	**Protocol Title**	**Protocol**	**PPPO**	**Handout**
~~U~~**MYDARCBDF**	Treatment of Previously Untreated Multiple Myeloma and Not-Eligible for Stem Cell Transplant using Daratumumab, Cyclophosphamide, Bortezomib and Dexamethasone	*Protocol Code, Eligibility, Exclusions, Tests, Premedications, Treatment, Dose Modifications and Precautions updated; subcutaneous daratumumab added*	*Protocol code updated; Premedications clarified; bortezomib dosing and subcutaneous daratumumab options added* **PPPOs:** **IV Cycle 1** **IV Cycle 2+** **subcut (*new*)**	-----
UMYDARLD	Treatment of Relapsed and Refractory Multiple Myeloma with Daratumumab in Combination with Lenalidomide and Dexamethasone	*Premedications, Treatment, Dose Modifications and Precautions updated; subcutaneous daratumumab added*	*Premedications clarified; subcutaneous daratumumab option added* **PPPOs:** **IV Cycle 1** **IV Cycle 2+** **subcut (*new*)**	*Subcutaneous daratumumab added*
~~U~~**MYDARLDF**	Treatment of Previously Untreated Multiple Myeloma and Not-Eligible for Stem Cell Transplant using Daratumumab, Lenalidomide and Dexamethasone	*Protocol Code, Eligibility, Tests, Premedications, Treatment, Dose Modifications and Precautions updated; subcutaneous daratumumab added*	*Protocol code updated; Premedications clarified; subcutaneous daratumumab option added* **PPPOs:** **IV Cycle 1** **IV Cycle 2+** **subcut (*new*)**	-----
SC | Supportive Care				
SCNAUSEA	Prevention and Treatment of Chemotherapy-Induced Nausea and Vomiting in Adults	*Hyperlink updated*	-----	-----
SM | Skin and Melanoma				
SMAJDT	Adjuvant Treatment of Stage III and IV, BRAF-Mutated, Fully Resected Melanoma using Dabrafenib and Trametinib	*Dose Modifications and Precautions updated (pyrexia)*	-----	*Side effects updated*
SMAVDT	Treatment of BRAF V600 Mutation-Positive Unresectable or Metastatic Melanoma using Dabrafenib and Trametinib	*Dose Modifications and Precautions updated (pyrexia)*	-----	*Side effects updated*

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		
Systemic Therapy Update Editor	604-877-6000 x 672649	bulletin@bccancer.bc.ca
Oncology Drug Information Cancer Drug Manual Editor Pharmacy Oncology Certification Nurse Educators	604-877-6275 250-519-5500 x 693742 250-712-3900 x 686820 604-877-6000 x 672638	druginfo@bccancer.bc.ca nbadry@bccancer.bc.ca rxchemocert@bccancer.bc.ca nursinged@bccancer.bc.ca
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
Manufacturer Patient Assistance Programs: http://www.bccancer.bc.ca/mpap		
Library/Cancer Information	604-675-8003	requests@bccancer.bc.ca toll free 888-675-8001 x 8003
Library Document Delivery	604-675-8002	requests@bccancer.bc.ca
Pharmacy Professional Practice Professional Practice, Nursing Provincial Systemic Therapy	604-877-6000 x 672247 604-877-6000 x 672623 604-877-6000 x 672247	mlin@bccancer.bc.ca BCCancerPPNAdmin@ehcnet.phsa.ca mlin@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
Community Oncology Network (CON) sites: To update your contact information, please contact: bulletin@bccancer.bc.ca		

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