



## For Health Professionals Who Care For Cancer Patients

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## EDITOR'S CHOICE

### NEW PROGRAMS

Effective 1 April 2018, the BC Cancer Provincial Systemic Therapy Program has approved the following programs.

#### Breast

**Palbociclib with Aromatase Inhibitor for Metastatic Breast Cancer (UBRAVPALAI)** – The BC Cancer Breast Tumour Group is introducing palbociclib as a new agent to patients with metastatic breast cancer. Palbociclib is an oral inhibitor of cyclin-dependent kinases associated with increased cellular proliferation and endocrine resistance in breast cancer. Funding for palbociclib is available for post-menopausal women in combination with first line anastrozole or letrozole therapy for metastatic breast cancer. Note that patients are funded to receive either palbociclib plus anastrozole/letrozole (UBRAVPALAI) or everolimus plus exemestane (UBRAVEVEX), but not sequential use of these two regimens. For more details, see the relevant protocols.

Compared to letrozole alone, addition of palbociclib is associated with increased progression free survival (24.8 vs. 14.5 mos) and response rate (55.3% vs. 42.1%). The most common serious toxicities include neutropenia (66.4%), leukopenia (24.8%) and anemia (5.4%). However, febrile neutropenia is uncommon (1.8%). Most patients can be managed with dose adjustment, and permanent discontinuation occurred in only 9.7% of patients in the trial.

#### Reference:

Finn RS, et al. Palbociclib and letrozole in advanced breast cancer. *N Engl J Med* 2016;375:1925-36.

**Capecitabine Adjuvant Therapy for Breast Cancer (BRAJCAP)** – The BC Cancer Breast Tumour Group is introducing capecitabine as an adjuvant therapy for patients with residual invasive disease after neoadjuvant anthracycline-taxane chemotherapy. In a phase III trial, addition of capecitabine to standard post-surgical treatments (endocrine, radiotherapy) was associated with increased 5-year disease free survival (74.1% vs. 67.6%) and overall survival (89.2% vs. 83.6%). As expected, the most significant toxicity with capecitabine is with hand-foot syndrome, which is manageable with dose modification in most patients.

Reference:

Masuda N, Lee SJ, Ohtani S, et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. *N Engl J Med* 2017;376:2147-59.

### **Lymphoma and Myeloma**

**Carfilzomib for Relapsed Multiple Myeloma (UMYCARDEX, UMYCARLD)** – The BC Cancer Lymphoma and Myeloma Group is introducing carfilzomib as a new proteasome inhibitor in two regimens for the treatment of myeloma. Carfilzomib with dexamethasone (UMYCARDEX) is superior to bortezomib with dexamethasone in progression free survival (18.7 vs. 9.4 mos) and overall survival (47.6 vs. 40.0 mos).<sup>1,2</sup> Similarly, addition of carfilzomib to lenalidomide and dexamethasone (UMYCARLD) is associated with increased progression free survival (26.3 vs. 17.6 mos) and overall survival (48.3 vs. 40.4 mos) compared to lenalidomide and dexamethasone.<sup>3,4</sup> Toxicity of carfilzomib is generally similar to bortezomib, but has lower risk of neurotoxicity. Carfilzomib has a higher incidence of severe hypertension (9% vs. 3%) and possibly heart failure (3.8% vs. 1.8%).

Both carfilzomib regimens are funded for relapsed myeloma. UMYCARDEX is funded for disease that may be refractory to lenalidomide but sensitive to bortezomib. UMYCARLD is funded for disease sensitive to lenalidomide and bortezomib. More details on eligibility can be found on the protocols.

References:

1. Dimopoulos MA, et al. Carfilzomib and dexamethasone versus bortezomib and dexamethasone for patients with relapsed or refractory multiple myeloma (ENDEAVOR): a randomised, phase 3, open-label, multicentre study. *Lancet Oncol* 2016;17(1):27-38.
2. Dimopoulos MA, et al. Carfilzomib or bortezomib in relapsed or refractory multiple myeloma (ENDEAVOR): an interim overall survival analysis of an open-label, randomised, phase 3 trial. *Lancet Oncol* 2017;18(10):1327-378.
3. Stewart KA, et al. Carfilzomib, lenalidomide, and dexamethasone for relapsed multiple myeloma. *N Engl J Med* 2015;372(2):142-52.
4. Stewart KA, et al. Improvement in overall survival with carfilzomib, lenalidomide, and dexamethasone in patients with relapsed or refractory multiple myeloma. *J Clin Oncol* 2018;36 (8):728-34.

### **Neuro-Oncology**

**Temozolomide Adjuvant Therapy for Grade III Malignant Gliomas (CNAJ12TZRT)** – The BC Cancer Neuro-Oncology Tumour Group is introducing a 12-cycle treatment for patients with grade III astrocytoma and oligodendroglioma. Currently, these patients are usually treated at BC Cancer with 6 cycles of temozolomide (CNAJ12TZRT) based on limited evidence. In a recent phase III trial, 12 cycles of adjuvant temozolomide therapy was associated with increased 5-year overall survival (55% vs. 44%) in a study population which included patients with grade III malignant gliomas compared to radiation therapy alone. The toxicity profile was as expected with temozolomide, with mainly reversible hematological adverse events.

Reference:

van den Bent MJ, et al. Interim results from the CATNON trial (EORTC study 26053-22054) of treatment with concurrent and adjuvant temozolomide for 1p/19q non-co-deleted anaplastic glioma: a phase 3, randomized, open-label intergroup trial. *Lancet Oncol* 2017;390(10103):1645-53.

## CANCER DRUG MANUAL

### REVISED MONOGRAPHS AND PATIENT HANDOUTS

#### **Mercaptopurine Monograph and Handout**

- *Interactions, Dosing, and Patient Information:* updated cow's milk interaction to allow mercaptopurine administration less restrictive

#### **Mitomycin Monograph**

- *Supply and Storage:* updated Canadian supplier information, deleted formulations no longer available in Canada

#### **Ibrutinib Monograph**

- *Dosing:* revised to include dosing for mantle cell lymphoma

#### **Pembrolizumab Monograph**

- *Supply and Storage:* added a new ready-to-use liquid formulation

#### **Temozolomide Monograph**

- *Supply and Storage:* deleted IV formulation (no longer available in Canada)

#### **Chemotherapy Preparation and Stability Chart**

- *Pembrolizumab:* added new ready-to-use liquid formulation
- *Temozolomide:* deleted IV formulation
- *Mitomycin:* added information for intravesical preparation, deleted unavailable products

## BENEFIT DRUG LIST

### NEW PROGRAMS

Effective 1 April 2018, these treatment programs have been added to the BC Cancer [Benefit Drug List](#):

Protocol Title	Protocol Code	Benefit Status
Therapy of adjuvant breast cancer using <b>capecitabine</b>	<b>BRAJCAP</b>	Class I
Therapy of advanced breast cancer using <b>palbociclib</b> with <b>aromatase inhibitor</b>	<b>UBRAVPALAI</b>	Restricted
Concomitant (dual modality) and 12 cycles of adjuvant <b>temozolomide</b> for newly diagnosed astrocytomas and oligodendrogliomas with radiation	<b>CNAJ12TZRT</b>	Class I
Alternative treatment of gynecological malignancies using <b>cisplatin</b> and <b>paclitaxel</b>	<b>GOCISP</b>	Class I
Therapy of multiple myeloma using <b>carfilzomib</b> and <b>dexamethasone</b>	<b>UMYCARDEX</b>	Restricted
Therapy of multiple myeloma using <b>carfilzomib</b> , <b>lenalidomide</b> with <b>dexamethasone</b>	<b>UMYCARLD</b>	Restricted

## BENEFIT DRUG LIST

### DELETED PROGRAMS

The following treatment programs have been reviewed by the BC Tumour Groups and will be deleted effective 1 April 2018 from the BC Cancer [Benefit Drug List](#):

Protocol Title	Protocol Code
Adjuvant therapy for breast cancer using <b>cyclophosphamide, epirubicin, fluorouracil</b> and <b>filgrastim</b>	<b>BRAJCEFG</b>
Adjuvant therapy of high risk breast cancer using <b>cyclophosphamide, methotrexate</b> and <b>fluorouracil</b>	<b>BRAJCMF</b>
Adjuvant therapy for breast cancer using <b>docetaxel</b> and <b>trastuzumab (HERCEPTIN)</b> , and <b>fluorouracil, epirubicin</b> and <b>cyclophosphamide</b>	<b>BRAJDTFEC</b>
Palliative therapy for metastatic breast cancer using <b>cyclophosphamide, doxorubicin</b> and <b>fluorouracil</b>	<b>BRAVCAF</b>
Palliative therapy for advanced breast cancer using <b>cyclophosphamide (oral), methotrexate</b> and <b>fluorouracil</b>	<b>BRAVCMFPO</b>
Palliative therapy for metastatic breast cancer using <b>docetaxel</b> and <b>capecitabine</b>	<b>BRAVDCAP</b>
Therapy for inflammatory breast cancer using <b>cyclophosphamide, epirubicin</b> and <b>fluorouracil</b>	<b>BRINFCEF</b>
Therapy for inflammatory breast cancer using <b>cyclophosphamide, epirubicin, fluorouracil</b> and <b>filgrastim</b>	<b>BRINFCEFG</b>
Locally advanced breast cancer using <b>cyclophosphamide, doxorubicin</b> and <b>fluorouracil</b>	<b>UBRLA2</b>
Therapy for locally advanced breast cancer using <b>cyclophosphamide, epirubicin, fluorouracil</b> and <b>filgrastim</b>	<b>BRLACEFG</b>
<b>Tamoxifen</b> for patients with recurrent brain tumours which are resistant to first line chemotherapy	<b>CNTAM</b>
Radioprotection in head and neck radiation using <b>amifostine</b>	<b>HNOTAMIRT</b>
Treatment of systemic light chain (AL) amyloidosis and multiple myeloma using <b>cyclophosphamide, thalidomide</b> and <b>dexamethasone</b>	<b>UMYCTD</b>
Therapy of multiple myeloma using <b>thalidomide</b>	<b>UMYTHALID</b>

### LIST OF NEW AND REVISED PROTOCOLS, PRE-PRINTED ORDERS AND PATIENT HANDOUTS

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

**NEW PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)**

CODE	Protocol	PPPO	Patient Handout	Protocol Title
BRAJCAP	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Therapy of adjuvant breast cancer using capecitabine
UBRAVPALAI	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Therapy of advanced breast cancer using palbociclib with aromatase inhibitor
CNAJ12TZRT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Concomitant (dual modality) and 12 cycles of adjuvant temozolomide for newly diagnosed astrocytomas and oligodendrogliomas with radiation
GOCISP	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Alternative treatment of gynecological malignancies using cisplatin and paclitaxel
UMYCARDEX	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Therapy of multiple myeloma using carfilzomib and dexamethasone
UMYCARLD	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Therapy of multiple myeloma using carfilzomib, lenalidomide with dexamethasone

**REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)**

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
UBRAJTTW	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Premedications clarified</i>	Adjuvant therapy for breast cancer using weekly paclitaxel and trastuzumab (HERCEPTIN)
BRAJZOL	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Booking clarified</i>	Adjuvant treatment of postmenopausal women using zoledronic acid
UBRAVERIB	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Test clarified, institutional name updated</i>	Palliative therapy for metastatic breast cancer using eribulin
BRAVEVEX	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Eligibility, institutional name, tests and dispensing quantity clarified</i>	Therapy for advanced breast cancer using everolimus and exemestane
BRAVPTRAT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Minor typo corrected, institutional name and tests updated</i>	Palliative therapy for metastatic breast cancer using pertuzumab, trastuzumab (HERCEPTIN), and paclitaxel as first-line treatment for advanced breast cancer
BRAVZOL	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Booking clarified</i>	Treatment of acute bone pain secondary to breast cancer metastases using IV zoledronic acid
CNAJTZRT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Eligibility and test updated</i>	Concomitant (dual modality) and adjuvant temozolomide for newly diagnosed malignant gliomas with radiation
GIAVPANI	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Minor typos corrected</i>	Palliative third line treatment of metastatic colorectal cancer using panitumumab
GIAVCETIR	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Minor typos corrected</i>	Third line treatment of metastatic colorectal cancer using cetuximab in combination with irinotecan
UGIFFOXPAN	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Magnesium sulfate dosing updated</i>	Palliative combination chemotherapy for metastatic colorectal cancer using oxaliplatin, fluorouracil, leucovorin and panitumumab

REVISED PROTOCOLS, PPPOs AND PATIENT HANDOUTS (AFFECTED DOCUMENTS ARE CHECKED)					
CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
UGOOVBEVG	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Minor typos corrected	Treatment of platinum resistant epithelial ovarian cancer with bevacizumab and gemcitabine
GUAJPG	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Test, institutional name and dose modifications updated	Adjuvant Therapy for Urothelial Carcinoma Using CISplatin and Gemcitabine
GUAVPG	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Test, institutional name and dose modifications updated	Palliative Therapy for Urothelial Carcinoma Using CISplatin and Gemcitabine
GUEDPM	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Minor typo and institutional name updated	Treatment of metastatic adrenocortical cancer with etoposide, doxorubicin, cisplatin and mitotane
GUNAJPG	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Test, institutional name, dose modifications and contact physician updated	Neo-adjuvant therapy for urothelial carcinoma using cisplatin and gemcitabine
UGUPRAD	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Exclusions institutional name updated	Therapy for metastatic castration resistant prostate cancer using radium-223
HNAVFUFA	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Cycle length, test and, institutional name updated	Fluorouracil and leucovorin for recurrent head and neck cancer (squamous cell carcinoma)
HNLACETRT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Magnesium sulfate dosing updated	Combined cetuximab and radiation treatment for locally advanced squamous cell carcinoma of the head and neck
HNAVFUFA	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Cycle length, test and, institutional name updated	Treatment of recurrent or metastatic nasopharyngeal cancer with fluorouracil and leucovorin
ULKPCVRUX	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Minor typos corrected	Treatment of polycythemia vera with ruxolitinib
LUAVDC	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Dose modifications clarified	First-line treatment of advanced non-small cell lung cancer with cisplatin and docetaxel
ULUAVNIV	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Tests clarified	Treatment of advanced non-small cell lung cancer using nivolumab
ULUAVPMBF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Eligibility clarified	First-line treatment of advanced non-small cell lung cancer using pembrolizumab
LYCHOPRMTX	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Methotrexate order clarified	Central nervous system prophylaxis with high dose methotrexate, CHOP and rituximab in diffuse large B-cell lymphoma

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