

# Systemic Therapy Update



BC Cancer Agency

CARE + RESEARCH

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## EDITOR'S CHOICE:

### HIGHLIGHTS OF CHANGES IN PROTOCOLS, PRE-PRINTED ORDERS AND PATIENT HANDOUTS

#### Caution Added for Interaction Between Phenytoin and Fluorouracil/Capecitabine

As mentioned in the last issue of the Systemic Therapy Update, a potential risk of an interaction between phenytoin and fluorouracil/capecitabine was identified as an example of medication misadventures. Therefore, a caution has now been added to all protocols and patient handouts which contain fluorouracil or capecitabine treatment. Healthcare providers are reminded of this possible drug-drug interaction to ensure appropriate monitoring of phenytoin blood levels. The added caution also informs patients to be aware of symptoms that they should report to the healthcare providers (e.g., hypotension, psychiatric changes, dizziness, bradycardia, drowsiness, headaches, insomnia, rash, nausea, vomiting).

Phenytoin toxicity has been described in case reports with patients taking concurrent phenytoin and fluorouracil or capecitabine (*Brickell K et al. Br J Cancer 2003;89:615-6; Gilbar PJ et al. Ann Pharmacother 2001;35:1367-70*). The presumed mechanism is that fluorouracil and capecitabine inhibit the cytochrome P450 2C9 (CYP2C9) isoenzyme, which is involved in the hydroxylation metabolism of phenytoin.

**Reformatting the Preprinted Doses of Chemotherapy Drugs in Physician Orders** The Provincial Pre-Printed Orders (PPPO) have been revised to improve the clarity in the treatment section when fixed doses of chemotherapy drugs are given. In place of a preprinted dose, a blank space has been added for the prescriber to specify the dose. To avoid reliance on memory, the standardized dose is included in brackets separately, e.g.,

*Previous version*

**Etoposide 50 mg** PO once daily x 21 days

*Revised version*

**Etoposide \_\_\_\_\_mg** PO (standard dose 50 mg) once daily x 21 days

The revised format is to help reduce the risk of inadvertently administering a drug which is to be omitted from the treatment plan. It takes advantage of the habit and pattern of completing other chemotherapy orders, while constraining the ability to process an order when a dose has not been specified.

The **Gastrointestinal Tumour Group** has introduced four new patient information handouts (GIFOLFIRI, GIGFOLFIRI, UGIFFIRB, UGIFFOXB).

The **Neuro-Oncology Tumour Group** has introduced two new patient information handouts for temozolomide-based protocols (CNAJZRT, CNTEMOZ).

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## CANCER DRUG MANUAL

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**Mitotane Monograph and Patient Handout** have been completely revised and updated. Expert review was provided by Dr. Joseph Connors (Lymphoma Tumour Group) and Dr. Jeff Davis (Pediatric Oncologist). Mitotane is an adrenal cytotoxic agent and primarily used in adrenocortical carcinoma. Highlights of the monograph and handout include the followings:

- Mitotane is stored primarily in fat tissue. Blood and tissue levels of mitotane may persist for weeks to months after treatment cessation due to a slow release from tissue storage sites.
- Enhanced absorption is seen when administered with fatty meals. Patients may take mitotane with or without food as long as they are consistent. Tablets should be taken at the same time each day.
- Ambulatory patients should be cautioned about driving or participating in activities requiring mental or physical alertness due to CNS side effects.
- The major toxic effects of mitotane are: gastrointestinal (80%), CNS (40-50%), and dermatologic (15%).
- Adrenal insufficiency is likely and adrenal steroid replacement should be considered for all patients treated with mitotane. At times of infection, shock, or severe trauma, treatment should be temporarily withheld and appropriate administration of additional exogenous steroids should be considered. Medical alert tags, bracelets, or wallet cards are advisable, to convey this information in the event of an emergency.
- Liver disease may impair metabolism of mitotane, and may cause drug accumulation. Caution is advised with severe hepatic impairment.

**Etoposide Monograph** has been updated to delete stability information that conflicted with recently added information in the Chemotherapy Preparation and Stability Chart. Detailed stability information is no longer included in Cancer Drug Manual monographs.

**Bevacizumab Monograph** has been revised to include an option of a more rapid infusion time of 10 minutes. The list of uses has also been updated to include breast, lung, and renal cell cancer.

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

**BC Cancer Agency Protocol Summaries, Provincial Pre-Printed Orders (PPPOs) and Patient Handouts** are revised periodically. New and revised protocols, PPPOs and patient handouts for this month are listed below. Protocol codes for treatments requiring “Compassionate Access Program” (previously Undesignated Indication Request) approval are prefixed with the letter U.

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

CODE	Protocol	PPPO	Patient Handout	Protocol Title
CNAJZRT	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Treatment of newly diagnosed malignant gliomas with concurrent Temozolomide and Radiation Therapy, followed by adjuvant Temozolomide
CNTEMOZ	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Treatment for Malignant Brain Tumours using Temozolomide
GIFOLFIRI	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	First Line Palliative Combination Chemotherapy For Metastatic Colon Or Rectal Cancer Using Irinotecan, Fluorouracil And Folinic Acid (Leucovorin)
GIGOLFIRI	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Second Line Palliative Combination Chemotherapy For Metastatic Gastric (Stomach) Or Esophageal Cancer Using Irinotecan, Fluorouracil And Folinic Acid (Leucovorin)
UGIFFIRB	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Palliative Chemotherapy For Metastatic Colon Or Rectal Cancer Using Irinotecan, Fluorouracil, Folinic Acid (Leucovorin) And Bevacizumab
UGIFFOXB	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Palliative Combination Chemotherapy For Metastatic Cancer Of The Colon Or Rectum Using Oxaliplatin, 5-Fluorouracil, Folinic Acid (Leucovorin) And Bevacizumab

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

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
UBRAJCAF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Breast Cancer using Cyclophosphamide, Doxorubicin and Fluorouracil
BRAJCAFG	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, Doxorubicin, Fluorouracil and Filgrastim (G-CSF)
BRAJCAFPO	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Breast Cancer using Oral Cyclophosphamide, Doxorubicin and Fluorouracil
BRAJCEF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, Epirubicin and Fluorouracil
BRAJCEFG	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF)
BRAJCMF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy of High Risk Breast Cancer using Cyclophosphamide, Methotrexate and Fluorouracil

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
BRAJCMFPO	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for High-Risk Breast Cancer using Cyclophosphamide (oral), Methotrexate and Fluorouracil
BRAJDTFEC	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Breast Cancer Using Docetaxel and Trastuzumab, and Fluorouracil, Epirubicin and Cyclophosphamide
BRAJFEC	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Breast Cancer Using Fluorouracil, Epirubicin and Cyclophosphamide
BRAJFECD	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Breast Cancer Using Fluorouracil, Epirubicin and Cyclophosphamide and Docetaxel
BRAVCAF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Palliative Therapy for Metastatic Breast Cancer using Cyclophosphamide, Doxorubicin and Fluorouracil
BRAVCMF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Palliative Therapy for Advanced Breast Cancer using Cyclophosphamide, Methotrexate and Fluorouracil
BRAVCMFPO	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Palliative Therapy for Advanced Breast Cancer using Cyclophosphamide (oral), Methotrexate and Fluorouracil
BRAVDCAP	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Palliative Therapy for Metastatic Breast Cancer using Docetaxel and Capecitabine
BRINFCAF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Inflammatory Breast Cancer using Cyclophosphamide, Doxorubicin and Fluorouracil
BRINFCEF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Therapy for Inflammatory Breast Cancer Using Cyclophosphamide, Epirubicin and Fluorouracil
BRINFCEFG	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Therapy for Inflammatory Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF)
BRLA2	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Locally Advanced Breast Cancer using Cyclophosphamide, Doxorubicin and Fluorouracil
BRLACEF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Therapy for Locally Advanced Breast Cancer Using Cyclophosphamide, Epirubicin and Fluorouracil
BRLACEFG	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Therapy for Locally Advanced Breast Cancer Using Cyclophosphamide, Epirubicin, Fluorouracil and Filgrastim (G-CSF)
CNETO	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Preprinted dose reformatted for clarity</i>	Palliative Treatment Of Patients With Recurrent Malignant Gliomas And Ependymoma Using Low Dose Etoposide

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
ENMITO	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Preprinted dose reformatted for clarity</i>	Treatment Of Adrenal Cortical Cancer (Using Mitotane)
GIAJFL	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy of Colon Cancer using Fluorouracil Injection and Infusion and Folinic Acid (Leucovorin) Infusion
GIAVFL	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Palliative Combination Chemotherapy for Metastatic Colorectal Cancer Using 5-Fluorouracil Injection and Infusion and Folinic Acid (Leucovorin) Infusion
GIEFUPRT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Combined Modality Therapy for Locally Advanced Esophageal Cancer using Cisplatin, Infusional Fluorouracil and Radiation Therapy
GIENAFUPRT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Neo-Adjuvant Combined Modality Therapy for Resectable Esophageal and Gastro-Esophageal Junction Cancer using Cisplatin, Infusional Fluorouracil and Radiation Therapy
GIFUART	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Curative Combined Modality Therapy for Carcinoma of the Anal Canal using Mitomycin, Infusional Fluorouracil and Radiation Therapy
GIFUFA	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Palliative Therapy of Advanced Colorectal Cancer using Leucovorin and Fluorouracil
GIFUINF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Palliative Chemotherapy for Metastatic Colorectal Adenocarcinoma using Infusional Fluorouracil
GIFUIP	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Chemotherapy of Pseudomyxoma Peritonei using Intraperitoneal Mitomycin and Fluorouracil
GIGAIRT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Combined Modality Adjuvant Therapy for Completely Resected Gastric Adenocarcinoma using Fluorouracil + Folinic Acid (Leucovorin) + Radiation Therapy
UGIGDCF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Palliative Treatment of Metastatic or Locally Advanced Gastric, Esophagogastric Junction, or Esophageal Adenocarcinoma using with Docetaxel, Cisplatin and Infusional Fluorouracil
GIGECC	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Perioperative Treatment of Resectable Adenocarcinoma of the Stomach, Gastroesophageal Junction or Lower 1/3 Esophagus using Epirubicin, Cisplatin and Capecitabine
GIGFOLFIRI	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Second Line Palliative Combination Chemotherapy for Metastatic Gastric or Esophageal Adenocarcinoma Using Irinotecan, Fluorouracil and Folinic Acid (Leucovorin)
GIPAJFF	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Adjuvant Therapy for Resected Pancreatic Cancer Using Leucovorin and Fluorouracil
GOBEP	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Preprinted dose reformatted for clarity</i>	Therapy Of Non-Dysgerminomatous Ovarian Germ Cell Cancer Using Bleomycin, Etoposide And Cisplatin

CODE	Protocol	PPPO	Patient Handout	Changes	Protocol Title
GOCXCRT	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Adjustment for creatinine revised; platelet criteria added; acetaminophen and loperamide removed</i>	Treatment of High Risk Squamous Carcinoma, Adenocarcinoma, or Adenosquamous Carcinoma of the Cervix with Concurrent Cisplatin and Radiation
GUAVPG	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Clarification of CAP requirement for re-treatment with GUAVPG</i>	Palliative Therapy for Urothelial Carcinoma Using Cisplatin and Gemcitabine
GUFUPRT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Combined Modality Therapy for Squamous Cell Cancer of the Genitourinary System Using Fluorouracil and Cisplatin with Radiation
UGUSUNI	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Amount of dispensed medication clarified</i>	Palliative Therapy for Renal Cell Carcinoma Using Sunitinib
HNFUFA	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	5-Fluorouracil and Leucovorin for Recurrent Head and Neck Cancer
HNFUP	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Advanced Head and Neck Cancer Using Cisplatin and Fluorouracil
HNFURT	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<i>Drug interactions updated in Precautions</i>	Combined Modality Therapy for Advanced Head and Neck Cancer using Mitomycin, Fluorouracil and Split Course Radiation Therapy
LUPOE	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Preprinted dose reformatted for clarity</i>	Therapy For Small Cell Lung Cancer Using Oral Etoposide
LYIT	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<i>Preprinted dose reformatted for clarity</i>	Treatment Of Lymphoma Using Intrathecal Methotrexate And Cytarabine

### ERRATUM

**Head and Neck Protocol** In our last issue, the revised protocol should have been **HNLPRT**, and *not* HNLNPRT.

## WEBSITE RESOURCES AND CONTACT INFORMATION

WEBSITE RESOURCES	<a href="http://www.bccancer.bc.ca">www.bccancer.bc.ca</a>
REIMBURSEMENT AND FORMS: BENEFIT DRUG LIST, CLASS II, BC CANCER AGENCY COMPASSIONATE ACCESS PROGRAM	<a href="http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms">www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Forms</a>
CANCER DRUG MANUAL	<a href="http://www.bccancer.bc.ca/cdm">www.bccancer.bc.ca/cdm</a>
CANCER MANAGEMENT GUIDELINES	<a href="http://www.bccancer.bc.ca/CaMgmtGuidelines">www.bccancer.bc.ca/CaMgmtGuidelines</a>
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SYSTEMIC THERAPY PROGRAM POLICIES	<a href="http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies">www.bccancer.bc.ca/HPI/ChemotherapyProtocols/Policies</a>
SYSTEMIC THERAPY UPDATE	<a href="http://www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate">www.bccancer.bc.ca/HPI/ChemotherapyProtocols/stupdate</a>

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OSCAR HELP DESK .....	1-(888)-355-0355 .....	<a href="mailto:oscar@bccancer.bc.ca">oscar@bccancer.bc.ca</a>
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