CAPECITABINE

INSTRUCTIONS FOR THE PHARMACIST

**Prescription**
- All orders should be written on a **pre-printed order**; if not, compare prescription to standard regimens in the Systemic Therapy Manual to confirm the dosing and instructions
  - The order must be signed by BOTH the prescriber (at the bottom) AND at least one other oncology health professional (nurse or hospital pharmacist) who has verified the order
  - Measure the patient’s height (cm) and weight (kg), then recalculate body surface area (BSA)
- The prescription may **not** be refilled (unless specifically ordered by the oncologist) and it may **not** be filled as a continuing care prescription
  - If the prescriber has written for refills, do **not** dispense until the oncology team authorizes the refill; blood work must be checked before the start of each cycle.

**Handling and Dispensing**
- It is strongly recommended that this medication be **dispensed in pill packs** prepackaged for this drug alone. Adherence is very important and toxicities from double dosing may be serious.
- Always check for drug-drug interactions, especially before the first cycle, as described below. Consult the **Drug Interactions** section (page 4), and consider an online drug interactions checking program.
  - Check with patient for any other medications filled at a different pharmacy
- When handling this drug, disposable gloves should be worn at all times by any woman of child-bearing potential. Counting trays and other equipment directly exposed to the drug should be cleaned with **soap and water**, followed by rinsing with copious amounts of water (wear gloves).
- Do not crush tablets in an open air environment and risk inhalation of powder.
- ALWAYS affix the auxiliary label to identify this medication as “Cancer Chemotherapy”- this is an important warning label for other health professionals caring for the patient.

**Patient Counseling and Follow-up**
- Counsel the patient, including the key messages listed below. Use the **Initial Assessment and Patient Counseling Visit- Pharmacist Guide** and the **Medication Info Sheet** for this drug. Be sure that you know the specific treatment schedule and that this is clearly communicated to the patient.
  - Call the patient within the first week to identify any problems with adverse reactions or adherence.
  - Continuing follow up calls between clinic visits are necessary for ADR identification and prevention and for adherence management. Contact the oncology clinic nurse or hospital pharmacist to negotiate who will do follow-up calls between clinic visits. Tell the patient that you plan to call back to check on their progress. Consider the suggested call-back schedule (pg. 2), with specific questions for each contact.
- If the patient reports any adverse effects, consider the management strategies suggested in the **Adverse Drug Reaction Management Guide**.
- ALWAYS document your findings in the patient profile of your pharmacy computer system
- ALWAYS contact the patient’s cancer care team of any findings and actions you have taken.
• ALWAYS watch for any unusual or unexpected symptoms or problems (such as an adverse reaction that appears too soon or too severe) and contact the cancer care team promptly if something seems wrong with the patient experience.

CLINICAL INDICATIONS
Capecitabine is clinically indicated for:
• Breast cancer and Colorectal cancer (alone, or in combination with other chemotherapy or radiotherapy)

DRUG ADMINISTRATION
• Capecitabine may be given twice daily (12 hours apart) for 14 consecutive days, followed by a 7 day rest period before resuming treatment. In other words, Capecitabine is given in a 3 week cycle: 2 weeks of treatment followed by 1 week of rest (except when given as neoadjuvant treatment with radiotherapy).
• Capecitabine should be taken with a glass of water within 30 minutes after a meal.
• Keep capsules in blister pack until time of ingestion.
• Do not crush tablets. Keep out of reach of children.
• If a dose is missed, do not take a double dose the next day to make up for it.

PATIENT COUNSELLING- INITIAL AND FOLLOW-UP CALLS
• In addition to other printed materials, use the Medication Info Sheet from the Cancer Care Nova Scotia website, and consider the more detailed suggestions in this toolkit.

<table>
<thead>
<tr>
<th>Key Messages</th>
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<tbody>
<tr>
<td><strong>Initial counselling- At time of dispensing</strong></td>
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<tr>
<td>• How to take the medication properly (including treatment-free breaks)</td>
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<tr>
<td>• Prevention measures for Hand-Foot Skin Reaction and skin rashes</td>
</tr>
<tr>
<td>• Good oral hygiene</td>
</tr>
<tr>
<td>• When to call back to the cancer care team for urgent care</td>
</tr>
<tr>
<td>• Use the Initial Assessment and Patient Counseling Visit- Pharmacist Guide and the drug-specific Medication Info Sheet</td>
</tr>
<tr>
<td><strong>First call-back – Within first week:</strong></td>
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<tr>
<td>• Identify any initial problems with understanding or adherence</td>
</tr>
<tr>
<td>• Use the First Follow-Up Call/Visit- Pharmacist Guide and the Medication Info Sheet (if needed)</td>
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<tr>
<td>• Reinforce key messages in the Pharmacist Guide</td>
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<td>o Suggest strategies to ensure adherence.</td>
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<tr>
<td>• Identify any early adverse effect symptoms; suggest management strategies</td>
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<tr>
<td><strong>Second call-back – After 2-3 weeks: (telephone or return visit to Pharmacy)</strong></td>
</tr>
<tr>
<td>• Identify any adverse effects or problems with understanding or adherence</td>
</tr>
<tr>
<td>• Use the Continuing Follow-Up Calls/Visits- Pharmacist Guide</td>
</tr>
<tr>
<td>o If any adverse effects identified, contact oncologist or oncology nurse</td>
</tr>
<tr>
<td>• Identify any continuing problems with adherence</td>
</tr>
<tr>
<td>• Reinforce key messages, if there continue to be any questions or concerns</td>
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<tr>
<td><strong>End of Treatment call-back or 3 weeks from start:</strong></td>
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<tr>
<td>• Remind patient to stop taking pills after 14 days (unless otherwise instructed)- ask if there are any pills left over; if so, PROBE to determine any barriers to treatment adherence</td>
</tr>
<tr>
<td>• Identify any adverse effects, as above</td>
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</tbody>
</table>
**Key Messages**

| Subsequent cycles- (at least one call during each cycle): | • Negotiate with patient and cancer care team for ongoing needs for counseling and timely follow up calls  
• Use the Continuing Follow-Up Calls/Visits- Pharmacist Guide[1]  
• Adherence assessment and support is an important issue for reinforcement at each visit and mid-cycle call-back as treatment continues |

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**ADVERSE EFFECTS: PREVENTION AND MANAGEMENT SUGGESTIONS**

If you identify any of the following, you should contact the oncologist and tell the patient to call the oncologist or go directly to the Emergency Department of the nearest hospital right away[1]:

- Signs of infection (fever, chills, body aches, flu symptoms)
- Severe diarrhea (more than 4 times per day, or during the night)
- Signs of coagulopathy (bloody, black, or tarry stools; coughing up blood or vomit that looks like coffee grounds)
- Symptoms of blood clots (pain or swelling in arm, thigh, or calf)
- Symptoms of cardiotoxicity (chest pain, rapid or irregular heart beats, shortness of breath)
- Symptoms of DPD deficiency (stomatitis, diarrhea, neutropenia and neurotoxicity)- there is no lab test for DPD (dihydropyrimidine dehydrogenase)
- Jaundice (yellowing of skin or eyes)

The following are the common adverse effects from Capecitabine.

### More Common

**Dermatologic disorders**
- Hand and foot syndrome*, dermatitis*
- Alopecia*

**Gastrointestinal disorders**
- Diarrhea*, nausea*, vomiting*, abdominal pain
- Stomatitis*, loss of appetite/anorexia*

**Hematologic disorders**
- Myelosuppression* - neutropenia, thrombocytopenia, anemia

**Hepatic disorders**
- Hyperbilirubinemia (jaundice) ✓

**General disorders**
- Fatigue*, fever*, pain*, edema+
- Asthenia*, fatigue/lethargy*

### Less Common

**Cardiovascular disorders**
- Blood clots ✓ (usually patients on stable warfarin dosing)
- Cardiotoxicity ✓ - angina, dysrhythmia, heart failure, MI- rare

**Skin disorders**
- Rash*, red skin✓

**Gastrointestinal disorders**
- Taste disturbance*

**Neuromuscular & Skeletal disorders**
- Myalgia*, arthralgia*, back pain*

**General disorders**
- Cough†, viral infection✓
- Headache*, dizziness†

* For detailed recommendations on the management of these adverse drug reactions, see the [Adverse Drug Reaction Management Guide](#)

† For management of these symptoms, the patient should see his physician

✓ These symptoms require urgent attention- advise the patient to go to the Emergency Department or contact their doctor (see instructions above)
DRUG INTERACTIONS
Capecitabine is a strong inhibitor of CYP2C9

- Take a thorough medication history (call other pharmacies if necessary) and determine the potential for all other drugs to increase or decrease Capecitabine plasma concentration.
- Drug interactions are often missed by community pharmacy computer systems
- REPORT any potential interaction to the prescribing oncologist- either the Capecitabine or the interacting drug may need to be dose altered or discontinued.

It is strongly recommended that you check any concurrent medications identified for interactions with this oral chemotherapy agent. Try one of the following comprehensive programs for checking drug interactions.

<table>
<thead>
<tr>
<th>Online Programs for Drug Interaction Checking—Publicly available:</th>
<th>Other Interaction Checkers—Subscription required:</th>
</tr>
</thead>
<tbody>
<tr>
<td><a href="http://www.drugs.com/drug_interactions.php">http://www.drugs.com/drug_interactions.php</a></td>
<td>Lexicomp</td>
</tr>
<tr>
<td><a href="http://www.healthline.com/druginteractions">http://www.healthline.com/druginteractions</a></td>
<td>eCPS</td>
</tr>
<tr>
<td><a href="http://cpref.goldstandard.com/inter.asp?r=8084">http://cpref.goldstandard.com/inter.asp?r=8084</a></td>
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<tr>
<td><a href="http://umm.edu/health/medical/drug-interaction-tool">http://umm.edu/health/medical/drug-interaction-tool</a></td>
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<tr>
<td><a href="http://online.epocrates.com/">http://online.epocrates.com/</a> (free account required)</td>
<td></td>
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</tbody>
</table>

Some common interactions with Capecitabine are:

- Carvedilol: Capecitabine may increase the serum concentration of Carvedilol
- Cimetidine: may increase serum concentrations of the active metabolite of Capecitabine (specifically, fluorouracil)
- CloZAPine: Capecitabine may increase the toxicity of Clozapine (specifically, agranulocytosis)
- CYP2C9 substrates: Capecitabine may decrease the metabolism of CYP2C9 substrates
- Diclofenac (systemic): may increase the serum concentration of Diclofenac. Consider using a lower dose of Diclofenac when used together with Capecitabine. Arthrotec labeling specifically recommends limiting the total daily dose to a maximum of 50 mg BID.
- Echinacea: may decrease the therapeutic effect of Capecitabine
- Leflunomide: may increase toxicity of Leflunomide (specifically, the risk of hematologic toxicity). Consider not using a leflunomide loading dose in patients receiving Capecitabine. Monitor patient for bone marrow suppression at least monthly if using these drugs concurrently.
- Leucovorin: may increase toxicity of Capecitabine
- Phenytoin, Fosphenytoin: may increase the serum concentration of Phenytoin and Fosphenytoin
- Tacrolimus (topical): may increase the toxicity of Capecitabine (avoid combination)
- Vaccines (inactivated, live): may increase toxicity and decrease therapeutic effect of vaccines (avoid combination)
- Vitamin K Antagonists (e.g. Warfarin): may increase the serum concentration of Vitamin K Antagonists