



## ETOPOSIDE

### 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
- 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 for each cycle.
- 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 Table**, in this Toolkit.

#### Handling and Dispensing

- 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 a **sodium hypochlorite (bleach)** solution (or soap and water), followed by rinsing with copious amounts of water (wear gloves). Do not open capsules in an open air environment and risk inhalation.
- ALWAYS affix the auxiliary label to identify this medication as “Cancer Chemotherapy”
  - This is an important warning label for other health professionals.



#### Patient Counseling and Follow-up

- Counsel the patient, including the key messages listed below. Use the **Initial Assessment and Patient Counseling Visit- Pharmacist Guide ①** and the **Medication Info Sheet ②** 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.
  - When speaking with the patient and during call backs, ask the patient to identify any problems with medication adherence. Use the **First Follow-Up Call/Visit- Pharmacist\_Guide ①**.
- 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.
  - When speaking with the patient and during call backs, ask the patient to identify any problems with medication adherence. Use the **Continuing Follow-Up Calls/Visits - Pharmacist\_Guide ①**.
- If the patient reports any adverse effects, consider the management strategies suggested in the **Adverse Drug Reaction Management Guide ②**.
- 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

Etoposide is clinically indicated for many different types of cancer, including:

- Lung cancer
- Non-Hodgkin's lymphoma
- Ovarian cancer
- Testicular cancer

## DRUG ADMINISTRATION

- Etoposide may be given **once or more daily**, depending on dose. Doses less than or equal to 200 mg/day may be given as a single daily dose.
- Capsules should be swallowed whole with a glass of water on an empty stomach.
- Keep capsules in blister pack until time of ingestion. Keep capsules out of reach of children.
- Do not open or chew capsules.
- 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.

	Key Messages
<p><b>Initial counselling- At time of dispensing</b></p>	<ul style="list-style-type: none"> <li>• How to take the medication properly (including treatment-free breaks)</li> <li>• Good oral hygiene</li> <li>• When to call back to the cancer care team for urgent care</li> <li>• Use the <b>Initial Assessment and Patient Counseling Visit- Pharmacist Guide ❶</b> and the drug-specific <b>Medication Info Sheet ❷</b></li> </ul>
<p><b>First call-back – Within first week:</b></p> 	<ul style="list-style-type: none"> <li>• Identify any initial problems with understanding or adherence</li> <li>• Use the <b>First Follow-Up Call/Visit- Pharmacist Guide ❶</b> and the <b>Medication Info Sheet ❷</b> (if needed)</li> <li>• Reinforce initial key messages <ul style="list-style-type: none"> <li>○ How and when treatment is taken</li> <li>○ Barriers to adherence- remembering to take medication; reluctance to take treatment; financial issues; nausea, vomiting or other adverse effects; trouble with packaging; felt better off medication; other concerns</li> <li>○ Suggest strategies to ensure adherence; reminder that full dose is needed for cancer control- partial doses may be ineffective.</li> </ul> </li> <li>• Management of diarrhea- ensure patient has some Loperamide at home</li> <li>• Identify any early adverse effect symptoms; suggest management strategies</li> </ul>
<p><b>Second call-back – After 2-3 weeks: (telephone or return visit to Pharmacy)</b></p> 	<ul style="list-style-type: none"> <li>• Ask if there are any capsules left over and, if so, <b>PROBE</b> to determine any barriers to treatment adherence (see above)</li> <li>• Identify any adverse effects (<b>PROBE</b> for evidence of nausea and vomiting; mouth sores; diarrhea)</li> <li>• Use the <b>Continuing Follow-Up Calls/Visits- Pharmacist Guide ❶</b> <ul style="list-style-type: none"> <li>○ If any ADR identified, contact oncologist or oncology nurse, and consider the information below under Adverse Effects</li> </ul> </li> <li>• Reinforce initial key messages, if there continue to be any questions or concerns</li> </ul>

Continued...

	<b>Key Messages (continued)</b>
<b>Subsequent cycles- (at least one call during each cycle):</b>	<ul style="list-style-type: none"> <li>• Negotiate with patient and cancer care team for ongoing needs for counseling and timely follow up calls (every 1-3 months)</li> <li>• Use the <b>Continuing Follow-Up Calls/Visits- Pharmacist Guide ①</b></li> <li>• Adherence assessment and support is an important issue for reinforcement at each visit and mid-cycle call-back as treatment continues</li> </ul>

**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 ⚡:

- Pale skin, light-headedness, shortness of breath, trouble concentrating
- Symptoms of infection (fever, chills, body aches, flu symptoms, sores in mouth and throat)
- Symptoms of hepatotoxicity (upper stomach pain, itching, loss of appetite, dark urine, clay-coloured stools, jaundice)
- Seizures
- Sudden chest pain or discomfort, wheezing, dry cough or hack

The following are the common adverse effects from Etoposide.

<b>More Common</b> <u>Dermatologic disorders</u> <ul style="list-style-type: none"> <li>• Alopecia★</li> </ul> <u>Gastrointestinal disorders</u> <ul style="list-style-type: none"> <li>• Nausea★, vomiting★, diarrhea★</li> <li>• Anorexia★</li> </ul> <u>Hematologic disorders</u> <ul style="list-style-type: none"> <li>• Myelosuppression★- leukopenia, thrombocytopenia, anemia</li> </ul>	<b>Less Common</b> <u>Gastrointestinal disorders</u> <ul style="list-style-type: none"> <li>• Stomatitis★, abdominal pain</li> </ul> <u>Hepatic disorders</u> <ul style="list-style-type: none"> <li>• Hepatotoxicity♦ - severe⚡</li> </ul> <u>Neuromuscular &amp; Skeletal disorders</u> <ul style="list-style-type: none"> <li>• Peripheral neuropathy (rare)</li> </ul> <u>General disorders</u> <ul style="list-style-type: none"> <li>• Allergic reaction (rare, usually with IV drug) ⚡</li> <li>• Infection⚡</li> </ul>
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★ For detailed recommendations on the management of these adverse drug reactions, see the **Adverse Drug Reaction Management Guide ②**

♦ 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

Etoposide is a major substrate of CYP3A4 and a minor substrate of CYP1A2, CYP2E1, and P-glycoprotein. Etoposide weakly inhibits CYP2C9 and CYP3A4.

- Take a **thorough medication history** (call other pharmacies if necessary) and determine the potential for all other drugs to increase or decrease Thalidomide plasma concentration.



It is strongly recommended that you check any concurrent medications for interactions with this oral chemotherapy agent. The pharmacy IT system may not provide a complete interaction cross-check. Try one of the following comprehensive programs for checking drug interactions.

<p><b>Online Programs for Drug Interaction Checking-Publicly available:</b></p> <ul style="list-style-type: none"> <li>• <a href="http://www.drugs.com/drug_interactions.php">http://www.drugs.com/drug_interactions.php</a></li> <li>• <a href="http://reference.medscape.com/drug-interactionchecker">http://reference.medscape.com/drug-interactionchecker</a></li> <li>• <a href="http://www.healthline.com/druginteractions">http://www.healthline.com/druginteractions</a></li> <li>• <a href="http://cpref.goldstandard.com/inter.asp?r=8084">http://cpref.goldstandard.com/inter.asp?r=8084</a></li> <li>• <a href="http://umm.edu/health/medical/drug-interaction-tool">http://umm.edu/health/medical/drug-interaction-tool</a></li> <li>• <a href="http://online.epocrates.com/">http://online.epocrates.com/</a> (free account required)</li> </ul>	<p><b>Other Interaction Checkers-Subscription required:</b></p> <ul style="list-style-type: none"> <li>• Lexicomp</li> <li>• Micromedex</li> <li>• eCPS</li> </ul>
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Some common interactions with Etoposide are:

- ARIPiprazole: may increase serum concentration of Aripiprazole by inhibiting CYP3A4. Monitor patient; dose adjustments may or may not be required.
- Atovaquone: may increase serum concentration of Etoposide. Separate administration of atovaquone and etoposide by at least 1-2 days.
- Barbiturates: may decrease serum concentration of Etoposide
- CloZAPine: may increase toxicity of Clozapine, specifically the risk of agranulocytosis (*avoid combination*)
- Cyclosporine (systemic): may decrease metabolism of Etoposide. Consider a 50% dose reduction of Etoposide if the patient is receiving, or has recently received, Cyclosporine. Monitor for increase effects of Etoposide.
- CYP3A4 inducers: may increase metabolism of Etoposide
- CYP3A4 inhibitors: may decrease metabolism of Etoposide
- Leflunomide: may increase toxicity of Leflunomide (specifically, the risk of hematologic toxicity). Consider not using a leflunomide loading dose in patients receiving Etoposide. Monitor patient for bone marrow suppression at least monthly if using these drugs concurrently.
- P-glycoprotein/ABCB1 inducers: may decrease serum concentration of Etoposide and may also limit distribution of Etoposide to sites high in p-glycoprotein, such as brain, T-cells, testes, etc.
- P-glycoprotein/ABCB1 inhibitors: may increase serum concentration of Etoposide and may increase distribution of Etoposide to brain, T-cells, testes, etc.
- Phenytoin, Fosphenytoin: may decrease the serum concentration of Etoposide
- Pimozide: may increase the serum concentration of Pimozide by inhibiting CYP3A4
- Tacrolimus (topical): may increase the toxicity of Etoposide (*avoid combination*)
- Vaccines (inactivated, live): may increase toxicity and decrease therapeutic effect of vaccines (*avoid combination*)
- Vitamin K Antagonists (e.g. Warfarin): may increase/decrease anticoagulant effect of Vitamin K Antagonists.

*Note: Drinking alcohol while taking Etoposide may increase GI irritation and should be avoided.*

*The patient should avoid taking St John's wort.*

**\* REPORT any potential interaction** to the prescribing oncologist- either the Etoposide or the interacting drug may need to be dose-altered or discontinued.