



EVEROLIMUS

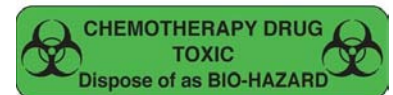
INSTRUCTIONS FOR THE PHARMACIST

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, contact the oncology team and do **not** dispense until they call back to authorize the refill; Blood work must be checked for each cycle.
- **Always check for drug-drug interactions, especially before the first cycle. There is a strong potential for Everolimus to interact with other drugs, foods or natural health products**, so a thorough drug interaction check (including medications filled at different pharmacies) is recommended before dispensing the first dose of Everolimus and after each new drug is considered for concomitant use. Consult the **Drug Interactions Table**, in this Toolkit.
 - Drug interactions are often missed by community pharmacy computer systems
 - Check with patient for any other medications filled at different pharmacies, OTCs, NHPs

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 **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 who may need to care 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 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 drug 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 with any findings and your actions.
- 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

Everolimus is clinically indicated for:



- Advanced renal cell carcinoma after failure of initial treatment with either Sunitinib or Sorafenib

DRUG ADMINISTRATION

- Everolimus is taken **once daily**, with or without food. Take Everolimus at the same time each day.
- Do not crush or chew the tablets.
- Patients should not eat grapefruits or Seville oranges or drink grapefruit juice while taking Everolimus.
- 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.

	Key Messages
<p>Initial counselling- At time of dispensing</p>	<ul style="list-style-type: none"> • How to take the medication properly (including the importance of adherence over the years of treatment) • When to call back to the cancer care team for urgent care • Use the Initial Assessment and Patient Counseling Visit- Pharmacist Guide ❶ and the drug-specific Medication Info Sheet ❷
<p>First call-back – Within first week:</p> 	<ul style="list-style-type: none"> • Identify any initial problems with understanding or adherence • Use the First Follow-Up Call/Visit- Pharmacist Guide ❶ and the Medication Info Sheet ❷ (if needed) • Reinforce initial key messages <ul style="list-style-type: none"> ○ How and when treatment is taken ○ 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 ○ Suggest strategies to ensure adherence; reminder that full dose is needed for cancer control- partial doses may be ineffective. • Identify any early adverse effect symptoms; suggest management strategies
<p>Second call-back – After 2-3 weeks: (telephone or return visit to Pharmacy)</p> 	<ul style="list-style-type: none"> • Identify any adverse effects (PROBE for evidence of hot flushes; gynecologic symptoms; skin rashes; peripheral edema; mood disturbances; nausea and/or vomiting; musculoskeletal problems) • Use the Continuing Follow-Up Calls/Visits- Pharmacist Guide ❶ <ul style="list-style-type: none"> ○ If any ADR identified, contact family physician, oncologist or oncology nurse, and consider the information below under Adverse Effects • Identify any continuing problems with adherence (see above) • Reinforce initial key messages, if there continue to be any questions or concerns

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

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 **↗**:

- Gastrointestinal hemorrhage, bowel perforation (abdominal pain and constipation/vomiting). This is life-threatening and early detection is critical.
- Hemorrhage (vaginal, retinal, lung, bloody stool, bloody urine)
- Infection (bacterial, fungal, viral, protozoal, or opportunistic)- may be fatal
- Symptoms of acute respiratory failure - Shortness of breath, fever, cough
- Symptoms of acute renal failure (low urine output, swollen body, fatigue, abdominal pain)

The following are the common adverse effects from Everolimus.

<p>More Common</p> <p><u>Myelosuppression</u>★</p> <ul style="list-style-type: none"> • Anemia, thrombocytopenia <p>Cardiovascular disorders</p> <ul style="list-style-type: none"> • swelling <p><u>Gastrointestinal disorders</u></p> <ul style="list-style-type: none"> • Stomatitis★, mucositis★ • Nausea★, vomiting★, diarrhea★ <p><u>General disorders</u></p> <ul style="list-style-type: none"> • Weakness, fatigue★, asthenia★ • Headache★ <p><u>Infection</u>↗</p> <ul style="list-style-type: none"> • Fever, sore throat <p><u>Metabolic disorders</u></p> <ul style="list-style-type: none"> • Hyperglycemia◆ • Hyperlipidemia◆ • Hypercholesterolemia◆ <p><u>Respiratory disorders</u></p> <ul style="list-style-type: none"> • Cough†, breathing problems↗ • Shortness of breath↗ <p><u>Skin disorders</u></p> <ul style="list-style-type: none"> • Rash★, dry skin★, itchy skin★ 	<p>Less Common</p> <p><u>Cardiovascular disorders</u></p> <ul style="list-style-type: none"> • Hypertension◆ • Tachycardia↗, congestive cardiac failure↗ <p><u>Respiratory disorders</u></p> <ul style="list-style-type: none"> • Pneumonitis↗ • Pleural effusion◆ <p><u>Gastrointestinal disorders</u></p> <ul style="list-style-type: none"> • Abdominal pain◆, dry mouth★, dysphagia◆ <p><u>Genitourinary disorders</u></p> <ul style="list-style-type: none"> • Acute renal failure↗ <p><u>General disorders</u></p> <ul style="list-style-type: none"> • Jaw pain◆ • Sleeplessness◆ • Pain (arms, legs, chest, back, abdomen, joints)★ • Taste disturbance★, weight loss • Wound-healing complications◆ <p><u>Skin disorders</u></p> <ul style="list-style-type: none"> • Hand-foot syndrome★
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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

DRUG INTERACTIONS

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

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



LIST OF IMPORTANT DRUG-DRUG INTERACTIONS WITH EVEROLIMUS- *This is not a complete list*

Everolimus is metabolized primarily in the CYP3A4 pathway in the liver. Significant interactions are possible with other drugs that affect the same metabolic pathway.

Everolimus is also a moderate inhibitor of the multidrug efflux pump PGP and mixed inhibitor of CYP2D6.

*Avoid live vaccines and close contact with people who receive them (BCG, varicella, yellow fever, typhoid, mumps, measles, and rubella).

- Anticoagulants (Anisindione, Ardeparin, Dalteparin, Dicoumarol, Enoxaparin, Heparin, Tinzaparin, Warfarin) - may increase risk of bleeding from Everolimus
- Bisphosphonate agents (Alendronate, Etidronate, Ibandronate, Pamidronate, Risedronate, Zoledronic Acid)- may increase risk of osteonecrosis of the jaw from bisphosphonates
- **CYP 3A4 inducer** medications (e.g., dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital or St. John's Wort): consider dose increase of Everolimus if co-administered with a strong CYP3A4 inducer (may decrease Everolimus plasma concentrations)
- **CYP 3A4 inhibitor** medications (e.g., ketoconazole, itraconazole, erythromycin, clarithromycin): consider dose reduction of Everolimus if co-administered with a strong CYP3A4 inhibitor (may increase Everolimus plasma concentrations)
- Dabigatran- Increased levels of Dabigatrin in the blood
- Denosumab- Increased risk of serious infections
- Echinacea- Reduced Everolimus levels
- Grapefruit or grapefruit juice- Increased Everolimus blood levels
- Hepatotoxic drugs (Black Cohosh, Clofarabine, Interferon beta-1a, Interferon beta-1b, **Leflunomide**, Methotrexate, Naltrexone, **Teriflunomide**) - Increased risk of hepatotoxicity
- PR prolongation- medications that cause a change in the heart rhythm
- QT prolongation- medications that cause a change in the heart rhythm
- Silodosin- Increased silodosin blood levels
- Statins- Everolimus may inhibit metabolism, increased blood levels and higher risk of developing rhabdomyolysis.
- Tacrolimus ointment- Increased risk of serious infections, lymphoma and skin cancers

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.

Online Programs for Drug Interaction Checking-Publicly available:

- http://www.drugs.com/drug_interactions.php
- <http://reference.medscape.com/drug-interactionchecker>
- <http://www.healthline.com/druginteractions>
- <http://cpref.goldstandard.com/inter.asp?r=8084>
- <http://umm.edu/health/medical/drug-interaction-tool>
- <http://online.epocrates.com/> (free account required)

Other Interaction Checkers-

Subscription required:

- Lexicomp
- Micromedex
- eCPS