Oral Systemic Therapy Pharmacy Toolkit

VEMURAFENIB

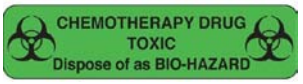
INSTRUCTIONS FOR THE PHARMACIST

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.
- **Always check for drug-drug interactions, especially before the first cycle**. **There is a strong potential for Vemurafenib 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 Enzalutamide and after each new drug is considered for concomitant use. 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 **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 Guide❶** and the **Medication Info Sheet❷** 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 Guide❶**.
- 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 Guide❶**.
- If the patient reports any adverse effects, consider the management strategies suggested in the **Adverse Drug Reaction Management Guide❷**.

- 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

Vemurafenib is clinically indicated for:

- Unresectable or metastatic melanoma with $BRAF^{V600E}$ mutation

DRUG ADMINISTRATION

- Vemurafenib is taken ***twice daily***, consistently with or without food.
- Patients should not eat grapefruits or drink grapefruit juice while taking Vemurafenib.
- Swallow whole tablets with a glass of water- Do not crush, split, or dissolve the 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.

	Key Messages
Initial counselling- At time of dispensing	• How to take the medication properly (including treatment-free breaks) • Prevention measures for skin rashes* • When to call back to the cancer care team for urgent care • Use the **Initial Assessment and Patient Counseling Visit- Pharmacist Guide❶** and the drug-specific **Medication Info Sheet❷**
First call-back – Within first week: 	• Identify any initial problems with understanding or adherence • Use the **First Follow-Up Call/Visit- Pharmacist Guide❶** and the **Medication Info Sheet❷** (if needed) • Reinforce initial key messages o How and when treatment is taken o 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 o 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
Second call-back – After 2-3 weeks: (telephone or return visit to Pharmacy) 	• Identify any adverse effects (**PROBE** for evidence of skin rashes; pruritis; QT prolongation-irregular heartbeats; nausea and vomiting; diarrhea) • Use the **Continuing Follow-Up Calls/Visits- Pharmacist Guide❶** o If any identified, contact oncologist or oncology nurse, and consider the information below under Adverse Effects • Identify any continuing problems with adherence (see above) • Reinforce initial key messages
Second call-back – After 2-3 months: (telephone or return visit to Pharmacy)	• Ask if there are any pills left over and, if so, PROBE to determine any barriers to treatment adherence (see above) • Identify any adverse effects, as above • Plan for return to Pharmacy at start of next cycle

	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 Guide❶** • Adherence assessment and support is an important issue for reinforcement at each visit 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🗲:

- Hypersensitivity reactions (generalized rash or redness, feeling faint, trouble breathing or swallowing, fast heartbeat, swelling of face, lips, or tongue, throat tightness or hoarseness)
- Severe skin reactions (blistering, blisters or sores in mouth, red and swollen face, hands, or soles of feet, fever, sunburn)
- Heart rhythm disturbance (dizziness, palpitations, fainting, or seizures)

The following are the common adverse effects from Vemurafenib.

More Common	**Less Common**
<u>Gastrointestinal disorders</u> • Nausea✶, vomiting✶, diarrhea✶, constipation✶ • Decreased appetite <u>General disorders</u> • Fatigue✶, fever, fluid retention† • Headache✶ <u>Musculoskeletal & Connective tissue disorders</u> • Joint and muscle pain in extremities✶ <u>Skin & Subcutaneous tissue disorders</u>🗲 • Hair loss✶, rash✶, photosensitivity reaction✶, sunburn✶, itch✶, hyperkeratosis†, dry skin✶	<u>Cardiovascular disorders</u> • QT prolongation🗲 <u>Hepatic disorders</u> • Liver laboratory abnormalities†, liver problems (jaundice, upper right quadrant pain) ♦ <u>Skin & Subcutaneous tissue disorders</u>🗲 • Skin redness • Neoplasms (cysts, polyps, benign and cancerous growths) ♦ • Skin papilloma♦, cutaneous squamous cell carcinoma♦, seborrheic keratosis🗲 <u>General disorders</u> • Hypersensitivity reactions🗲 • Taste disturbance✶

✶ For detailed recommendations on the management of these adverse drug reactions, see the **Adverse Drug Reaction Management Guide❷**

♦ 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

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

- Drug interactions are often missed by community pharmacy computer systems
- ***REPORT any potential interaction*** to the prescribing oncologist- either the Vemurafenib or the interaction drug may need to be dose altered or discontinued.

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

Vemurafenib is metabolized primarily in the CYP3A4 pathway in the liver. It is a CYP3A4 inducer, moderate CYP1A2 inhibitor, and weak CYP2D6 inhibitor. It inhibits the CYP2C9 pathway, which may impact the use of Warfarin. Significant interactions are possible with other drugs that affect the same metabolic pathway.

- Anticoagulants (Anisindione, Ardeparin, Dalteparin, Dicoumarol, Enoxaparin, Heparin, Tinzaparin, Warfarin) - may increase risk of bleeding from Vemurafenib
- 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 Vemurafenib if co-administered with a strong CYP3A4 inducer (may decrease Vemurafenib plasma concentrations)
- **CYP 3A4 inhibitor** medications (e.g., ketoconazole, itraconazole, erythromycin, clarithromycin): consider dose reduction of Vemurafenib if co-administered with a strong CYP3A4 inhibitor (may increase Vemurafenib plasma concentrations)
- Dabigatran- Increased levels of Dabigatrin in the blood
- Denosumab- Increased risk of serious infections
- Echinacea- Reduced Vemurafenib levels
- Grapefruit or grapefruit juice- Increased Vemurafenib blood levels
- Hepatotoxic drugs (Black Cohosh, Clofarabine, Interferon beta-1a, Interferon beta-1b, **Leflunomide,** Methotrexate, Naltrexone, **Teriflunomide**) - Increased risk of hepatotoxicity
- "Live" vaccinations
- PGP inhibitors (Cyclosporine, Nifedipine)- increase plasma levels of Vemurafenib
- 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
- 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. Try one of the following comprehensive programs for checking drug interactions.

Online Programs for Drug Interaction Checking-Publicly available:	**Other Interaction Checkers-Subscription required**:
• 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)	• Lexicomp • Micromedex • eCPS