Oral Systemic Therapy Pharmacy Toolkit

SORAFENIB

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 Sorafenib 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, 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.

CLINICAL INDICATIONS

Sorafenib is clinically indicated for:

- Hepatocellular Carcinoma (unresectable)
- Advanced/Metastatic Renal Cell Carcinoma (failed or intolerant to previous systemic therapy)

DRUG ADMINISTRATION

- Sorafenib is generally taken as ***twice daily***, with low-fat food or without food.
- Sorafenib absorption is reduced if taken with high fat food. Avoid grapefruit and grapefruit juice.
- Swallow whole tablets with water- Do not crush or chew.
- Keep out of reach of children.
- Sorafenib is usually taken continuously, without a break.
- 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 Hand-Foot Skin Reaction and 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. • Management of diarrhea- ensure patient has some Loperamide at home • 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 HFSR; skin rashes; thrombosis, hypertension, CHF- trouble breathing, swollen ankles, QT prolongation-irregular heartbeats; mouth sores; diarrhea) • Use the **Continuing Follow-Up Calls/Visits- Pharmacist Guide❶** o If any identified, contact oncologist or oncology nurse • Management of mild HFSR- ensure patient uses appropriate moisturizer • Identify any continuing problems with adherence. At end of treatment, ask if there are any pills left over; if so, PROBE to determine any barriers to treatment adherence. • Reinforce initial key messages

	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🗲:

- Bleeding problems (blood in urine or stool; nose bleeds) and infection
- Blood clots (severe pain, swelling, or redness in legs or severe chest pain with shortness of breath)
- Heart problems (shortness of breath, fatigue, swollen feet and ankles)
- Pancreatitis (abdominal pain, fever, nausea, vomiting)

The following are the common adverse effects from Sorafenib.

More common	**Less Common**
<u>Bleeding disorders</u>🗲 • Bleeding from mouth, nose, stomach or gut, rectum, lungs or windpipe, nail beds, blood blisters <u>Cardiovascular disorders</u> • Hypertension† <u>Gastrointestinal disorders</u> • Diarrhea✶, nausea✶, vomiting✶, constipation✶, loss of appetite/anorexia✶, loss of weight, stomatitis✶ <u>General disorders</u> • Fatigue✶, weakness✶ • Hair loss✶ • Pain (abdominal pain, headache; joint, bone or muscle pain) ✶ <u>Hematologic disorders</u> • Myelosuppression✶ (lymphopenia, neutropenia, anemia, thrombocytopenia) <u>Respiratory disorders</u> • Breathlessness♦ <u>Skin disorders</u> • Hand-foot skin reaction✶, rash✶; pruritus✶; inflamed, dry, or scaly skin that sheds✶	<u>Cardiovascular disorders</u> • Flushing, heart attack🗲 (cardiac ischemia/infarction) • Left ventricular failure🗲, QT prolongation🗲 • Thromboembolism🗲 <u>CNS disorders</u> • Cerebral hemorrhage🗲, transient ischemic attack <u>General disorders</u> • Flu-like illness♦, fever♦ • Depression♦, hoarseness♦, impotence♦ • Sensory neuropathy♦ <u>Gastrointestinal disorders</u> • Indigestion, heartburn♦, difficulty swallowing♦, infection or inflammation of gallbladder or bile ducts♦ • Elevated pancreatic enzymes♦ , pancreatitis🗲 <u>Kidney disorders</u> • Kidney failure♦ <u>Skin disorders</u> • Acne

✶ 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 SUNItinib plasma concentration.

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

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

- Anti-neoplastic agents- Use caution if Sorafenib given with other anti-neoplastic agents
- Capecitabine- increased levels of Capecitabine and 5FU, possible increased toxicity
- Carboplatin and Paclitaxel- increased levels of Paclitaxel, possible increased risk of death from lung cancer when used together with Sorafenib
- **CYP 2B6 substrate** medications (Sorafenib inhibition of this CYP450 enzyme may cause increased levels of the substrates and possible increased effect or toxicity)
- **CYP 2C8 substrate** medications (Sorafenib inhibition of this CYP450 enzyme may cause increased levels of the substrates and possible increased effect or toxicity)
- **CYP 2C9 substrate** medications (Sorafenib inhibition of this CYP450 enzyme may cause increased levels of the substrates and possible increased effect or toxicity)
- **CYP 3A4 inducer** medications (may decrease Sorafenib plasma concentrations)
- **CYP 3A4 inhibitor** medications (may increase Sorafenib plasma concentrations)
- Docetaxel- increased levels of Docetaxel, possible increased toxicity
- Doxorubicin- increased levels of Doxorubicin, possible increased toxicity
- Everolimus- Increased blood levels of Everolimus
- Fluorouracil- May change fluorouracil levels (increase or decrease)
- Irinotecan- increased levels of SN-38, possible increased toxicity
- **Leflunomide** - Increased risk of myelosuppression
- "Live" vaccinations
- Neomycin- may decrease levels of Sorafeninb
- P-glycoprotein substrate drugs (e.g. Aliskiren, Ambrisentan, Cabazitaxel, Colchicine, Dabigatran, Loperamide, Maraviroc, Mibefradil, Mitoxantrone, *Raltegravir,* **Sirolimus,** Tipranavir, Tolvaptan, Vinblastine, Vincristine, Vinorelbine, Vismodegib) may have increased levels and toxicity when co-administered with Sorafenib
- QT prolongation- medications that cause a change in the heart rhythm
- Tacrolimus ointment- Increased risk of serious infections, lymphoma and skin cancers
- **UGT1A9 inhibitor** medications (may increase Sorafenib plasma concentrations by reducing glucuronidation:
- Warfarin- possible changes in PT-INR; monitor regularly

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