BUSULFAN

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, as described below. Consult the Drug Interactions Table, in this Toolkit.
  - 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 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 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.
- 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.
- 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 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.

Go to [www.cancercare.ns.ca](http://www.cancercare.ns.ca) - Health Professionals section, click on Systemic Therapy (left side list), select Oral Systemic Therapy (Pharmacy) or Systemic Therapy Manual- select drug  Choose link to PDF document.  Revision Date: 09/14
**CLINICAL INDICATIONS**
Busulfan is clinically indicated for:

- Chronic myelogenous leukemia

**DRUG ADMINISTRATION**

- Busulfan may be given **once daily** for days or weeks at a time. Doses may be repeated by the hematologist depending on blood results in response to treatment. Dosing may vary.
- Tablets should be swallowed whole with a glass of water.
- 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.

<table>
<thead>
<tr>
<th>Key Messages</th>
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</thead>
</table>
| **Initial counselling- At time of dispensing** | How to take the medication properly (including treatment-free breaks)  
When to call back to the cancer care team for urgent care  
Use the Initial Assessment and Patient Counseling Visit- Pharmacist Guide and the drug-specific Medication Info Sheet |
| **First call-back – Within first week:** | Identify any initial problems with understanding or adherence  
Use the First Follow-Up Call/Visit- Pharmacist Guide and the Medication Info Sheet (if needed)  
Reinforce initial key messages  
- 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 |
| **Second call-back – After 2-3 weeks: (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 (PROBE for evidence of seizures; skin rashes or darkening; back pain or joint pain; irregular heartbeats; mouth sores or dry mouth)  
Use the Continuing Follow-Up Calls/Visits- Pharmacist Guide  
- If any identified, contact oncologist or oncology nurse, and consider the information below under Adverse Effects  
Reinforce initial 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(every 1-3 months)  
Use the Continuing Follow-Up Calls/Visits- Pharmacist Guide  
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:

- Signs of allergic reaction (hives, trouble breathing, swollen face, lips, tongue, or throat).
- Symptoms of liver toxicity (weight gain, stomach swelling or tenderness, jaundice).
- Respiratory symptoms (shortness of breath, coughing up blood).
- Fast, slow, or uneven heart rate - Cardiac tamponade.
- Symptoms of pulmonary fibrosis (weak pulse, confusion, fainting, seizure; or persistent cough, congestion, low fever, shortness of breath; may occur several months/years after taking Busulfan).
- Seizure.

The following are some adverse effects from Busulfan.

<table>
<thead>
<tr>
<th>More Common</th>
<th>Less Common</th>
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</thead>
<tbody>
<tr>
<td><strong>Hematologic disorders</strong></td>
<td><strong>Cardiovascular disorders</strong></td>
</tr>
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<td>• Myelosuppression (anemia, leukopenia, thrombocytopenia)</td>
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<td><strong>Cardiovascular disorders</strong></td>
<td><strong>Endocrine &amp; Metabolic disorders</strong></td>
</tr>
<tr>
<td>• Cardiac tamponade</td>
<td>• Hyperbilirubinemia, hyperuricemia, hyperuricosuria</td>
</tr>
<tr>
<td><strong>CNS disorders</strong></td>
<td><strong>Gastrointestinal disorders</strong></td>
</tr>
<tr>
<td>• Seizures</td>
<td>• Clinical syndrome similar to adrenal insufficiency</td>
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<td><strong>Gastrointestinal disorders</strong></td>
<td><strong>Hepatic disorders</strong></td>
</tr>
<tr>
<td>• Dry mouth, mucositis</td>
<td>• Cholestatic jaundice; hepatic veno-occlusive disease</td>
</tr>
<tr>
<td><strong>Gynecologic disorders</strong></td>
<td><strong>Musculoskeletal disorders</strong></td>
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<td><strong>Ophthalmologic disorders</strong></td>
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<td><strong>Respiratory disorders</strong></td>
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<tr>
<td>• Back pain; arthralgia</td>
<td>• Interstitial pulmonary fibrosis; pneumonia</td>
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<td><strong>Ophthalmologic disorders</strong></td>
<td><strong>Skin disorders</strong></td>
</tr>
<tr>
<td>• Cataract, corneal thinning, lens changes</td>
<td>• Hyperpigmentation of skin</td>
</tr>
<tr>
<td><strong>Respiratory disorders</strong></td>
<td>• Very dry and fragile skin</td>
</tr>
<tr>
<td>• Interstitial pulmonary fibrosis; pneumonia</td>
<td>• Rash, urticaria</td>
</tr>
</tbody>
</table>

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).

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DRUG INTERACTIONS

Busulfan is metabolized by CYP3A4.

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

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

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.

<table>
<thead>
<tr>
<th>Online Programs for Drug Interaction Checking</th>
<th>Other Interaction Checkers - Subscription required</th>
</tr>
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<tbody>
<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://online.epocrates.com/">http://online.epocrates.com/</a> (free account required)</td>
<td></td>
</tr>
</tbody>
</table>

Some common interactions with Busulfan are:

- Acetaminophen: may increase the serum concentration of Busulfan
- Antifungal agents (Azole derivatives, systemic- e.g. Metronidazole): may decrease metabolism of Busulfan
- CloZAPine: may increase toxicity of Clozapine (**avoid combination**)
- CYP3A4 Inducers: may increase metabolism of Busulfan and thus lower serum concentration of Busulfan
- CYP3A4 Inhibitors: may decrease metabolism of Busulfan and thus increase serum concentration of Busulfan
- Dabrafenib, Dasatinib, Deferasirox, Denosumab, Trastuzumab?
- Echinacea: may decrease the therapeutic effect of Busulfan
- Leflunomide: may increase toxicity of Leflunomide, especially the risk of hematologic toxicity. Consider not using a Leflunomide loading dose and monitor for bone marrow suppression if given concurrently
- Phenytoin, Fosphenytoin: may decrease the serum concentration of Busulfan
- Tacrolimus (topical): may increase toxicity of Busulfan (**avoid combination**)
- Vaccines (live and inactivated): Busulfan 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 Busulfan may increase GI irritation and should be avoided. St John’s wort should not be taken while taking Busulfan.*