PROCARBAZINE

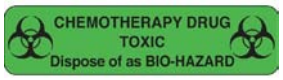
INSTRUCTIONS FOR THE PHARMACIST

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
  - Measure the patient's height (cm) and weight (Kg), then recalculate body surface area (BSA)
- 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** section (page 4), and consider an online drug interactions checking program.
- Check with patient for any other medications filled at a different pharmacy

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 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

Procarbazine is clinically indicated for:

- Hodgkin's disease, Non-Hodgkin's lymphoma
- Brain cancers- glioma, oligodendroglioma, CNS Lymphoma

DRUG ADMINISTRATION

- Procarbazine capsules may be given ***once daily*** for several days (usually between 7 and 28 days), alone or as part of a combined chemotherapy regimen- usually each dose is multiple capsules
- Avoid food/beverages that contain tyramine (aged cheese, air-dried or cured meats such as sausages and salamis, tap/draft beers, soy sauce, etc.). See Medication Info Sheet for a list of dietary restrictions.
- Do not crush capsules.
- Keep capsules out of reach of children and protect from light.
- 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) • 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 or second week: 	• Identify any initial problems with understanding, adherence, or adverse effects (**PROBE** for evidence of any adverse effect listed below) • 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.
Second call-back – After 2-3 weeks: (telephone or return visit to Pharmacy)	• Remind patient to continue taking pills on a regular basis, and to stop taking pills at end of prescribed cycle (variable for each regimen) • At end of treatment, ask if there are any pills left over; if so, PROBE to determine any barriers to treatment adherence. • Use the **Continuing Follow-Up Calls/Visits- Pharmacist Guide❶** • 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 • 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↗:

- Signs of allergic reaction (hives, trouble breathing, swollen face, lips, tongue, or throat.
- Watery diarrhea
- Confusion, hallucinations, problems with vision or speech, trouble walking or doing daily activities
- Feeling unsteady, loss of coordination or balance
- Tremors, seizures
- Cough, chest pain, trouble breathing
- Signs of infection (fever, chills, body aches, flu symptoms)

The following are some adverse effects from Procarbazine.

<u>Cardiovascular disorders</u> • Edema♦, flushing♦, hypotension♦ • Syncope↗, tachycardia↗ <u>CNS disorders</u> • Coma↗, confusion↗, hallucination↗ • Depression, dizziness, fatigue, fever • Headache✶, general pain✶ • Insomnia✶, lethargy✶, nervousness • Apprehension, ataxia, chills • Nightmares, seizures↗, slurred speech↗ <u>Dermatologic disorders</u> • Alopecia✶, dermatitis✶, hyperpigmentation, • Rash✶, itchy skin✶, red or purple spots on skin, hives✶ <u>Gastrointestinal disorders</u> • Abdominal pain✶, anorexia✶, constipation✶, diarrhea✶ • Trouble swallowing↗, vomiting blood↗ • Black, tarry stools or blood in stools† • Nausea and vomiting✶, stomatitis✶, dry mouth✶ <u>Genitourinary disorders</u> • Blood in urine♦, nocturia♦, polyuria♦ • Reproductive dysfunction♦	<u>Hematologic disorders</u> • Myelosuppression✶- neutropenia, thrombocytopenia, anemia <u>Hepatic disorders</u> • Hepatic dysfunction↗, jaundice♦ <u>Neuromuscular & Skeletal disorders</u> • Arthralgia✶, falling, foot drop, myalgia✶ • Paresthesia↗, decreased reflexes♦ • Muscle tremor ♦, unsteadiness♦, weakness <u>Ocular disorders</u> • Double vision♦, inability to focus vision♦ • Involuntary eye movement♦ • Swelling of optic disc♦ • Light intolerance♦, retinal hemorrhage♦ <u>Respiratory disorders</u> • Cough♦, nose bleed♦, coughing up blood✶ • Hoarseness, pleural effusion↗, pneumonitis↗ <u>General disorders</u> • Hearing loss† • Allergic reaction↗ • Excessive sweating♦ • Herpes, infection↗, secondary malignancies

✶ 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

Procarbazine inhibits Monoamine Oxidase. Foods and beverages containing tyramine should be avoided. Take a ***thorough medication history*** (call other pharmacies if necessary) and determine the potential for all other drugs to increase or decrease Procarbazine plasma concentration.

- Drug interactions are often missed by community pharmacy computer systems
- ***REPORT any potential interaction*** to the prescribing oncologist- either the Procarbazine 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. 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

NOTE: Patients taking Procarbazine should avoid drinking alcohol.

Supplements that contain caffeine, tyrosine, tryptophan, or phenylalanine may increase the risk of severe side effects and should be avoided. Echinacea should also be avoided.

Some common drug-drug interactions with Procarbazine are:

- Alpha-/Beta-Agonists (indirect-acting, ophthalmic): may increase hypertensive effect of alpha-/beta-agonists (*avoid combination*)
- Altretamine: may increase orthostatic hypotensive effect of Procarbazine
- Amphetamines: may increase hypertensive effect of amphetamines (*avoid combination*)
- Anilidopiperidine Opioids (e.g. Fentanyl, Sufentanil): may increase the serotonergic effect of Procarbazine. This could cause serotonin syndrome. Avoid use of Fentanyl (and others) when possible in patients who have used Procarbazine in the past 14 days. (*avoid combination*)
- Antidepressants (SSRIs, SNRIs, MAOIs, TCAs, Serotonin Modulators): may increase the toxicity of antidepressants or Procarbazine (*avoid combination*)
- Antihypertensives: may increase hypotensive effect of antihypertensives
- Antipsychotics: may increase serotonergic effect of Serotonin Modulators. This could cause serotonin syndrome (acute symptoms include- tachycardia, shivering, sweating, dilated pupils, myoclonus/overactive reflexes, hyperactive bowel, hypertension, and/or hyperthermia), which can be life-threatening.
- AtoMOXetine: may increase neurotoxic effect of Atomoxetine (*avoid combination*)
- Cardiac Glycosides: may decrease absorption of cardiac glycosides (may only affect Digoxin tablets; does not affect Digitoxin)
- CloZAPine: Capecitabine may increase the toxicity of Clozapine (specifically, agranulocytosis). (*avoid combination*)
- CNS depressants (eg, narcotics, analgesics, alcohol, antiemetics, benzodiazepines, sedatives, tranquilizers): concurrent use may potentiate CNS effects
- COMT (catechol-O-methyl transferase) inhibitors (e.g. entacapone, tolcapone): may increase toxicity of Procarbazine (*avoid combination*)

- Cyclobenzaprine: may increase serotonergic effect of Procarbazine and could cause serotonin syndrome (*avoid combination*)
- Dexmethylphenidate: may increase hypertensive effect of Dexmethylphenidate (*avoid combination*)
- Dextromethorphan: may increase serotonergic effect of Dextromethorphan and could cause serotonin syndrome (*avoid combination*)
- Digoxin: may result in a decrease in digoxin plasma levels, even several days after stopping Procarbazine
- Domperidone: may increase toxicity and decrease therapeutic effect of Domperidone. Domparidone may decrease therapeutic effect of Procarbazine.
- Doxapram: may increase hypertensive effect of Doxapram
- Doxylamine: may increase anticholinergic effect of Doxylamine. The manufacturer of Diclegis lists is use in combination with MAOIs as contraindicated.
- Echinacea: may decrease the therapeutic effect of Capecitabine
- EPINEPHrine (Nasal, systemic, oral inhalation): may increase hypertensive effect of Epinephrine
- Hydromorphone: may increase toxicity of Hydromorphone (*avoid combination*)
- Hypoglycemic agents: may increase hypoglycemic effect of hypoglycemic agents
- Leflunomide: may increase toxicity of Leflunomide (specifically, the risk of hematologic toxicity). Consider not using a leflunomide loading dose in patients receiving Procarbazine. Monitor patient for bone marrow suppression at least monthly if using these drugs concurrently.
- Levodopa: may increase toxicity of Procarbazine. Of particular concern are the hypertensive reactions when levodopa is used with a non-selective MAOI.
- Linezolid: may increase toxicity of Linezolid (*avoid combination*)
- Lithium: may increase toxicity of Lithium (*avoid combination*)
- MAOIs: may increase orthostatic hypotensive effect of Procarbazine (*avoid combination*). If MAO inhibitor therapy is required, use naratriptan, eletriptan, or frovatriptan.
- Methadone: may increase toxicity of methadone. Initial safety testing giving small incremental doses of methadone while the patient is closely monitored is recommended if methadone is to be used with (or within 14 days of) Procarbazine. Avoid transdermal selegiline.
- Methotrexate: may increase methotrexate-induced nephrotoxicity
- Methyldopa: may increase the toxicity of Methyldopa
- Methylene blue: may increase serotonergic effect of Methylene blue (*avoid combination*)
- Methylphenidate: may increase hypertensive effect of Methylphenidate (*avoid combination*)
- Metoclopramide: may increase toxicity of metoclopramide
- Mirtazapine: may increase neurotoxic effect of Mirtazapine (*avoid combination*)
- Norepinephrine: may increase hypertensive effect of Norepinephrine.
- OxyCODONE: may increase toxicity of Oxycodone.
- Oxymorphone: may increase toxicity of Procarbazine
- Serotonin 5-HT1D Receptor Agonists (e.g. sumatriptan): may decrease metabolism of Serotonin 5-HT1D Receptor Agonists. (*avoid combination*)
- Tacrolimus (topical): may increase the toxicity of Capecitabine (*avoid combination*)
- Tetrahydrozoline (Nasal): may increase hypertensive effect of tetrahydrozoline (nasal). *Avoid combination*.
- TraMADol: may increase neuroexcitatory and/or seizure-potentiating effect and serotonergic effect of Procarbazine

- Tricyclic antidepressants: Severe toxic and fatal reactions including excitability, fluctuations in BP, convulsions, and coma may occur.
- Tryptophan: may increase neutropenic effect of Procarbazine
- 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