



TRETINOIN

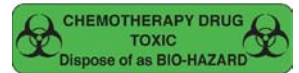
INSTRUCTIONS FOR THE PHARMACIST

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.
- It is strongly recommended that this medication be dispensed in pill packs prepackaged for this drug alone. Adherence is very important and toxicities from double dosing may be serious.
- 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.

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 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 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 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

Tretinoin is clinically indicated for:



- Leukemia, acute promyelocytic

DRUG ADMINISTRATION

- Tretinoin may be given **twice daily**, with a meal.
- Capsules should be swallowed whole with a glass of water.
- Keep capsules in blister pack until time of ingestion.
- Keep capsules out of reach of children and protect from light.
- 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.

	Key Messages
<p>Initial counselling- At time of dispensing</p>	<ul style="list-style-type: none"> • 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 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>End of Treatment call-back – (telephone or return visit to Pharmacy)</p> 	<ul style="list-style-type: none"> • 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 retinoic acid syndrome, or any symptoms listed below) • Use the Continuing Follow-Up Calls/Visits- Pharmacist Guide ❶ <ul style="list-style-type: none"> ○ If any identified, contact oncologist or oncology nurse, and consider the information below under Adverse Effects • Reinforce initial key messages
<p>Subsequent cycles- (at least one call during each cycle):</p>	<ul style="list-style-type: none"> • 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 Guide ❶ • 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 ✓

Patients are generally followed closely during the first weeks of treatment, to watch for symptoms of APL Retinoic Acid Syndrome. If Tretinoin is given concurrent with injectable chemotherapy, patients will be seen on a regular basis by the hematologist. If you identify any of the following once the patient is at home, 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:

- APL Retinoic Acid Syndrome (fever, dyspnea, short of breath, respiratory distress, hyperleukocytosis, hypotension, pleural effusions, multi-organ failure- occurs within first few days of treatment- patients usually admitted to hospital)
- Fever, breathing problems, weight gain, swelling of hands and feet
- Sudden and severe pain behind your eyes with nausea, vomiting, and vision problems

The following are the common adverse effects from Tretinoin.

<p>More Common</p> <p><u>APL Retinoic Acid Syndrome</u>★</p> <p>fever, dyspnea, short of breath, respiratory distress, hyperleukocytosis, hypotension, pleural effusions, multi-organ failure</p>	<p>Less Common</p> <p><u>Bleeding disorders</u></p> <ul style="list-style-type: none"> • Thrombosis ✓ (risk during first month of treatment)- cerebrovascular accident, myocardial infarctions • Disseminated intravascular coagulation (DIC) ♦, nosebleed♦ <p><u>Cardiovascular disorders</u></p> <ul style="list-style-type: none"> • Enlarged heart, heart murmur, heart failure (rare) ✓ <p><u>CNS disorders</u>♦</p> <ul style="list-style-type: none"> • Dizziness, confusion, light headed feeling, flank pain, • Numbness of extremities, hyporeflexia, paresthesia <p><u>Dermatologic disorders</u></p> <ul style="list-style-type: none"> • Dermal bleeding♦, pruritus★, photosensitivity reaction♦ • Increased sweating★, alopecia★ • Dry scalp†, nasal dryness♦ <p><u>Genitourinary disorders</u></p> <ul style="list-style-type: none"> • Dysuria♦, frequent urination♦, cystitis♦, kidney failure♦ <p><u>EENT</u></p> <ul style="list-style-type: none"> • Blurred vision♦, visual disturbance♦, photophobia♦, conjunctivitis♦, changes in visual acuity♦ • Ear fullness♦, earache♦, ear buzzing♦ <p><u>Respiratory disorders</u></p> <ul style="list-style-type: none"> • Dyspnea★, coughing♦ • Pleural effusion♦, pulmonary infiltration♦ <p><u>General disorders</u></p> <ul style="list-style-type: none"> • Headache★, fever★, fatigue★ • Back pain★, chest pain★ • Intracranial hypertension/pseudotumor cerebri ✓
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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 (see instructions above)

DRUG INTERACTIONS

Tretinoin is metabolized by CYP2C8. Tretinoin is also a weak substrate of CYP2A6, CYP2B6, CYP2C9. Tretinoin is a weak inhibitor of CYP2C9 and a weak/moderate inducer of CYP2E1.

- Take a **thorough medication history** (call other pharmacies if necessary) and determine the potential for all other drugs to increase or decrease Tretinoin plasma concentration.
- Drug interactions are often missed by community pharmacy computer systems
- **REPORT any potential interaction** to the prescribing oncologist- either the Tretinoin 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:

- 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

Some common interactions with Tretinoin are:

- Antifibrinolytic agents: may increase thrombogenic effect
- Contraceptives (Estrogens, Progestins): may decrease therapeutic effect/serum concentration of these contraceptives. Two forms of effective contraception are recommended in females of child-bearing potential during Tretinoin therapy. Particularly, microdosed progesterone-only preparations may be inadequately effective.
- CYP2C8 inducers: may decrease metabolism of Tretinoin
- CYP2C8 inhibitors: may decrease metabolism of Tretinoin
- Echinacea: may decrease the therapeutic effect of Tretinoin
- Leflunomide: may increase toxicity of Leflunomide (specifically, the risk of hematologic toxicity). Consider not using a leflunomide loading dose in patients receiving Tretinoin. Monitor patient for bone marrow suppression at least monthly if using these drugs concurrently.
- Multivitamins/Fluoride/Minerals (with ADEK, Folate, Iron): may increase toxicity of Tretinoin (*avoid combination*)
- Tacrolimus (topical): may increase the toxicity of Tretinoin (*avoid combination*)
- Tetracycline derivatives: may increase toxicity of Tretinoin. The development of pseudotumor cerebri is especially concerning. (*Avoid combination*)
- Vaccines (inactivated, live): may increase toxicity and decrease therapeutic effect of vaccines (*avoid combination*)

Note: Drinking alcohol while taking Tretinoin may increase CNS depression. Caution patients about effects and monitor for increased effects when patients drink alcohol while taking this medication.

The patient should avoid taking dong quai, St John's wort, and additional Vitamin A supplementation.