

PART III: CONSUMER INFORMATION

PrTOCTINO (alitretinoin) Soft Capsules

This leaflet is part III of a three-part "Product Monograph" published when TOCTINO was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about TOCTINO. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

TOCTINO is used for adults with severe chronic hand eczema that has not improved after topical treatments, including steroids.

TOCTINO capsules are not to be given to children or adolescents less than 18 years old.

TOCTINO should be used under the care of a doctor who is knowledgeable in the use of systemic retinoids.

What it does:

The active substance in TOCTINO is alitretinoin. It belongs to a group of medicines known as retinoids which are related to vitamin A. Alitretinoin is believed to modify the immune system and have an anti-inflammatory effect on the eczematous lesions by reducing the production of some substances responsible for inflammation, thereby reducing and helping to clear eczema.

When it should not be used:

Do not use TOCTINO if you:

- are pregnant or if you can become pregnant and are not using two effective birth control measures
- are breast feeding
- have liver disease
- have severe kidney disease
- have high blood cholesterol or raised triglycerides
- have uncontrolled thyroid disease
- have very high levels of vitamin A in your body (*hypervitaminosis A*)
- are allergic (*hypersensitive*) to alitretinoin or to other retinoids (such as isotretinoin), soya, peanuts, or any of the other ingredients of TOCTINO (other nonmedicinal ingredients are listed below).
- are taking tetracycline (a type of *antibiotic*)
- have a hereditary problem of fructose intolerance, as this product contains sorbitol

If any of these apply to you, **go back to your doctor without taking TOCTINO.**

What the medicinal ingredient is:

alitretinoin

What the important nonmedicinal ingredients are:

DL- α -tocopherol, Gelatin, Glycerol, Medium chain triglycerides, Partially hydrogenated soybean oil, Sorbitol, Soybean oil, Water, Yellow wax, iron oxide red, iron oxide black (10 mg capsules only), iron oxide yellow (30 mg capsules only).

What dosage forms it comes in:

Soft capsule, 10 mg (brown) and 30 mg (red-brown).

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

All Women: Birth defects:

TOCTINO can cause birth defects (deformed babies). It can also cause miscarriage, premature birth, or death of the baby. Therefore, adequate birth control measures are essential when taking TOCTINO. See "What are the important warnings for women taking TOCTINO?"

Treatment with systemic retinoids, including alitretinoin, may cause increased pressure in the brain, with symptoms such as headache, nausea, vomiting and visual disturbances.

For other serious side effects of TOCTINO, see "SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM" Table below.

What are the important warnings for women taking TOCTINO?

- Do not take TOCTINO if you are pregnant
- If you become pregnant, stop taking TOCTINO and contact your doctor immediately
- TOCTINO can cause deformed babies. There is an extremely high risk that your baby will be deformed if you are pregnant while taking TOCTINO. This risk exists even if TOCTINO is taken for a short time. If you are a woman of childbearing potential, your physician should have discussed this risk with you, and explained how to avoid becoming pregnant while taking TOCTINO.
- You must avoid becoming pregnant while you are taking TOCTINO and for at least one month after you stop taking TOCTINO.
- You must discuss effective birth control with your doctor before beginning TOCTINO treatment, and you must use effective birth control:
 - For at least one month before you start TOCTINO;
 - While you are taking TOCTINO; and
 - For at least one month after you stop taking TOCTINO;

Bearing in mind that any method of birth control can fail.
- You must use two effective and complementary methods of birth control at the same time, even if you have a history of infertility or are not sexually active.

- Microdosed progesterone preparations (minipills) are not a suitable method of contraception during TOCTINO therapy.
- Do not take TOCTINO until you are sure that you are not pregnant.
- You must have two negative pregnancy tests at least 3 weeks apart before you start TOCTINO. Take pregnancy tests at doctor's visits on a monthly basis while on the drug and take a pregnancy test at a doctor's visit one month after stopping treatment with TOCTINO. If your menstrual period is abnormal in length and intensity, tell your doctor. You must wait until the second or third day of your next normal menstrual period before you start TOCTINO.
- Your doctor can write a prescription for no more than 30 days of treatment. A new prescription is needed for more treatment. Each new prescription must be started within 11 days from the last negative pregnancy test.
- Stop taking TOCTINO and contact your doctor immediately if you do become pregnant while taking TOCTINO or during the first month after treatment has stopped, if you miss your period, or if you have sexual intercourse without using effective birth control. You should discuss with your doctor the serious risk of your baby having severe birth deformities because you are taking or have taken TOCTINO. You should also discuss the desirability of continuing with your pregnancy.
- Do not breastfeed while taking TOCTINO.
- Do not take the supplement St John's Wort (*Hypericum perforatum*) if you are taking an oral contraceptive. St. John's Wort (*Hypericum perforatum*) can interact with oral contraceptives and may decrease their effectiveness in preventing pregnancy.

You should have been counseled using the manufacturer's Patient Information and Pregnancy Prevention Program which includes:

- Comprehensive information about the risks of this drug
- A checklist of criteria you had to meet before receiving this drug
- Detailed information on birth control options
- An acknowledgement form for you to review and sign

Advice for men taking TOCTINO

Very low amounts of alitretinoin are present in the semen of men taking TOCTINO, but too little to harm the unborn baby of your partner.

All patients should read the rest of this Consumer Information.

Do not take TOCTINO unless you completely understand its possible risks and are willing to follow all of the instructions in this Consumer Information.

BEFORE you use TOCTINO tell your doctor or pharmacist if:

- you have ever had any mental health problems, including depression, suicidal behaviour or psychosis, or if you take medicines for any of these conditions.
- you have high blood cholesterol or triglycerides or have a blood lipid (fats) disorder, risk of heart problems or are obese, you may need blood tests more often. If your blood cholesterol or triglycerides stay high, your doctor may lower your dose, or take you off TOCTINO.
- you have been suffering from thyroid disease. TOCTINO may lower your thyroid hormone levels. If your thyroid hormone level is low, your doctor may prescribe supplements.
- you plan vigorous physical activity during treatment with TOCTINO.
- you have any food or drug allergies.
- you are taking any vitamin preparations or health food supplements that contain Vitamin A.
- what brand of contraceptives you are taking. There are certain types of contraceptives that should not be taken while on TOCTINO.
- you are taking an antibiotic (particularly tetracyclines).
- you have liver disease, kidney disease or high lipid levels in your blood
- you have diabetes. TOCTINO may increase blood sugar levels. Your doctor may request periodic tests for blood sugar levels during treatment, particularly if you already have diabetes or are overweight.

While taking TOCTINO:

- **Do not donate blood** while you take TOCTINO and for one month after stopping TOCTINO. If someone who is pregnant gets your donated blood, her baby may be exposed to TOCTINO and may be born with birth defects.
- **Do not share TOCTINO with other people.** It can cause birth defects and other serious health problems.
- **Minimise your exposure to sunlight** and avoid exposure to sun lamps. Your skin may become more sensitive to sunlight. Before you go out in the sun, use a sun protection product with a high protection factor (SPF 15 or higher).
- **Cut down on intensive physical activity:** TOCTINO can cause muscle and joint pain.
- **If you develop dry eyes,** contact your doctor as soon as possible. This can be helped by the application of a lubricating eye ointment or tear replacement drops. If you wear contact lenses and experience dry eyes you may need to wear glasses for the duration of TOCTINO treatment. Dry eyes and sight problems normally return to normal once treatment is stopped
- **If you experience any problems with your sight, tell your doctor immediately.** You should not drive or operate machinery. TOCTINO may need to be stopped and your sight monitored.
- **If you get a persistent headache,** nausea or vomiting (feeling or being sick) and blurred vision, these may be

signs of a condition called benign intracranial hypertension. **Stop taking TOCTINO immediately** and contact your doctor as soon as possible.

- **If you have bloody diarrhea, severe diarrhea, abdominal pain or rectal bleeding, stop taking TOCTINO immediately** and contact your doctor as soon as possible.
- TOCTINO may change your liver enzyme levels, cholesterol or triglyceride levels, blood sugar levels or thyroid function. Your doctor will test these during treatment.
- If you have a rash, swelling of your face or mouth, difficulty breathing, or feel unwell, you may be allergic to the ingredients in TOCTINO. Contact your doctor immediately.
- If your mood changes, you feel sad, angry, or notice other emotional problems, contact your doctor immediately.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist about all the medicines you take or have taken recently, including non-prescription or herbal medicines.

Tell your doctor or pharmacist if:

- you are taking ketoconazole, fluconazole, or miconazole (medicines used to treat fungal infections). Your doctor may decide to adjust your dose of TOCTINO.
- you are taking gemfibrozil (a medicine which is used to lower cholesterol), diosmin (used to treat hemorrhoids) or oxandrolone (an anabolic steroid). Your doctor may decide to adjust your dose of TOCTINO
- you are taking St John’s Wort (a herb extract used to treat depression), protease inhibitors (used to treat HIV or hepatitis C) or any medicines for epilepsy or seizures. These may reduce how well the contraceptive pill works.
- you are taking methotrexate, which can increase the risk of liver toxicity when taken with retinoids (such as TOCTINO).

Don’t take TOCTINO with these medicines:

- vitamin A supplements or tetracyclines (a type of antibiotic). This increases the risk of side effects.
- other retinoid medicines, such as isotretinoin or tazarotene

TOCTINO is not recommended with amiodarone (a medicine that helps to regulate heart rate).

TOCTINO can also affect how some other medicines work. These include:

- paclitaxel (used to treat cancer),
- rosiglitazone or repaglinide (used to treat diabetes).

Tell your doctor if you are taking any of these.

What brand of oral contraceptives (“birth control pill”) are you taking? There are certain types of contraceptives that should not be taken while on TOCTINO, such as the low-dose, progesterone only “mini-pill”. These may not work while you are

taking TOCTINO. Please talk to your doctor about what would be the most effective type of contraceptive while you are taking TOCTINO.

PROPER USE OF THIS MEDICATION

Usual Adult Dose:

- Read your prescription label carefully and be sure to take the exact amount of medicine prescribed by your doctor, usually either 10mg or 30mg once a day. Your doctor may change your prescribed dose from time to time, therefore, it is important that you check the label each time you fill your TOCTINO prescription. If you have any questions, call your doctor.
- Swallow each capsule whole and don’t chew them.
- It is important to take TOCTINO with a main meal, preferably at the same time each day. Be sure to return to your doctor as scheduled. It is important for your doctor to see you regularly, (every month for women of child bearing potential), when you are taking TOCTINO. Discuss your progress and any concerns with your doctor.
- A course of treatment usually lasts for 12 to 24 weeks depending on your disease. If your first treatment was successful, your doctor may prescribe another course of treatment if symptoms return.

Overdose:

In cases of overdose or suspected overdose, contact a healthcare practitioner (or doctor), hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

If you are a woman and have taken an overdose of TOCTINO, ask your doctor to test if you are pregnant. If *you* find out you are pregnant, stop taking TOCTINO and contact your doctor immediately.

Missed Dose:

If you forget to take a dose of TOCTINO it may be taken later the same day, but do not take more TOCTINO in one day than your doctor has prescribed. Do not double dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, TOCTINO can cause side effects, although not everybody gets them.

- **Headache**
- **Raised blood fats:** higher levels of fats (triglycerides) and cholesterol in the blood
- **Blood cell disorders:** increase in the number of blood platelets (cells that help blood to clot), decrease in the number of red and white blood cells seen in blood tests
- **Thyroid problems:** decreased levels of thyroid hormones
- **Eye problems:** inflammation of the eye and eyelid area (conjunctivitis); eyes feel dry and irritated. **Ask a pharmacist**

for suitable eye drops. If you wear contact lenses and get dry eyes, you may need to wear glasses instead.

- **Blood and circulation:** flushing, high blood pressure, inflammation of blood vessels, swelling of the hands, lower legs and feet
- **Muscle and joint pain:** back pain, muscle pain, joint pain. High levels of muscle breakdown products in your blood if you exercise vigorously.
- **Skin, nail and hair problems:** dryness of the skin, especially of the lips and face, inflamed skin, redness of the skin, itchy skin, skin peeling, rash, dry skin eczema, itchy skin rash, hair loss, increased sensitivity of the skin to sunlight, nail disorders, abnormal hair texture (e.g. curling of the hair)
- **Liver problems:** raised liver enzymes seen in blood tests
- **Sensory problems:** dizziness, persistent noise in the ears
- **General:** nausea, vomiting, dry mouth, lack of energy (fatigue)
- **Ear, nose and throat problems:** nose bleeding
- **Bone disorders:** extra growth of bone, including the spine disorder ankylosing spondylitis
- **Stomach problems:** indigestion
- **Vision:** blurred, distorted vision, difficulty seeing at night. If you suffer these problems, do not drive or operate machinery until these symptoms have passed. If vision problems persist, contact your doctor and your doctor may stop TOCTINO treatment and may refer you to an eye specialist.

Side effects of other medicines in the same family of medications as TOCTINO.

The following effects haven't yet been seen in TOCTINO but have occurred in this product class and may occur.

- **Diabetes**
Excessive thirst; frequent need to urinate; blood tests show an increase in your blood sugar.
- **Bone disorders**
Arthritis; bone disorders (delayed growth, changes to bone density); growing bones may stop growing.
- **Visual disorders**
Colour blindness and colour vision gets worse.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist right away	Stop taking drug and call your doctor or pharmacist right away
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Symptom / effect	Talk with your doctor or pharmacist right away	Stop taking drug and call your doctor or pharmacist right away
<p>Common</p> <p>Depression and other mental problems including sad or empty mood, mood changes, tearfulness, and emotional disorder.</p> <p>Some people have had thoughts about harming themselves or ending their lives, have attempted suicide or committed suicide. These people may not appear to be depressed. Your doctor can arrange help.</p> <p>You should tell a family member or close friend that you can become depressed, or have significant changes in mood or behaviour, and ask them to read this leaflet. You might ask them to look after you.</p>	✓	
<p>Uncommon</p> <p>Sight problems including blurred vision, distorted vision, cloudy surface on the eye (corneal opacity, cataracts).</p>		✓
<p>Rare</p> <p>Severe allergic reaction including swelling of the face or mouth causing difficulty in breathing (angioedema), raised and itchy rash (hives).</p> <p>Immune reaction including vasculitis (swelling of the blood vessel) with symptom such as bruises and red patches.</p>		✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist right away	Stop taking drug and call your doctor or pharmacist right away
Rare	<p>Benign Intracranial Hypertension</p> <p>Lasting headache along with feeling sick (nausea), being sick (vomiting), and changes in your eyesight including blurred vision.</p>		✓
Very rare	<p>Stomach disorders</p> <p>Severe abdominal (tummy) pain, with or without bloody diarrhea, feeling sick (nausea) and being sick (vomiting). These can be signs of serious abdominal conditions.</p>		✓
Unknown	<p>Keratitis (inflamed cornea).</p>		✓
	<p>Pancreatitis (inflammation of the pancreas) which can be fatal, with symptoms such as abdominal pain, nausea, vomiting, diarrhea and fatty stool.</p>		✓

This is not a complete list of side effects. For any unexpected effects while taking TOCTINO, contact your doctor or pharmacist.

HOW TO STORE IT

- **Keep out of the sight and reach of children**
- TOCTINO blister strips should be stored in its cardboard package at 15-30°C and protected from sunlight and heat
- Return any unused capsules to your pharmacist at the end of treatment

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document, along with the full product monograph, (prepared for health professionals) and the TOCTINO Patient Information and Pregnancy Prevention Program materials can be found at: www.toctino.ca or can be obtained by contacting the sponsor, GlaxoSmithKline Inc. 7333 Mississauga Road Mississauga, Ontario L5N 6L4 1-800-387-7374

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