



Dear Healthcare Professional,

Toctino® (alitretinoin): Important Information on the Pregnancy Prevention Program

Toctino (alitretinoin oral, 10 mg or 30 mg) is indicated for use in adults who have severe chronic hand eczema, unresponsive to treatment with potent topical corticosteroids.

Like other retinoids, Toctino is a teratogen. Treatment with Toctino during pregnancy is contraindicated and special precautions must be taken when treating women of childbearing potential. Stringent contraception measures must be followed while patients are on Toctino therapy and for one month after stopping treatment. No special contraception requirement is indicated for male patients taking Toctino. Please review the attached Summary of Product Characteristics (SmPC) and the 'Checklist for Prescribing to Female Patients', detailing actions required for prescribing Toctino.

A Pregnancy Prevention Program (PPP) has been developed to assist you in fulfilling the requirements for Toctino treatment. It is important to note that Toctino is strictly contraindicated in women of childbearing potential unless all the requirements of the PPP are fulfilled. The PPP is supported by the following documents:

- 'Guidance for Doctors and Pharmacists'
- 'Patient Information Brochure'
- 'Information About Contraception'
- 'Checklist for Prescribing to Female Patients'
- 'Acknowledgement Form for Female Patients'

These documents should enhance the awareness and understanding of the teratogenic risks associated with the use of Toctino.

When prescribing Toctino, consider the following:

- The patient has to be informed and fully understand the term teratogenicity and the potential risks of using the product during pregnancy
- The patient must sign the 'Acknowledgement Form for Female Patients', or similar patient information/consent form that contains warnings about the risk of potential birth defects if the foetus is exposed to alitretinoin
- Check the patient understands the requirement to use effective contraception for one month before starting treatment, during treatment and for one month after stopping treatment with Toctino, using at least one and preferably two effective methods of contraception
- The need to conduct pregnancy testing before, and during the treatment as determined according to local practice and 5 weeks following the end of treatment with Toctino
- Mandatory reporting of all pregnancy cases to the applicable Health Authorities and to Neopharm Israel

In addition there are controls on the distribution of Toctino:

- Prescriptions for female patients prescribed under the PPP must be limited to 30 days of treatment
- Prescriptions are only valid for 7 days

Further copies of the materials contained in this pack are available and can be reordered from Neopharm's Medical Affairs Department 1-800-250-255. We will continue to inform you of important developments and changes. If you have any questions about Toctino, please contact Neopharm Medical Dept. Tel: 1-800-250-255

PRESCRIBING INFORMATION: TOCTINO® (ALITRETINOIN) 10mg OR 30mg CAPSULES. Before prescribing Toctino please refer to the full Summary of Product Characteristics. **Name of the medicinal product:** Toctino (alitretinoin) 10mg or 30mg Capsules. **Non proprietary name:** Alitretinoin. **Presentation:** Soft capsules containing 10mg or 30mg of alitretinoin. **Indication:** TOCTINO is indicated for use in adults who have severe chronic hand eczema that is unresponsive to treatment with potent topical corticosteroids. Patients in whom the eczema has predominantly hyperkeratotic features are more likely to respond to treatment than in those in whom the eczema predominantly presents as pompholyx. **Dosage and administration:** Toctino should only be prescribed by dermatologists or physicians with experience in the use of systemic retinoid therapy. The recommended dose range is 10-30mg once daily, to be taken orally with a meal. The recommended starting dose is 30mg once daily. A dose reduction to 10mg once daily may be considered in patients with unacceptable adverse reactions to the higher dose. "High risk" patients with diabetes, obesity, cardiovascular risk factors or lipid metabolism disorders should be initiated on 10mg once daily and titrated up to 30mg once daily if necessary. A treatment course can be given for 12 to 24 weeks depending on response. In the event of relapse, patients may benefit from further treatment courses. Prescriptions for women of childbearing potential should be limited to 30 days and dispensed within 7 days of the prescription in accordance with the Pregnancy Prevention Program.

Contraindications:

Pregnancy is an absolute contraindication to treatment with Toctino. Use during pregnancy or in women of childbearing potential is contraindicated unless all conditions of Pregnancy Prevention Program are met. If pregnancy does occur in spite of the pregnancy prevention precautions during treatment with Toctino or in the month following discontinuation of therapy, there is a high risk of very severe and serious malformation of the foetus. Please refer to the Toctino Summary of Product Characteristics for further details.

If pregnancy occurs, Toctino should be stopped immediately and the patient referred to a physician specialising or experienced in teratology for advice. Toctino is contraindicated during breastfeeding.

Toctino is contraindicated in patients with hepatic insufficiency, severe renal insufficiency, uncontrolled hypercholesterolaemia, hypertriglyceridaemia, hypothyroidism, hypervitaminosis A, hypersensitivity to alitretinoin, other retinoids or excipients, allergy to peanut or soya, hereditary fructose intolerance and concomitant tetracycline treatment.

Precautions and warnings: Not recommended in patients under 18 years of age. Male fertility may be compromised. Patients should be reminded not to share medication or donate blood during therapy or for 1 month following therapy with Toctino. Psychiatric disorders have been seen with other retinoids, therefore particular care should be taken in patients with a history of depression. Patients should be observed for signs of depression and referred for appropriate treatment if necessary. Effects of UV light may be enhanced and patients should avoid excessive exposure to sunlight, unsupervised use of sun lamps and should use appropriate sun protection of at least SPF 15. Patients experiencing visual difficulties should be referred to an ophthalmologist and treatment discontinuation may be required. Decreased night vision has been reported and patients should be warned to be cautious when driving or operating machinery. Patients who develop signs and symptoms of benign intracranial hypertension including headache, nausea and vomiting, visual disturbances and papilloedema should discontinue treatment immediately. Serum cholesterol and triglycerides should be monitored. Treatment should be discontinued if hypertriglyceridaemia cannot be controlled at an acceptable level or if symptoms of pancreatitis occur. In "high risk" patients with diabetes, obesity, cardiovascular risk factors or lipid metabolism disorders, more frequent serum lipid checks may be necessary. Dose reduction or discontinuation should be considered in the event of persistent clinically relevant elevation of liver transaminases. If severe diarrhoea is observed, diagnosis of inflammatory bowel disease should be considered and treatment discontinued immediately. Severe allergic reactions necessitate interruption of therapy and careful monitoring.

Interactions: Concomitant use of St John's Wort may cause failure of combined hormonal contraceptives. Concomitant use of vitamin A or other retinoids may cause hypervitaminosis A. Concomitant use of tetracyclines may increase the risk of benign intracranial hypertension. **Common adverse effects: Very common (≥10%):** headache, hypertriglyceridaemia, hypercholesterolaemia, decreased HDL. **Common (≥1%; <10%):** anaemia, increased iron binding capacity, decreased monocytes, increased thrombocytes, decreased TSH, decreased free T4, conjunctivitis, dry eyes, eye irritation, flushing, increased liver transaminases, dry skin and lips, cheilitis, eczema, dermatitis, erythema, alopecia, arthralgia, myalgia, increased blood creatine phosphokinase. **Adverse effects: Uncommon (≥ 0.1%; <1%):** blurred vision, cataract, epistaxis, pruritus, rash, skin exfoliation, asteatotic eczema, exostosis, (hyperostosis), ankylosing spondylitis. **Rare (≥0.01; <0.1%):** benign intracranial hypertension, vasculitis. **Overdose:** reversible adverse effects consistent with retinoid toxicity, including severe headache, diarrhoea, facial flushing and hypertriglyceridaemia. **Storage instructions:** Store in original packaging and protect from light.

Registration number: TOCTINO 10 MG: 145-92-33163-00/TOCTINO 30 MG: 146-64-33164-00

Name and address of registration holder: Neopharm Scientific Ltd, P.O.Box 7063 Petach Tikva.

Date of approval of prescribing information: November 2011.

Please refer to the Toctino Summary of Product Characteristics for further details.

Adverse events should be reported to Neopharm to Tel: 1-800-250-255 or at drugsafety@neopharmgroup.com

