



Pregnancy
Prevention
Programme

Toctino[®] (alitretinoin)

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1. Guidance for doctors prescribing Toctino

Please read this guidance document carefully before discussing the possibility of treatment with Toctino with your patient. This document informs you about the contraceptive precautions which are essential in patients treated with Toctino. Additional comprehensive information regarding the prescription of Toctino and about possible adverse events is summarised in the Summary of Product Characteristics (SmPC), which has been provided to you. Please read and follow the guidance and monitoring instructions given in the SmPC.

1.1 Important facts

- Alitretinoin, the active ingredient of Toctino, is a retinoid. Retinoids are known to be highly teratogenic
- Treatment with Toctino during pregnancy and during breastfeeding is strictly contraindicated
- Patients must 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
- Pregnancy testing in patients wishing to take Toctino should be performed one month before treatment, monthly during treatment, and 5 weeks after stopping treatment. The dates and results of the pregnancy tests should be recorded in the 'Checklist for Prescribing to Female Patients'
- The 'Checklist for Prescribing to Female Patients' contains a checklist which should be completed for each female patient prior to prescribing Toctino. This checklist is then maintained throughout the treatment course

1.2 Teratogenic risk

Toctino is indicated for patients with severe chronic hand eczema that is unresponsive to treatment with potent topical corticosteroids. Foetal exposure to alitretinoin, even for short periods, presents a high risk of congenital malformations.

The following malformations have been observed with retinoids when taken during pregnancy:

- Defects of the central nervous system, e.g., hydrocephaly
- Cerebral malformations
- Microcephaly
- Defects of the face, e.g., depressed bridge of nose
- Cleft palate
- Deformed or absent ears
- Defective eye formation, e.g., microphthalmia
- Cardiovascular abnormalities
- Defects of thymus gland and parathyroid gland

Furthermore the risk of miscarriage is increased.

Toctino is therefore strictly contraindicated in women of childbearing potential, unless all conditions in the Pregnancy Prevention Programme are fulfilled.

2. The Pregnancy Prevention Programme

The Pregnancy Prevention Programme is intended to minimise the risks associated with the use of Toctino during pregnancy for you and your patients.

It 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.

There are also a number of requirements in relation to therapy management.

- Female patients prescribed Toctino under the PPP must have clinic appointments every 4 weeks throughout the treatment course
- Female patients are subject to medically supervised pregnancy tests before, during and 5 weeks after treatment has been completed
- Female patients of childbearing potential must commit to use at least one, preferably two methods of effective contraception

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

3. Informing patients

Treatment with Toctino is strictly contraindicated during pregnancy (see also contraindications in the Summary of Product Characteristics). In the event of pregnancies occurring despite all preventive measures, the high risk of serious foetal malformations must be considered.

Discuss in detail the requirements of pregnancy prevention and pregnancy testing and provide the patient with the 'Information About Contraception' brochure.

The role of the sexual partner in contraception should be stressed and the patient should be encouraged to share the information given in the 'Patient Information Brochure' with their partner.

Inform the patient about everything she should know concerning treatment with Toctino and the potential adverse events. Special attention should be given to the product's teratogenicity and the need for at least one and preferably two effective methods of contraception.

3.1 Pregnancy testing

Medically supervised pregnancy tests with a minimum sensitivity of 25mIU/ml have to be performed prior to treatment, during treatment and 5 weeks after treatment. Dates and results of the tests should be recorded in the table in the 'Checklist for Prescribing to Female Patients'.

As the prescribing doctor you should ensure there are arrangements in place for your patients to receive medically supervised pregnancy tests either within the clinic setting or from another source. These tests should be conducted on the clinic appointment day or in the 3 days prior to the patient's appointment.

Pregnancy testing does not have to be performed in cases of documented irreversible sterility or hysterectomy.

3.1.1 Pregnancy testing before starting treatment

1st pregnancy test: An initial medically supervised pregnancy test has to be performed and recorded during the first 3 days of the patient's menstrual cycle. This test should rule out a potential pregnancy prior to starting contraception. In case of irregular menstrual periods the test should be performed about 3 weeks after the patient last had unprotected sexual intercourse.

2nd pregnancy test: A second medically supervised pregnancy test should be performed after the patient has used effective contraception for at least one month. If this second test is also negative the patient can start taking Toctino.

3.1.2 Pregnancy testing during treatment

Medically supervised pregnancy tests should be performed for each of the patient's 4 weekly follow-up appointments. In the ideal situation pregnancy testing, prescription and the dispensing of Toctino should be done on the same day.

3.1.3 Pregnancy testing at the end of treatment

Final pregnancy test: Patients have to undergo a final pregnancy test 5 weeks after the end of treatment, in order to complete the monitoring process.

3.2 Contraceptive counselling

It is very important to help your patient in the selection of appropriate contraceptive methods, stressing that not all methods are suitable when taking Toctino and that at least one and preferably two effective methods of contraception should ideally be used.

Please read the 'Information About Contraception' brochure in order to be prepared for questions from your patients.

The patient may be referred to a family planning expert for contraceptive counselling.

Remind your patients to strictly follow all instructions. Contraception has to be used for one month before starting treatment, during treatment and for one month after stopping treatment. Since no contraceptive method is 100% effective, patients should be informed comprehensively about the available methods and about the need for at least one and preferably two effective methods of contraception. Primary and secondary contraceptive methods are described in the 'Information About Contraception' brochure.

Even when using contraception, patients can still become pregnant if the selected methods are not applied appropriately and consistently. The patient should be aware of their responsibility when taking Toctino. Please make sure that your patient understands and follows all the requirements of the Pregnancy Prevention Programme and obtain a written confirmation that they have understood the contraceptive measures required (see 'Acknowledgement Form for Female Patients').

3.3 Reporting requirements

If you become aware of a pregnancy during Toctino treatment, report it immediately to Basilea Pharmaceuticals Ltd and submit a report through the Yellow Card Scheme (www.yellowcard.gov.uk).

Basilea Pharmaceuticals Ltd, 14/16 Frederick Sanger Road, The Surrey Research Park, Guildford, Surrey, GU2 7YD, Tel 01483 790023.

4. Additional precautions

4.1 Female patients not at risk of pregnancy

It is important that female patients not considered to be at risk of pregnancy are warned of the teratogenic risks of Toctino. The importance of contraception should also be discussed with these patients as a woman not at risk of pregnancy at the start of Toctino therapy may have a change in circumstances. All women should sign the 'Acknowledgement Form for Female Patients' to confirm that they have been informed of the risks of teratogenicity with Toctino.

All female patients should receive both the 'Patient Information Brochure' and the 'Information About Contraception' brochure.

4.2 Male patients

Studies have shown small quantities of Toctino in semen. These levels are considered too low to harm the unborn baby of your female partner. Based on limited animal studies male fertility may be affected by treatment with Toctino.

Full patient information about the teratogenic risk of Toctino and the strict pregnancy prevention measures should be given to male patients.

4.3 All patients

Patients should be instructed never to give Toctino to another person and to return any unused capsules to their pharmacist at the end of treatment.

Patients should be instructed not to donate blood during treatment or within one month after stopping treatment, since the person to whom their blood will be transfused could be pregnant and this would place their unborn baby at risk of birth defects.

4.4 Failures resulting in pregnancies under treatment with retinoids

Experience with similar Pregnancy Prevention Programmes, in particular that of isotretinoin, indicate that the following issues led to failure of the applied Pregnancy Prevention Programme:

- 14% of patients reporting pregnancies during oral retinoid treatment were already pregnant at the time of prescription. Pregnancy tests had not been performed or the drug had been prescribed prior to the availability of the test result. **A negative pregnancy test must be available prior to starting with the selected contraception**
- 12% of patients became pregnant after starting treatment, but before their next menstrual cycle. **An additional pregnancy test has to be performed immediately prior to prescription**
- 64% of patients who became pregnant during treatment did so as a result of non-compliance with contraception. **Continuous contraceptive counselling on a monthly basis is of utmost importance to avoid pregnancies**

5. Dispensing requirements, Instructions to the pharmacist

Under the Pregnancy Prevention Programme the following dispensing restrictions apply to Toctino prescriptions:

1. Prescriptions of Toctino for women should be limited to 30 days of treatment and the prescription is only valid for 7 days.
 - Under the Pregnancy Prevention Programme prescriptions presented more than 7 days after the prescription date should be considered expired and the patient should be told to get a new prescription from their prescriber. For some female patients this may require a further negative pregnancy test
 - If a prescription for more than 30 days' treatment is received for a female patient, the prescriber should be contacted to confirm whether or not the patient is in the Pregnancy Prevention Programme. If the patient is not being treated under the Pregnancy Prevention Programme, Toctino must not be dispensed
 - If in doubt check with the prescriber
2. Prescriptions for male patients do not have a limit on the duration of treatment to be dispensed or restrictions on the period the prescription is considered valid.
3. Do not accept:
 - Telephone or computer-transmitted prescriptions for Toctino
 - Repeat prescriptions
 - Free sample distribution

Checklist for pharmacists

- Check that the female patient is on at least one and preferably two effective methods of contraception
- Check she has received the 'Patient Information Brochure' and the 'Information About Contraception' brochure

