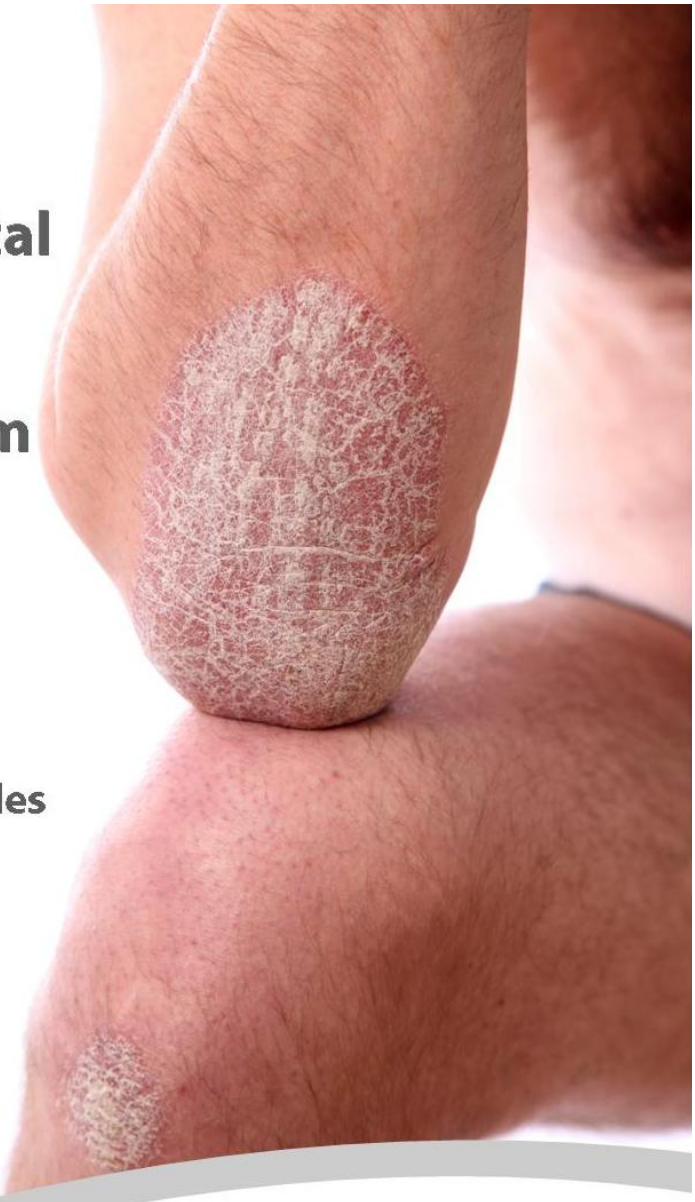
Pregnancy and Foetal Exposure Prevention Program



Neotigason®

Acitretin

10mg and 25mg hard capsules

actavis
think smart medicine

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Doctor Guide:

Neotigason® (Acitretin) 10 mg and 25 mg capsules
Pregnancy and Foetal Exposure Prevention

Introduction:
Neotigason® contains the active substance acitretin, which is a teratogenic derivative of retinoic acid. This brochure sets out a program for doctors to ensure safe use of Neotigason® in relation to pregnancy and foetal exposure. It describes measures for women of childbearing potential to avoid pregnancy and for other patient groups to decrease the risk of foetal exposure. It also contains checklists of topics which should be covered at specific clinic visits. For full prescribing information including details of undesirable effects, please refer to the currently approved Summary of Product Characteristics (SmPC) for Neotigason®.

- Acitretin is highly teratogenic. There is a very high risk that foetal exposure to acitretin will result in severe malformations (e.g. craniofacial defects, cardiac and vascular or CNS malformations, skeletal and thymic defects) and spontaneous abortions.
- There is a risk that acitretin (half-life approx. 50 hours) can be transformed to etretinate which is also teratogenic and has a very long half-life of approx. 120 days.
- There is a high risk of severe malformation of the foetus should women become pregnant during treatment, or within a 2 year period after cessation of treatment.
- Women of childbearing potential must not receive blood from patients being treated with acitretin. Therefore donation of blood by a patient being treated with acitretin is prohibited during and for two years after completion of treatment with acitretin.

Neotigason® must not be used by women who are pregnant. The same applies to women of childbearing potential unless strict contraception is practiced 4 weeks before, during and for 2 years after treatment. Please notify Actavis of all pregnancies occurring during and after therapy, by telephone: +356 22483330 or by fax: +356 22483350.

Other material available to support successful Neotigason® treatment:
Neotigason® – Patient guide, Pregnancy & Foetal Exposure Prevention. Consent forms, one for women of child bearing potential and another form for other patient groups. Brochures and consent forms are available from your local drug representative or from Actavis (fax: +356 22483350).

Neotigason® should only be prescribed by physicians experienced in the use of systemic retinoids.

Healthcare professionals should report any adverse event suspected to be associated with the use of Neotigason to Actavis by email on phv@actavis.com.mt, by phone: +356 22483330; Fax: +356 22483350 or by post to: Actavis M&S Office, Tarxien Road, Tarxien TXN 1095, Malta.

Any suspected adverse reaction can also be reported to the Medicines Authority. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gzira GZR 1368, Malta, or sent by email to postlicensing.medicinesauthority@gov.mt

Women of childbearing potential:

First Visit

Assess the need for treatment and the suitability of Neotigason® for the patient, e.g. the severity of the disease, the resistance to other therapies and if she can be relied on to understand and follow instructions about the therapy.

Emphasise the significance of contraception during and after therapy due to the high risk of malformation of the child. Give the patient a copy of the Neotigason® – patient guide for pregnancy & foetal exposure prevention and discuss at least the following topics:

- **Adequate contraception:** For women of child-bearing age, discuss the most suitable forms of effective contraception (preferably 2 complementary forms) and agree on implementation. Primary contraceptive method is a combination hormonal contraceptive product or an intrauterine device and it is recommended that a condom or diaphragm (cap) is also used. Effective contraception without interruption must be used for at least four weeks before start of treatment and for 2 years after discontinuation of treatment. Note that due to possible interference with their contraceptive effect, low dose progesterone-only products (minipills) are not recommended.

- **Regular pregnancy testing:** Therapy should start on the second or third day of a menstrual period. To make sure the patient is not pregnant; pregnancy tests (minimum sensitivity 25 mIU/ml) will have to be carried out within 3 days before the first dose is given, and should be repeated every 28 days during treatment and at 1-3 monthly intervals for 2 years after end of treatment. A negative pregnancy test not older than 3 days is also mandatory before each prescription renewal.

- **What to do in case of pregnancy:** The patient should immediately contact the prescribing doctor or the nearest health care centre for advice. Note that the teratogenic risk applies especially during treatment with acitretin and for 2 months after end of treatment. For up to 2 years after discontinuation, the risk is lower but cannot be entirely excluded due to possible formation of etretinate.

- **Alcohol use:** Advise the patient that she must not consume alcohol and should avoid all products containing alcohol (drink, food, medicines) during treatment and for 2 months after stopping treatment. Concomitant use of acitretin and alcohol has been found to lead to formation of the highly tertogenic etretinate, which eliminates more slowly from the body than acitretin.

- **Giving blood is prohibited:** Patients must not give blood while taking Neotigason® and for 2 years after completion of therapy, as blood transfusions containing acitretin might harm unborn babies if given to pregnant women.

- **This medication is prescribed solely for the patient's personal use:** Due to the risk of foetal malformations, the medicine must not be passed on to other people. Instruct the patient to return unused or expired products to a pharmacy for disposal.

Initial Checklist

☐ **Advise the patient on the expected benefit versus risk of treatment with Neotigason®**

☐ **Make sure the patient understands the instructions and is capable of using the agreed contraceptive measures reliably**

☐ **Give the patient a copy of the Patient guide, Pregnancy & Foetal Exposure Prevention to take home and explain a consent form needs to be signed before start of treatment**

☐ **Perform a pregnancy test**

☐**Schedule the second visit to allow the patient to use the agreed form of contraception for at least four weeks before treatment with Neotigason® is started**

Start of Treatment Checklist

☐ **Check on the use of contraceptives**

☐ **Remind the patient that she immediately needs to inform of any omission of contraception, unprotected sexual contact or suspected pregnancy**

☐ **Perform a pregnancy test. A negative pregnancy test not older than 3 days is mandatory before prescription**

☐ **Prepare the consent form available for women of child bearing potential, and ask the patient to sign the form. Keep the signed form for future reference**

☐ **Arrange pregnancy tests at 28-day intervals**

☐ **Schedule the next visit to ensure the continued success of the treatment**

☐ **Make sure that the patient understands all risk issues**

Follow-up Checklist

☐ **Check on the use of contraceptives**

☐ **Arrange a pregnancy test. A negative pregnancy test not older than 3 days is mandatory before renewed prescription**

☐ **Remind the patient that she immediately needs to inform of any omission of contraception, unprotected sexual contact or suspected pregnancy**

☐ **Schedule the next visit to ensure the continued success of the treatment.**

Termination of Treatment Checklist

☐ **Discuss the termination time for therapy.**

☐ **Agree on contraception for a minimum of 2 years following discontinuation of therapy.**

☐ **Remind the patient that she immediately needs to inform suspected pregnancy.**

☐ **Add information about end of treatment to the consent form, and ask the patient to sign the form. Keep the signed form for future reference.**

☐ **Agree on follow-up pregnancy tests every 1-3 months for 2 years after stopping therapy.**

All other patient groups:

Explain the high risk of malformation in case of foetal exposure to acitretin and discuss at least the following topics:

- **Giving blood is prohibited:** Patients must not give blood while taking Neotigason® and for 2 years after completion of therapy, as blood transfusions containing acitretin might harm unborn babies if given to pregnant women.

- **This medication is prescribed solely for the patient's personal use:** Due to the risk of foetal malformations, the medicine must not be passed on to other people. Instruct the patient to return unused or expired products to a pharmacy for disposal.

Additional information: For male patients treated with acitretin, available data, based on the level of maternal exposure from the semen and seminal fluid indicate a minimal, if any, risk of teratogenic effects.

☐ **Prepare a consent form before start of treatment (the form for all patients except women of childbearing potential), and ask the patient to sign the form. Keep the signed form for future reference.**

☐ **When the treatment is terminated, add information thereof to the consent form, and ask the patient to sign the form. Keep the signed form for future reference.**

Patient Guide: For Women of Child Bearing Potential

Neotigason® (acitretin) 10 mg and 25 mg capsules
Pregnancy & Foetal Exposure Prevention

What this brochure is for
This brochure contains important information for women of child-bearing age, as the risk of birth defects is high if Neotigason® is taken during pregnancy or for a period after treatment has finished. Please read this brochure carefully before you start taking Neotigason®.

Neotigason® contains the active ingredient acitretin, which causes severe birth defects in pregnancy and is also slowly removed from the body. **Therefore if you are a woman of child-bearing age, you must not be or become pregnant during treatment or for 2 years after stopping treatment.**

Adequate contraception is essential

- Discuss suitable, effective and ongoing contraception with your doctor.
- The best contraceptive method is an intrauterine device (coil) or a combination hormonal contraceptive product such as the 'Pill'. It is recommended that a second form of contraception such as a condom or diaphragm (cap) is also used.
- Low-dose progesterone-only contraceptives ("minipills") are not recommended.
- Start using contraceptives at least 4 weeks before starting treatment with Neotigason®
- Use your contraception continuously. Do not stop using contraceptives at any point during treatment with Neotigason®.
- You must not get pregnant for two years after stopping treatment, so you must continue to use the recommended contraceptives for 2 years after you have finished treatment with Neotigason®.

Regular pregnancy testing

To make sure you are not pregnant during treatment, your doctor will carry out a pregnancy test before treatment starts with Neotigason®. A pregnancy test should be repeated at 28 days intervals during treatment. Before each renewal of Neotigason® prescription, your doctor will also want you to have a pregnancy test. After completion of treatment, you will need to have a pregnancy test every 1-3 months for a period of 2 years.

If you become pregnant during or after treatment

If despite precautions, you become pregnant during treatment or within the 2 years after stopping Neotigason®, the risk of extremely severe foetal malformations in the unborn baby is high. Contact your prescribing doctor or your nearest healthcare centre without delay for support and advice.

Avoid alcohol

If alcohol is taken during treatment with Neotigason®, a compound called etretinate can form, which may be harmful to an unborn child and is removed very slowly from the body. Therefore women of child-bearing age must not consume alcohol and should avoid all products containing alcohol (drinks, foods, and medicines) during treatment and for 2 months after stopping treatment.

Giving blood during Neotigason® treatment

Neotigason® is carried in the blood. Neotigason® in blood transfusions might harm unborn babies if given to pregnant women. Therefore both women and men treated with Neotigason® must not give blood during treatment and for two years after completion of treatment.

This medicine has been prescribed only for your personal use

You should never give this medicinal product to anyone else. You should return any unused or expired medicines to the pharmacy for disposal.

Other information

While this brochure gives important facts about Neotigason® that you need to be aware of, it does not replace the advice given to you by your dermatologist, doctor or pharmacist.

Further information (such as how to take Neotigason®, special warnings and possible side effects) is included in the patient information leaflet, which is supplied in each pack of Neotigason®. Please read this leaflet carefully.

If you have any further questions or concerns about taking Neotigason® after you have read this brochure, talk to your dermatologist/doctor.

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Consent form for women of childbearing potential:

Neotigason® (Acitretin) 10 mg and 25 mg capsules
Pregnancy & Foetal Exposure Prevention

Name of the patient/identification: (please use block letters)	
Name of the doctor/identification: (please use block letters)	

Before start of treatment
I confirm that my doctor has informed me about what treatment with Neotigason® involves in respect of pregnancy prevention, and

☐ I understand the risk of birth defects related to pregnancy during treatment and for 2 years after stopping treatment with Neotigason®.

☐ I understand the importance of using contraception during and for 2 years after stopping treatment with Neotigason®.

☐ I understand the importance of regular pregnancy testing during and for 2 years after stopping treatment with Neotigason®.

☐ I understand the importance of avoiding alcohol consumption during and for 2 months after stopping treatment with Neotigason®.

☐ I understand that I must not give blood during treatment and for two years after stopping treatment with Neotigason®.

☐ I understand that I should never give this medicinal product to anyone else, but return any unused or expired medicines to the pharmacy for disposal.

☐ I have been given a copy of the Neotigason® Patient Guide, Pregnancy & Foetal Exposure Prevention.

Signed and confirmed by the patient/date:

Start of treatment (date):	
Use of contraception started (date):	
Signed and confirmed by the patient/date:	**Signed and confirmed by the doctor/date:**

Termination of treatment (date):	
Contraception to be used and blood donation avoided until (date):	
Signed and confirmed by the patient/date:	**Signed and confirmed by the doctor/date:**

General Consent Form

Neotigason® (Acitretin) 10 mg and 25 mg capsules
Foetal Exposure Prevention

Name of the patient/identification: (please use block letters)	
Name of the doctor/identification: (please use block letters)	

Before start of treatment

I confirm that:

☐ I understand that I must not give blood during treatment and for two years after stopping treatment with Neotigason®.

☐ I understand that I should never give this medicinal product to anyone else, but return any unused or expired medicines to the pharmacy for disposal.

Signed and confirmed by the patient/date:

Termination of treatment (date):	
Blood donation to be avoided until (date):	
Signed and confirmed by the patient/date:	**Signed and confirmed by the doctor/date:**