Roaccutane®: Pregnancy Prevention Programme

Physician’s guide to prescribing Isotretinoin (Roaccutane®)

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For further information, refer to the Summary of Product Characteristics available on www.medicines.ie
Introduction ......................................................................................................... 4

The teratogenic risks of isotretinoin .............................................................5

Pregnancy Prevention Programme for Isotretinoin .................................5

Conditions of prescribing isotretinoin to women at risk of pregnancy......7

Reporting Side Effects....................................................................................10

Further Information..........................................................................................10
Introduction

Isotretinoin is highly teratogenic. There is an extremely high risk that foetal exposure to isotretinoin will result in life threatening congenital abnormalities. The isotretinoin Pregnancy Prevention Programme (PPP) has therefore been developed to ensure that female patients are not pregnant when starting isotretinoin and do not become pregnant during isotretinoin therapy or for at least one month after stopping isotretinoin treatment.

This guide provides a summary of the Pregnancy Prevention Programme. For full details of the Pregnancy Prevention Programme please refer to the isotretinoin Summary of Product Characteristics (SmPC) under section 4.4 Special warnings and special precautions for use.

This brochure should be used in conjunction with the Physician’s checklist for prescribing to female patients.

PLEASE NOTE THAT THIS GUIDE PROVIDES INFORMATION RELATING TO ROACCUTANE PREGNANCY PREVENTION ONLY – FOR FULL PRESCRIBING INFORMATION INCLUDING ADVERSE EVENT LISTINGS, PLEASE REFER TO THE ROACCUTANE SmPC.
The teratogenic risks of isotretinoin

Isotretinoin is indicated for severe forms of acne (such as nodular or conglobate acne or acne at risk of permanent scarring) resistant to adequate courses of standard therapy with systemic anti-bacterials and topical therapy.

Isotretinoin is TERATOGENIC. The foetal malformations associated with exposure to isotretinoin include:

- Central nervous system abnormalities (hydrocephalus, cerebellar malformation/abnormalities, microcephaly),
- facial dysmoria,
- cleft palate,
- external ear abnormalities (absence of external ear, small or absent external auditory canals),
- eye abnormalities (microphthalmia),
- cardiovascular abnormalities (conotruncal malformations such as tetralogy of Fallot, transposition of great vessels, septal defects),
- thymus gland abnormality and parathyroid gland abnormalities.
- There is also an increased incidence of spontaneous abortion.

Isotretinoin is contraindicated in women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met. Isotretinoin is contraindicated in women who are pregnant or breast feeding.

If pregnancy occurs in a woman treated with isotretinoin, treatment must be stopped and the patient should be referred to a physician specialised or experienced in teratology for evaluation and advice.

Pregnancy Prevention Programme for Isotretinoin

Evidence supports the following as key issues in identifying female patients for treatment with Roaccutane:

1. identifying those who are already pregnant when you are considering Roaccutane
2. identifying those who may not be reliable in avoiding pregnancy for the required period before, during and after therapy.

The patient should accept the risks and precautionary measures involved to avoid exposing an unborn baby to Roaccutane.

The patient must understand the critical responsibility she assumes in electing to undertake therapy with Roaccutane, and that any method of birth control can fail. You must verify that each individual patient receives adequate counselling about all her pregnancy prevention options, and that she knows how to select and use at least one and preferably two effective contraceptive methods.
The Pregnancy Prevention Programme consists of 3 parts:

- Educational programme
- Therapy management
- Distribution control

Roaccutane must be prescribed to female patients of childbearing potential under the Roaccutane Pregnancy Prevention Programme (PPP). The goal of the PPP is to prevent the foetus from exposure to isotretinoin.

**Educational programme**

The purpose of the educational programme is to:

- enhance the understanding of the teratogenic risks of isotretinoin by both patients and physicians
- enhance female patient information and awareness.

As part of the educational programme the following brochures are provided:

- Physician’s guide to prescribing isotretinoin (this document)
- Physician’s checklist for prescribing to female patients
- Pharmacist’s Guide to Dispensing
- Acknowledgement form for female patients
- Patient information brochure
- Brochure on contraception

**Therapy management**

The basic components of therapy management in the isotretinoin Pregnancy Prevention Programme are:

- provision of educational material to patients
- medically supervised pregnancy testing before, during and 5 weeks after end of treatment
- use of at least one method of contraception and preferably 2 complementary forms of contraception including a barrier method for at least one month before initiating therapy, continuing throughout the treatment period, and then for at least one month after stopping therapy.

**Distribution control**

Under the Pregnancy Prevention Programme the prescription of isotretinoin for women should be limited to a 30 day supply. In addition the prescription for isotretinoin will only be valid for 7 days.
Conditions of prescribing isotretinoin to women at risk of pregnancy

Isotretinoin is contraindicated in women of childbearing potential unless all of the following conditions of the Pregnancy Prevention Programme are met:

- She has severe acne (such as nodular or conglobate acne or acne at risk of permanent scarring) resistant to adequate courses of standard therapy with systemic anti-bacterials and topical therapy (refer to section 4.1 of the SmPC).
- She understands the teratogenic risk.
- She understands the need for rigorous follow-up, on a monthly basis.
- She understands and accepts the need for effective contraception, without interruption, 1 month before starting treatment, throughout the duration of treatment and 1 month after the end of treatment. At least one and preferably two complementary forms of contraception including a barrier method should be used.
- Even if she has amenorrhea she must follow all of the advice on effective contraception.
- She should be capable of complying with effective contraceptive measures.
- She is informed and understands the potential consequences of pregnancy and the need to rapidly consult if there is a risk of pregnancy.
- She understands the need and accepts to undergo pregnancy testing before, during and 5 weeks after the end of treatment.
- She has acknowledged that she has understood the hazards and necessary precautions associated with the use of isotretinoin.

These conditions also concern women who are not currently sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy.

The prescriber must ensure that:

- The patient complies with the conditions for pregnancy prevention as listed above, including confirmation that she has an adequate level of understanding.
- The patient has acknowledged the aforementioned conditions.
- The patient has used at least one and preferably two methods of effective contraception including a barrier method for at least 1 month prior to starting treatment and is continuing to use effective contraception throughout the treatment period and for at least 1 month after cessation of treatment.
- Negative pregnancy test results have been obtained before, during and 5 weeks after the end of treatment. The dates and results of pregnancy tests should be documented.
**Contraception**
Female patients must be provided with comprehensive information on pregnancy prevention and should be referred for contraceptive advice if they are not using effective contraception.

As a minimum requirement, female patients at potential risk of pregnancy must use at least one effective method of contraception. Preferably the patient should use two complementary forms of contraception including a barrier method. Contraception should be continued for at least 1 month after stopping treatment with isotretinoin, even in patients with amenorrhea.

**Pregnancy testing**
According to local practice, medically supervised pregnancy tests with a minimum sensitivity of 25 mIU/mL are recommended to be performed in the first 3 days of the menstrual cycle, as follows.

**Prior to starting therapy**
In order to exclude the possibility of pregnancy prior to starting contraception, it is recommended that an initial medically supervised pregnancy test should be performed and its date and result recorded. In patients without regular menses, the timing of this pregnancy test should reflect the sexual activity of the patient and should be undertaken approximately 3 weeks after the patient last had unprotected sexual intercourse. The prescriber should educate the patient about contraception.

A medically supervised pregnancy test should also be performed during the consultation when isotretinoin is prescribed or in the 3 days prior to the visit to the prescriber, and should have been delayed until the patient had been using effective contraception for at least 1 month. This test should ensure the patient is not pregnant when she starts treatment with isotretinoin.

**Follow-up visits**
Follow-up visits should be arranged at 28 day intervals. The need for repeated medically supervised pregnancy tests every month should be determined according to local practice including consideration of the patient’s sexual activity and recent menstrual history (abnormal menses, missed periods or amenorrhea). Where indicated, follow-up pregnancy tests should be performed on the day of the prescribing visit or in the 3 days prior to the visit to the prescriber.

**End of treatment**
Five weeks after stopping treatment, women should undergo a final pregnancy test to exclude pregnancy.

**Prescribing and dispensing restrictions**
Prescriptions of isotretinoin for women of childbearing potential should be limited to 30 days of treatment and continuation of treatment requires a new prescription. Ideally, pregnancy testing, issuing a prescription and dispensing of isotretinoin should occur on the same day. Dispensing of isotretinoin should occur within a maximum of 7 days of the prescription.
**Male patients**

The available data suggest that the level of maternal exposure from the semen of the patients receiving isotretinoin, is not of a sufficient magnitude to be associated with the teratogenic effects of isotretinoin.

Male patients should be reminded that they must not share their medication with anyone, particularly not females.

**Additional precautions**

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

Patients should not donate blood during therapy and for 1 month following discontinuation of isotretinoin because of the potential risk to the foetus of a pregnant transfusion recipient.

**Female patients not at risk of pregnancy**

It is important that female patients not at risk of pregnancy are warned of the teratogenic risks of isotretinoin. The importance of contraception should also be discussed with these patients as a woman not at risk of pregnancy at the start of isotretinoin therapy may have a change in circumstances. All women should sign the acknowledgement form to confirm that they have been informed of the risks of teratogenicity with isotretinoin. Full patient information about the teratogenic risk of isotretinoin and the strict pregnancy prevention measures should be given to female patients not at risk of pregnancy.
Reporting Side Effects

Reporting of suspected adverse events or reactions

Reporting suspected adverse events or reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse events or reactions (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

In the event of a suspected adverse event, please report it to:
The Drug Surveillance Centre
Roche Products (Ireland) Limited
3004 Lake Drive
Citywest
Naas Road
Dublin 24
Telephone: (01) 4690700
Fax: (01) 4690793
Email: ireland.drug_surveillance_centre@roche.com

Alternatively, suspected adverse reactions should be reported to:
HPRA Pharmacovigilance
The Health Products Regulatory Authority
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
Dublin 2
Telephone: (01) 6764971
Fax: (01) 6762517
Email: medsafety@hpра.ie
Website: www.hpra.ie

Further Information

For additional copies of this risk minimisation material, refer to www.hpra.ie and download the required material or alternatively if you would like hard copies, please contact Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24 by mail, telephone (01 4690700), fax (01 4690791) or email (Ireland.dra@roche.com).

For further information about Roaccutane, please contact Medical Information at Roche Products (Ireland) Limited by telephone (01 4690700), fax (01 4690791) or email (Ireland.druginfo@roche.com).