9th November 2023

Direct Healthcare Professional Communication (DHPC)

Oral isotretinoin▼: New safety measures following review into sexual and psychiatric adverse reactions

Dear Healthcare professional,

Roche Products Ltd, in agreement with the marketing authorisation holders of oral isotretinoin and the Medicines and Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- Initiation of isotretinoin treatment in patients under 18 years of age now requires agreement by two independent prescribers that there is no other appropriate effective treatment before it is prescribed.
- All patients must be counselled about the benefits and risks of treatment before isotretinoin is prescribed, including possible side effects relating to mental health and sexual function.
- Patients should also be monitored for these and other side effects during isotretinoin treatment.
- New risk minimisation materials have been developed to incorporate these new safety measures and support healthcare professionals and patients, as well as highlight the updates to the product information.
- The Acknowledgement of Risk Form is available for prescribers and should be completed with all patients. Patients should be provided with a copy of this as well as the Patient Reminder Card. A Pharmacist Checklist should be used by pharmacists as a reminder when dispensing isotretinoin.
- Applicability of the updated Pregnancy Prevention Programme must be assessed for all patients. Isotretinoin is contraindicated in women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met.

Background on the safety concern

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

The Commission on Human Medicines (CHM) Isotretinoin Expert Working Group conducted a review, published April 2023, to explore the complex relationship between isotretinoin, severe acne, mental health and sexual health.

This review concluded that the overall balance of risks and benefits for isotretinoin remains favourable but further action should be taken to ensure patients are fully informed about isotretinoin and are effectively monitored during and after treatment. Limitations in the data, including conflicting study data, lack of consistent patient level data or long term follow up information prevented the establishment of causal associations between the acute and longer term psychiatric and sexual side effects and the use of isotretinoin.

Following consideration of the data, the CHM has advised to further strengthen safety measures for isotretinoin through updates to the product information and risk minimisation materials. These changes are described below.

Changes to the product information

The product information (Summary of Product Characteristics and Patient Information Leaflet) has been updated to:

- Reflect that initiation of isotretinoin treatment in patients under 18 years of age now requires agreement by two independent prescribers that there is no other appropriate effective treatment before it is prescribed.
- Highlight that all patients must be counselled about the benefits and risks of treatment before isotretinoin is prescribed, including possible side effects relating to mental health and sexual function.
- Emphasise that patients should also be monitored for these side effects during isotretinoin treatment.

Updated risk minimisation materials

Updated risk minimisation materials have been created to incorporate these new safety measures and support healthcare professionals and patients, as well as highlight the updates to the product information. These materials are applicable to **all patients** and include:

1. Acknowledgement of Risk Form
2. Patient Reminder Card
3. Pharmacist Checklist

The Acknowledgement of Risk Form should be completed by the **prescriber** (to confirm that they have explained the risks of treatment) and by the **patient** (to confirm they have

understood these risks and the associated actions required). A copy of the completed Acknowledgement of Risk Form should be given to the patient by the prescriber, along with the Patient Reminder Card. **Pharmacists** should ensure the Pharmacist Checklist is suitably placed as a reminder each time an oral isotretinoin prescription is dispensed.

These new materials are available in electronic form at https://www.medicines.org.uk and hard copies will also be distributed.

Applicability of the updated Pregnancy Prevention Programme must be assessed for all patients. Isotretinoin is contraindicated in women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

You can report via:

- the Yellow Card website
- the free Yellow Card app available from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, timing onset, treatment dates, and product brand name.

Adverse events should also be reported to the manufacturer, using the contact details provided below.

Company contact point

Should you have any questions regarding the use of isotretinoin, please contact the manufacturer using the following contact details.

Manufacturer	**Email**	**Phone**
Roche Products Limited	Additional Information: medinfo.uk@roche.com Suspected adverse reactions: welwyn.uk_dsc@roche.com	Additional information: +44 (0)800 328 1629 Suspected adverse reactions: +44 (0)1707 367554
Ennogen Healthcare Limited	Additional information and suspected adverse reactions: info@ennogen.com	Additional information and suspected adverse reactions: +44 (0)1322 629 220
Sun Pharma	Additional information and suspected adverse reactions: medinfoeurope@sunpharma.com	Additional information and suspected adverse reactions: +44 (0) 208 848 8688

The Summary of Product Characteristics (SmPC) for oral isotretinoin is available at: www.medicines.org.uk/emc.

This Direct Healthcare Professional Communication is provided to you by:

Roche Products Limited
Ennogen Healthcare Limited
Sun Pharma

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