EMA starts review of retinoid medicines. Effectiveness of measures for pregnancy prevention and for minimising possible risk of neuropsychiatric disorders to be evaluated

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Information on Retinoid Medicines

- Retinoids are vitamin A derivatives that are available orally as capsules or topically as creams and gels to be applied to the skin.
- Retinoids taken by mouth are used to treat various forms of severe acne, severe hand eczema that does not respond to treatment with corticosteroids, severe forms of psoriasis and other skin conditions, and certain types of cancer.
- Retinoids applied to the skin are used to treat various skin conditions including mild to moderate acne.
- Most retinoids have been authorised nationally in the European Union (EU). Panretin (alitretinoin) has also been authorised centrally as for the treatment of skin lesions in AIDS patients with Kaposi's sarcoma (a type of skin cancer) while Targretin (bexarotene) has also been authorised centrally the treatment of the visible signs on the skin of cutaneous T-cell lymphoma (CTCL, a rare cancer of the lymph tissue).

In Malta the following products are authorised through various licensing procedures:

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	Marketing Authorization Holder
Bexarotene 75 mg	Targretin	Soft Capsule	POM	EU/1/01/178/001	Eisai Ltd.
Isotretinoin 10 mg	Decutan 10mg	Soft Capsule	POM	MA155/00501	Actavis h.f.
Isotretinoin 20mg	Decutan 20mg	Soft Capsule	POM	MA155/00502	Actavis h.f.
Isotretinoin 10 mg	Isotretinoin 10mg	Capsule	POM	AA908/13201	NeoFarma Pharmaceuticals Limited
Isotretinoin 20 mg	Isotretinoin 20mg	Capsule	POM	AA908/13202	NeoFarma Pharmaceuticals Limited

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Alitretinoin 10 mg	Toctino 10mg	Soft Capsule	POM	MA300/01501	Glaxo SmithKline UK Limited
Alitretinoin 30 mg	Toctino 30mg	Soft Capsule	POM	MA300/01502	Glaxo SmithKline UK Limited
Alitretinoin 0.1% w/w	Panretin Gel	Gel	POM	EU/1/00/149/001	Eisai Ltd
Adapalene 0.1% w/w	Differine Cream	Cream	POM	MA117/00201	Galderma International
Adapalene 0.1% w/w	Differine Gel	Gel	POM	MA117/00202	Galderma International
Adapalene 1 mg/ml and benzoyl peroxide 25 mg/g	Epiduo Gel	Gel	POM	AA117/01201	Galderma International

Information about the EMA's review of retinoid medicines

The European Medicines Agency (EMA) has started a review of retinoid medicines to evaluate measures currently in place for pregnancy prevention and for minimising the possible risk of neuropsychiatric disorders.

- Retinoids taken by mouth can have harmful effects on the unborn child and therefore must not be used in pregnant women. To facilitate this, pregnancy prevention programmes (PPPs) for retinoids have been set up across the European Union (EU).
- For retinoids applied to the skin, the evidence of these effects is less robust; however, it is generally recommended that these medicines should not be used during pregnancy.
- Although PPPs have helped reduce the number of pregnancies in women taking retinoids by mouth, pregnancies still occur. A recent analysis of the effectiveness of the isotretinoin PPP, which considered post-marketing data and published studies, raised concerns about how well PPPs are followed in practice, and about the lack of consistency at EU level.
- Concerns around the measures in place for pregnancy prevention have also been raised with regard to retinoids applied to the skin.

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) will review the measures currently in place for pregnancy prevention, including the warnings and recommendations in the product information for all retinoid medicines, to ensure that they are effective and appropriate. The PRAC will also review the possible risk of neuropsychiatric disorders such as

depression, anxiety, psychotic disorders and suicidal behaviour with retinoids. Warnings about this possible risk are already included in the product information for some of these medicines. The Committee will review the extent and nature of these warnings to ensure that they reflect the available evidence for retinoids taken by mouth, as well as for those applied to the skin.

The PRAC's recommendations will be sent to Committee for Medicinal Products for Human Use (CHMP), which will issue the Agency's final opinion in due course.

While the review is ongoing, patients who have any concerns about their medication should discuss them with their healthcare professional and for more information on review of retinoid medicines please refer to the European Medicines Agency's press release

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on retinoid containing medicines. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or online to **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate
Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

The Medicines Authority thanks you for your time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. Your feedback may be returned by folding this page address side up, stapling the ends and then posting (no stamp required)

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Pharmacovigilance Section

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