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EMA starts review of retinoid medicines

Effectiveness of measures for pregnancy prevention and for minimising possible risk of neuropsychiatric disorders to be evaluated

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 (which include the active substances acitretin, adapalene, alitretinoin, bexarotene, isotretinoin, tazarotene and tretinoin) are taken by mouth or applied as creams or gels to treat several conditions mainly affecting the skin, including acne and psoriasis. Some retinoids are also used to treat certain forms of cancer.

Retinoids taken by mouth can have harmful effects on the unborn child. These medicines therefore must not be used in pregnant women, and 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[1] 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[2].

Following a request from the United Kingdom's medicines agency, 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

[1] http://www.ema.europa.eu/docs/en_GB/document_library/Minutes/2016/03/WC500202623.pdf#page=47
[2] http://www.ema.europa.eu/docs/en_GB/document_library/Minutes/2016/06/WC500207977.pdf#page=43

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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.

While the review is ongoing, patients who have any concerns about their medication should discuss them with their healthcare professional.

More about the medicines

Retinoids are vitamin A derivatives that are available as capsules to be taken by mouth or 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.

The following retinoids have been authorised nationally in a number of Member States of the EU and are covered by this review: acitretin, adapalene, alitretinoin, isotretinoin, tazarotene and tretinoin. Alitretinoin has also been authorised centrally as Panretin for the treatment of skin lesions in AIDS patients with Kaposi's sarcoma (a type of skin cancer). Bexarotene has been authorised centrally as Targretin for the treatment of the visible signs on the skin of cutaneous T-cell lymphoma (CTCL, a rare cancer of the lymph tissue).

More about the procedure

The review of retinoids has been initiated at the request of the United Kingdom, under Article 31 of Directive 2001/83/EC.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. The PRAC recommendations will then be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt an opinion. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.