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New review of risks with high-strength estradiol-containing creams

EMA has started a new review of high-strength estradiol-containing creams (0.01% w/w) that are used inside the vagina for treating women with vaginal atrophy who have been through menopause.

The review will assess the risk of estradiol being absorbed systemically (throughout the body) from these creams. Systemic absorption is of concern because it may result in similar side effects to those associated with the use of estradiol in systemic hormone replacement therapy (HRT), which include venous thromboembolism (formation of blood clots in the veins), stroke and endometrial cancer (cancer of the lining of the womb).

In 2014, EMA completed a review of the risk of systemic absorption with high-strength estradiol creams and recommended measures to minimise it, including limiting the use of the creams to a maximum duration of 4 weeks. However, in March 2019 the EU Court of Justice partially annulled the conclusions of the review on procedural grounds. Although the Court of Justice did not question the scientific conclusions, the partial annulment means that some of the measures taken to minimise the risk have been invalidated.

The European Commission has therefore asked EMA to reassess this risk, taking into account both the original data and any new data that have become available since the previous review, and to recommend measures that should be put in place to protect patients. The review will be carried out by EMA's safety committee (PRAC).

While the review is ongoing, women who have any questions or concerns about their treatment should speak to their doctor or pharmacist.

More about the medicine

The estradiol-containing creams covered by this review contain 100 micrograms of estradiol per gram (0.01% w/w).

They are a type of topical 'hormone replacement therapy': they contain a female hormone, estradiol, used to replace the estradiol hormone the body no longer makes after menopause.

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These high-strength estradiol-containing creams have been authorised in the EU for the treatment of vaginal atrophy in post-menopausal women through national procedures for over 40 years. They are marketed in Austria, Bulgaria, Croatia, Czech Republic, Estonia, Germany, Hungary, Latvia, Lithuania and Slovakia under the following trade names: Linoladiol, Linoladiol N, Linoladiol Estradiol, Estradiol Wolff and Montadiol.

More about the procedure

The review of high-strength estradiol-containing creams (0.01% w/w) has been initiated at the request of the European Commission, 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. As these medicines are all authorised nationally, the PRAC recommendations will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.