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EMA recommendations on the use of Linoladiol N and Linoladiol HN estradiol-containing creams

A limit to the duration of use and other measures put in place to manage potential risk of side effects

On 25 April 2014, the EMA's Committee for Medicinal Products for Human Use (CHMP) updated recommendations on the use of two high-strength estradiol-containing creams, Linoladiol N and Linoladiol HN.

The Linoladiol N cream is only to be used inside the vagina for treating postmenopausal women with vaginal atrophy due to a lack of the hormone estrogen, while the Linoladiol HN cream is for postmenopausal women with mild, inflammatory skin conditions around the genital area. Treatment with both creams should be limited to a maximum duration of 4 weeks.

In addition, Linoladiol HN is no longer to be used to treat lichen sclerosus, a skin condition that commonly affects the genital area, because of a lack of evidence of benefit in this condition.

In December 2013, the CHMP had concluded a review of the benefits and risks of both creams and made recommendations on their use.[1] Following a request by the company for a re-examination of Linoladiol N, the recommendations for this cream have been updated, taking into account new measures to manage the potential risk of side effects.

The CHMP reiterated the need to limit treatment with both creams to 4 weeks because of their relatively high estradiol content and the potential risks of side effects from estradiol being absorbed systemically (throughout the body). Systemic absorption of estradiol may be associated with risks similar to those seen in systemic hormone replacement therapy (HRT), including blood clots, stroke and endometrial (womb) cancer. The product information of Linoladiol N and Linoladiol HN have been updated to inform patients and healthcare professionals about these potential risks.

In addition, for Linoladiol N, the cream with the higher amount of estradiol, the CHMP has required the company to limit the amount of cream available in the packs to prevent patients from using them for longer than recommended.

The CHMP's recommendations were sent to the European Commission which endorsed them and issued a final, legally binding decision valid throughout the EU on 19 August 2014.

[1] For more information, see here.

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Information to patients

The European Medicines Agency has updated advice on how to use Linoladiol N and Linoladiol HN creams. Patients using these creams should be aware of the following:

- Linoladiol N is only to be used inside the vagina for treating postmenopausal women with vaginal atrophy due to a lack of estrogen.
- Linoladiol HN should only be used for treating postmenopausal women with mild, inflammatory skin conditions affecting the external genital area.
- Linoladiol HN was previously being used to treat a condition called lichen sclerosus. If you have been using Linoladiol HN for this condition, contact your doctor to discuss alternative treatments.
- Both creams should not be used for more than 4 weeks. This is because the creams contain the hormone estradiol which can be absorbed into the bloodstream and may increase your risks of side effects such as blood clots and strokes if the creams are used for extended periods.
- Linoladiol N should be applied into the vagina while Linoladiol HN should be applied to the external genital area.
- If you have any questions about your treatment, you should contact your doctor or pharmacist.

Information to healthcare professionals

The EMA has concluded a review of Linoladiol N and Linoladiol HN estradiol-containing creams and has updated recommendations on their use. The product information for both creams will be updated with the following recommendations:

- Linoladiol N is indicated for the treatment of vaginal atrophy due to estrogen deficiency in postmenopausal women.
- Linoladiol HN is indicated in the short-term treatment of acute, mild inflammatory skin diseases of the external genital area in postmenopausal women.
- Linoladiol HN should no longer be prescribed for lichen sclerosus.
- Both Linoladiol N and Linoladiol HN should not be used beyond four weeks due to the risks associated with possible systemic exposure to estradiol.

More about the medicine

The Linoladiol N cream (0.01 %w/w) contains 100 microgram of estradiol per gram, while Linoladiol HN (0.005 %w/w, 0.4 %w/w) contains 50 microgram of estradiol and 4 mg of the corticosteroid prednisolone per gram.

Linoladiol N and Linoladiol HN are a type of local ‘hormone replacement therapy’: they contain a female hormone, estradiol, used to replace the estradiol hormone the body no longer makes after menopause. Linoladiol HN also contains low-dose prednisolone, which acts as an anti-inflammatory agent.

Both medicines have been authorised in the EU through national procedures for over 40 years. Linoladiol N is marketed in Bulgaria, Czech Republic, Estonia, Germany, Hungary, Latvia, Lithuania and Slovakia, while Linoladiol HN is marketed in Estonia, Germany, Latvia and Lithuania.

More about the procedure

The review of the topical estradiol-containing medicines Linoladiol N and Linoladiol HN was triggered on 24 May 2012 by Germany, under Article 31 of Directive 2001/83/EC. The German medicines agency asked the CHMP to carry out a full assessment of the benefit-risk balance of these medicines and to issue an opinion on whether their marketing authorisations should be maintained, varied, suspended or withdrawn across the European Union.

The review has been carried out by the Committee for Medicinal Products for Human Use (CHMP) responsible for questions concerning medicines for human use.

The CHMP issued an opinion in December 2013. Following a request from the company, a re-examination of the opinion for Linoladiol N was carried out and concluded in April 2014. The final CHMP opinion was forwarded to the European Commission, which issued a final decision on 19 August 2014.

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