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Medicines containing nomegestrol or chlormadinone: PRAC recommends new measures to minimise risk of meningioma

EMA's safety committee (PRAC) has recommended new measures to minimise the risk of meningioma with medicines containing nomegestrol or chlormadinone, which are used for gynaecological and menstrual disorders, hormone replacement therapy and, at lower doses, as hormonal contraceptives (birth control). Meningioma is a tumour of the membranes covering the brain and spinal cord. It is usually benign and is not considered to be a cancer, but due to their location in and around the brain and spinal cord, meningiomas can in rare cases cause serious problems.

The PRAC has recommended that medicines containing high-dose chlormadinone (5 – 10 mg) or high-dose nomegestrol (3.75 – 5 mg) should be used at the lowest effective dose and for the shortest duration possible, and only when other interventions are not appropriate. In addition, low- and high-dose nomegestrol or chlormadinone medicines must not be used by patients who have, or have had, meningioma.

As well as restricting the use of the high-dose medicines, the PRAC has recommended that patients should be monitored for symptoms of meningioma, which can include change in vision, hearing loss or ringing in the ears, loss of smell, headaches, memory loss, seizures and weakness in arms or legs. If a patient is diagnosed with meningioma, treatment with these medicines must be permanently stopped.

The product information for the high-dose medicines will also be updated to include meningioma as a rare side effect.

The recommendations follow a review of available data, including post-marketing safety data and results from two recent epidemiological studies.[1,2] These data showed that the risk of meningioma increases with increasing dose and duration of treatment.

The PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP) for the adoption of EMA's final opinion. Further details will be published at the time of the CHMP opinion.

[1] Nguyen P, Hoisnard L, Neumann A, Zureik M, Weill A. Utilisation prolongée de l'acétate de chlormadinone et risque de méningiome intracrânien: une étude de cohorte à partir des données du SND. EPI-PHARE, 2021. https://www.epi-phare.fr/app/uploads/2021/04/epi-phare_rapport_acetate_chlormadinone_avril-2021-1.pdf
[2] Nguyen P, Hoisnard L, Neumann A, Zureik M, Weill A. Utilisation prolongée de l'acétate de nomégestrol et risque de méningiome intracrânien: une étude de cohorte à partir des données du SNDS. EPI-PHARE, 2021. https://www.epi-phare.fr/app/uploads/2021/04/epi-phare_rapport_acetate_nomegetrol_avril-2021.pdf

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More about the medicine

Medicines containing nomegestrol acetate or chlormadinone acetate are available as tablets to be taken by mouth. They are available on their own or in combination with oestrogens to treat gynaecological disorders such as amenorrhoea (absence of menstrual periods) and other menstrual disorders, uterine bleeding, endometriosis (a condition in which tissue similar to the lining of the womb grows elsewhere in the body), breast tenderness, and as hormone replacement therapy or contraceptives (birth control).

The medicines are marketed under several trade names including Belara, Lutenyl, Luteran, Naemis and Zoely and as generic medicines. With the exception of Zoely (nomegestrol acetate/estradiol), which is centrally authorised, all other medicines reviewed during this procedure have been authorised via national procedures. Warnings about the risk of meningioma are already included in the product information for some of them, although the wording may differ across EU Member States. The PRAC's recommendation will lead to alignment of the product information for these medicines across the EU.

More about the procedure

The review of products containing nomegestrol or chlormadinone was initiated at the request of France, under Article 31 of Directive 2001/83/EC.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations.

The PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt the Agency's 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.