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# New measures to minimise risk of meningioma with medicines containing nomegestrol or chlormadinone

EMA's human medicines committee (CHMP) has endorsed the recommendation of the Pharmacovigilance Risk Assessment Committee (PRAC), which concluded that the benefits of medicines containing nomegestrol or chlormadinone outweigh the risks, provided new measures are taken to minimise the risk of meningioma.

A 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 CHMP has recommended that medicines containing high-dose nomegestrol (3.75 – 5 mg) or high-dose chlormadinone (5 – 10 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-containing 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 CHMP 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 by the PRAC 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 CHMP endorsed the PRAC's assessment of this risk.

The CHMP opinion has been sent to the European Commission, which will issue a legally binding decision valid across the EU.

[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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**Information for patients**

- Meningiomas have been reported with the use of nomegestrol- or chlormadinone-containing medicines.
- This risk, which is very low, is increased when the medicines are used at high doses (3.75 - 5 mg for nomegestrol and 5 - 10 mg for chlormadinone) and for prolonged periods of time.
- EMA is therefore recommending that these medicines should only be used at the lowest effective dose and for the shortest duration possible. Higher doses (3.75 – 5 mg nomegestrol and 5 - 10 mg chlormadinone) should only be considered if other interventions are not possible.
- You should not use or be prescribed nomegestrol- or chlormadinone-containing medicines if you have a meningioma or have had one in the past.
- Contact your doctor immediately if you experience a change in vision (seeing double or blurriness), hearing loss or ringing in the ears, loss of smell, headaches that worsen with time, memory loss, seizures and weakness in your arms or legs.
- If you are diagnosed with a meningioma while using a nomegestrol- or chlormadinone-containing medicine, your doctor will stop your treatment with the medicine.
- The risk of meningioma may decrease after you stop treatment with a nomegestrol- or chlormadinone-containing medicine.

**Information for healthcare professionals**

- Meningiomas (single and multiple) have been reported with the use of nomegestrol- or chlormadinone-containing medicines, particularly at high doses and for prolonged time. The risk increases with increasing cumulative doses.
- The use of these medicines at high doses should be restricted to situations where other interventions are considered inappropriate, and they should be used at the lowest effective dose and for the shortest duration.
- Nomegestrol- or chlormadinone-containing medicines are contraindicated in patients with meningioma or a history of meningioma.
- Patients should be monitored for signs and symptoms of meningiomas in line with clinical practice. If a patient is diagnosed with meningioma, treatment with these medicines should be permanently stopped.
- Available evidence suggests that the risk of meningioma decreases after treatment discontinuation of the nomegestrol- or chlormadinone-containing medicine.

A direct healthcare professional communication (DHPC) will be sent in due course to healthcare professionals prescribing, dispensing or administering the medicine. The DHPC will also be published on a dedicated page on the EMA website.

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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 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 CHMP 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 was first carried out by the PRAC, the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations.

The PRAC recommendations were sent to the CHMP, responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP's opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States in due course.