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Ulipristal acetate for uterine fibroids: EMA recommends restricting use

On 12 November 2020, EMA's human medicines committee (CHMP) recommended restricting use of medicines containing ulipristal acetate 5 mg (Esmya and generic medicines) as a result of cases of serious liver injury. The medicines can now only be used to treat uterine fibroids in premenopausal women for whom surgical procedures (including uterine fibroid embolisation) are not appropriate or have not worked. The medicines must not be used for controlling symptoms of uterine fibroids while awaiting surgical treatment.

Information on the risk of liver failure (requiring liver transplantation in some cases) will be added to the summary of product characteristics and the package leaflets for ulipristal acetate 5 mg medicines as well as in educational material for doctors and cards for patients.

EMA's safety committee (PRAC) review of serious liver injury with ulipristal acetate 5 mg had found that it was not possible to identify either patients most at risk of liver injury or measures that could reduce the risk. The PRAC had therefore advised that these medicines should not be marketed in the EU.

The CHMP endorsed the PRAC's assessment of the risk of liver injury. However, it considered that the benefits of ulipristal acetate 5 mg in controlling fibroids may outweigh this risk in women who have no other treatment options. As a result, the CHMP recommended that the medicine remains available to treat premenopausal women who could not have surgery (or for whom surgery had not worked).

Ulipristal acetate is also authorised as a single-dose medicine for emergency contraception (ellaOne and other trade names). No concern has been raised about liver injury with these single-dose emergency contraception medicines and this recommendation does not affect them.

The CHMP's recommendation was sent to the European Commission which has issued a legally binding decision. The use of 5-mg ulipristal acetate medicines for uterine fibroids had been suspended as a precaution while awaiting the outcome of this review.

Information for patients

- Your doctor will prescribe ulipristal acetate 5 mg medicine for treating uterine fibroids (growths in the womb that are not cancerous) only if:
  - you have not reached the menopause and
  - you cannot have an operation for the condition or the operation has not worked.

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- Serious liver injury has occurred in women taking ulipristal acetate 5 mg, which can lead to liver transplantation in a few cases. Your doctor will discuss with you whether your need for treatment outweighs this risk.
- You will have a blood test to check your liver before you take ulipristal acetate 5 mg, during your treatment and after your treatment stops.
- Read the card you have been given with your ulipristal acetate 5 mg medicine because it tells you what to do if you have any signs of liver injury.
- You must stop treatment with ulipristal acetate 5 mg and speak with your doctor immediately if you get any signs of liver injury such as yellowing of the skin, dark urine, feeling sick or vomiting.
- Speak to your doctor or pharmacist if you have any questions and concerns about your treatment.

Information for healthcare professionals

- Ulipristal acetate 5 mg medicine must only be prescribed for treating uterine fibroids in premenopausal women who cannot have surgery or uterine fibroid embolisation, or the surgical procedure has failed.
- Use of ulipristal acetate 5 mg is restricted because of reports of serious liver injury, occasionally requiring liver transplantation.
- Before treatment with ulipristal acetate 5 mg:
  - prescribers should discuss all available treatment options with women
  - prescribers should counsel women on the risk of liver failure and subsequent need for liver transplantation.
- Although risk factors for liver injury with ulipristal acetate 5 mg or specific measures to reduce risk have not been identified, healthcare professionals should follow the summary of product characteristics (including contraindications and recommendations on liver function monitoring) as well as the physician's guide to prescribing that is available for the medicine.
- Patients should be advised to monitor for signs and symptoms of liver damage.

More about the medicine

Ulipristal acetate 5 mg was authorised (as Esmya and Ulipristal Acetate Gedeon Richter) for treating moderate to severe symptoms of uterine fibroids (non-cancerous tumours of the womb) in women who had not reached the menopause. It was used either for up to 3 months before surgery to remove the fibroids or over the long-term but with treatment breaks in women who could not have surgery.

Esmya (ulipristal acetate) was authorised throughout the EU in 2012. It was the subject of a previous review in 2018. Ulipristal Acetate Gedeon Richter was authorised throughout the EU in 2018. Generic ulipristal acetate medicines have been authorised via national procedures in several EU countries under various trade names.

More information on Esmya and Ulipristal Acetate Gedeon Richter is available on the EMA website.

More about the procedure

The review of Esmya, Ulipristal Acetate Gedeon Richter and generics was initiated at the request of the European Commission, under Article 31 of Directive 2001/83/EC.

The review was first carried out by the Pharmacovigilance Risk Assessment Committee (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 Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which adopted the Agency's opinion. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 11 January 2021.