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PRAC recommends new measures to minimise risk of rare but serious liver injury with Esmya for fibroids

Regular liver function testing required during treatment

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has completed its review of Esmya (ulipristal acetate), following reports of serious liver injury. After considering all the evidence, the PRAC concluded that the medicine must not be used in women with liver problems and that certain other patients may start new treatment courses provided they have regular liver tests.

Esmya is used to treat moderate to severe symptoms of uterine fibroids (benign tumours of the womb). The medicine has been shown to be effective at reducing bleeding and anaemia, as well as the size of the fibroids.

The PRAC has concluded that Esmya may have contributed to the development of some cases of serious liver injury.[1] The Committee has therefore made the following recommendations to minimise this risk:

- Esmya must not be used in women with known liver problems.
- A liver function test should be performed before starting each treatment course and treatment must not be started if liver enzyme levels are more than 2 times the upper limit of normal.
- Liver function tests should be performed once a month during the first two treatment courses and two to four weeks after stopping treatment. If the test is abnormal (liver enzyme levels more than 3 times the upper limit of normal), the doctor should stop treatment and closely monitor the patient.
- Esmya should be used for more than one treatment course only in women who are not eligible for surgery. Women who are about to have surgery should continue to use only one course.
- A card will be included in the box of the medicine to inform patients about the need for liver monitoring, and to contact their doctor should they develop symptoms of liver injury (such as tiredness, yellowing of the skin, darkening of the urine, nausea and vomiting).
- Studies should be performed to determine the effects of Esmya on the liver and whether these measures are effectively minimising the risks.

[1] In 8 cases of serious liver injury, a role of Esmya in contributing to these cases is possible. It is estimated that around 765,000 patients have been treated with Esmya to date.

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In February 2018, while the review was ongoing, the PRAC had issued temporary recommendations that no new patients should be started on Esmya. Having finalised its review, the Committee has now concluded that new patients can start treatment in line with the above recommendations to minimise the risk of liver injury.

The PRAC's recommendations will now be forwarded to the Committee for Medicinal Products for Human Use (CHMP) for the adoption of EMA's final opinion, and this will then go to the European Commission for a final legal decision. A letter will be sent to doctors to inform them of the new restrictions of use, which will become applicable after a Commission decision is issued.

More about the medicine

Esmya was authorised in the EU in 2012 for the treatment of moderate to severe symptoms of uterine fibroids, which are benign (non-cancerous) tumours of the womb, in women who have not reached the menopause.

The active substance in Esmya, ulipristal acetate, works by attaching to the targets on cells (receptors) that the hormone progesterone normally attaches to, preventing progesterone from having its effect. Since progesterone may promote the growth of fibroids, by preventing the effects of progesterone ulipristal acetate reduces the size of the fibroids.

More information on Esmya can be found here.

Ulipristal acetate is also the active substance of a single-dose medicine authorised for emergency contraception, ellaOne. No cases of serious liver injury have been reported with ellaOne and there are no concerns with this medicine at this time.

More about the procedure

The review of Esmya was initiated at the request of European Commission on 30 November 2017, under Article 20 of Regulation (EC) No 726/2004.

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 made a set of recommendations.

On 8 February 2018, while the review was ongoing, the PRAC issued temporary recommendations.

The PRAC's final recommendations will now be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt an 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. The new restrictions on the use of Esmya will become applicable after a Commission decision is issued.