

1st August 2018

New contraindication, requirements for liver monitoring and restricted indication for Esmya (ulipristal acetate)

Dear Healthcare Professional,

Gedeon Richter Plc. in agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

As treatment with Esmya may carry a risk of serious liver injury, the following measures apply from now on:

Restricted indication

- For the intermittent treatment of moderate to severe symptoms of uterine fibroids, Esmya should only be used in women of reproductive age and if they are not eligible for surgical treatment.
- Esmya continues to be indicated for one treatment course (up to 3-months) of pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age.

New contraindication

- Esmya is contraindicated in patients with underlying liver disorders.

Requirements for liver function monitoring

- Liver function tests should be performed before starting each treatment course, monthly during the first 2 treatment courses, and 2-4 weeks after stopping treatment.
- Do not start Esmya treatment if levels of alanine transaminase (ALT) or aspartate aminotransferase (AST) are > 2 times the upper limit of normal (ULN) (isolated or in combination with bilirubin > 2 x ULN)
- Stop treatment in patients whose ALT or AST levels are > 3 x ULN.

Advice to patients

- Advise patients to look out for signs and symptoms of liver injury. In case of signs or symptoms suggestive of such injury, treatment should be stopped. Patients should be investigated immediately including liver function testing.

Background on the safety concern

Four cases of serious liver injury leading to a hepatic transplantation and additional cases of hepatic impairment have been reported for Esmya (ulipristal acetate). In February 2018, as an interim precaution, EMA recommended that treatment with Esmya should not be initiated in new patients and in patients under intermittent treatment who have completed a previous treatment course. The risk of liver injury with Esmya has been further evaluated. It has been concluded that Esmya (ulipristal acetate) may carry a risk for serious liver injury. While uncertainties around causality remain, the very serious outcome of the reported cases of liver injury is recognised. Balancing this to the benefits of Esmya treatment of moderate to severe symptoms of uterine fibroids, EMA has concluded that the indicated population should be restricted for safety reasons, and measures to minimise a risk for liver injury are necessary.

While EMA has now concluded that certain patients can be treated, physicians should carefully consider if Esmya is an appropriate option for their patients, in view of the restricted indication, the new contraindication and the liver monitoring to be undertaken as described above. It has also been clarified that the pre-operative treatment comprises one treatment course. In addition, Esmya treatment is to be initiated and supervised by physicians experienced in the diagnosis and treatment of uterine fibroids. These measures will be introduced in the summary of product characteristics of Esmya, and the physician's guide of the medicine will also be updated. These can be found on the eMC website: <https://www.medicines.org.uk/emc/product/3951>.

It is important to tell the patients about the risk of serious liver injury and the possible signs and symptoms of liver injury. If they experience such symptoms they should stop treatment, and contact a doctor immediately. Patients should also be informed of the need for liver monitoring tests before, during and after treatment courses. For this reason, the card included in the medicine's package should be read carefully by patients.

Action for Pharmacists

Pharmacists are kindly requested to hand out a copy of the Patient Card with each pack dispensed. A downloadable version of the Patient Card is available for printing from the eMC website at <https://www.medicines.org.uk/emc/product/3951/rmms>. If printing facilities are not available, two hard copies of the patient card are enclosed with this letter. For additional hard copies, please contact the company (details below). This will only be required until packs with the pre-inserted Patient Card reach the market.

Call for reporting

Any suspected adverse reactions should be reported to: MHRA Yellow Card Scheme; Website: www.mhra.gov.uk/yellowcard.

Company contact point

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Yours sincerely,



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