GEDEON RICHTER

Direct Healthcare Professional Communication

23 March 2020

Esmya 5mg Tablets (ulipristal acetate 5 mg) for uterine fibroids not to be used during ongoing review of liver injury risk

Dear Healthcare Professional,

Gedeon Richter UK Ltd 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:

EMA is reviewing the benefits and risks with ulipristal acetate 5 mg for the treatment of uterine fibroids. The review was initiated following one new case report of serious liver injury leading to transplantation in a patient treated with ulipristal acetate 5mg. The following temporary measures have been agreed until the review is finalised.

Summary

- **Ulipristal acetate 5 mg is temporarily withdrawn from the market during the ongoing review.**
- **Ulipristal acetate 5 mg should not be initiated in new patients.**
- **For patients on treatment with ulipristal acetate 5 mg the treatment must be stopped.**
- **Liver monitoring should be performed within 2-4 weeks after treatment has stopped.**
- **Patients should be advised to immediately report signs and symptoms of liver injury (such as nausea, vomiting, right hypochondrial pain, anorexia, asthenia, jaundice), which could occur after stopping treatment.**

Background on the safety concern

Ulipristal acetate 5 mg is currently approved in the EU for the following indications:

- ulipristal acetate is indicated for one treatment course of pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age
- ulipristal acetate is indicated for intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age who are not eligible for surgery.

In 2018, the Pharmacovigilance Risk Assessment Committee (PRAC) finalised a review of Esmya 5 mg (ulipristal acetate) initiated due to reports of serious liver injury, including four cases requiring liver transplantation. To minimise the risk, the use of ulipristal 5 mg was restricted and recommendations for regular liver function tests were issued. In December 2019, EMA was informed of a new case of serious liver injury leading to liver transplantation following treatment with Esmya 5mg (ulipristal acetate).

In view of the seriousness of this case and its occurrence, despite adherence to the risk minimisation measures implemented in 2018, ulipristal acetate 5 mg-containing products must not be used while a review of the benefits and risks of these products is ongoing at EU level.

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Ulipristal acetate is also authorised as a single-dose medicine for emergency contraception. This review does not affect the single-dose ulipristal acetate emergency contraceptive (ellaOne and other trade names) and there is no concern of liver injury with these medicines.

Call for reporting

Any suspected adverse drug reactions should be reported through MHRA Yellow Card Scheme online through Yellow Card website, https://yellowcard.mhra.gov.uk/ or Yellow Card app available on Apple App Store or Google Play store.

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- by downloading and printing a form from the Yellow Card website (see link above)

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates and product brand name.

Company contact point

Any suspected adverse reactions should also be reported to the company:

Gedeon Richter UK Ltd
127 Shirland Road
London W9 2EP

Tel: +44 (0)207 604 8806

Email : medinfo.uk@gedeonrichter.eu

Annexes

The link below will connect with the area on the EMA's website, which provides further information on this issue.

https://www.ema.europa.eu/en/medicines/human/referrals/ulipristal-acetate-5mg-medicinal-products

Yours faithfully

Mr. Tamás Neubauer

Managing Director

Gedeon Richter UK Ltd