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Direct Healthcare Professional Communication

18th March 2020

Ulipristal acetate 5 mg for uterine fibroids not to be used during ongoing review of liver injury risk

Dear Healthcare Professional,

Gedeon Richter Plc in agreement with the European Medicines Agency (EMA) and the Malta Medicines Authority 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 Esmya 5 mg (ulipristal acetate). 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- **Ulipristal acetate 5 mg is temporarily withdrawn from the market during the ongoing review.**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 (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.

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

Healthcare professionals should report any adverse reactions associated with the use of ulipristal acetate 5 mg in accordance with the national spontaneous reporting system on Website: *www.medicinesauthority.gov.mt/adrportal*.

Company contact point

For any further information kindly send an email to pv@alfredgera.com.

Kind regards,

Jurgen Azzopardi

Resonsible Person