



GEDEON RICHTER

Direct Healthcare Professional Communication

29 January 2021

Esmya (ulipristal acetate) 5 mg: Indications for uterine fibroids restricted due to concerns of severe liver injury

Dear Healthcare Professional,

Gedeon Richter Plc. in agreement with the European Medicines Agency (EMA), and the Medicines and Healthcare product Regulatory Agency (MHRA) would like to inform you about new restrictions on the use of ulipristal acetate 5 mg and additional measures to minimise the risk of serious liver injury:

Summary

- **Cases of serious liver injury (including those necessitating liver transplantation) have followed the use of ulipristal acetate 5 mg for treating moderate to severe symptoms of uterine fibroids.**
- **Ulipristal acetate 5 mg must now be used only for intermittent treatment of moderate to severe symptoms of uterine fibroids in women who have not reached menopause and when uterine fibroid embolisation or surgery are not suitable or have failed.**
- **The physician must discuss with patients the risks and benefits of available alternative treatments so patients can make an informed decision.**
- **The risks of ulipristal acetate 5 mg should be fully explained to patients, especially the risk of liver injury, which could in rare cases lead to liver transplantation.**
- **Patients should be informed about possible signs and symptoms of liver injury, and that if they have such symptoms, they must stop treatment and contact their doctor immediately.**

Background on the safety concern

In 2018, a review of ulipristal acetate 5 mg was carried out in light of four cases of serious liver injury leading to liver transplantation. As a result, several measures were recommended to minimise the risk of serious liver injury, including restriction of the indication, a new contraindication in patients with an underlying liver disorder, and liver function monitoring.

Recently, a new (fifth) case of serious liver injury leading to liver transplantation was reported. Having ruled out other plausible aetiologies, ulipristal acetate was considered to be the most likely cause of acute hepatitis leading to acute liver failure and liver transplantation.

The marketing of ulipristal acetate 5mg was suspended while a second European review of the risk of liver injury took place. The review concluded that in addition to the previous measures, the indication of ulipristal acetate 5 mg should be further restricted. The risk of severe liver injury does not justify its use for pre-operative treatment of uterine fibroids.

Prior to prescribing, the prescriber must carefully explain the benefits and risks of ulipristal acetate 5 mg to patients as well as the benefits and risks of alternative treatments so that the patient can make a fully informed decision about the treatment which is most appropriate for her. In particular patients should be told about the risk of liver injury which has in rare cases required liver transplant. Patients should be told the signs and symptoms of liver injury and that if they experience such symptoms, they should stop treatment and contact their doctor immediately. Patients should also be informed of the need for liver monitoring before, during and after treatment courses. For this reason, patients should carefully read the patient alert card included in the medicine's package.

These measures will be introduced in the summary of product characteristics (SmPC) of ulipristal acetate 5 mg. The Physician's guide and the patient alert card will also be updated.

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Call for reporting

Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme.

Please report suspected ADRs electronically via:

- the Yellow Card website <https://yellowcard.mhra.gov.uk/>
- the free Yellow Card app available from the [Apple App Store](#) or [Google Play Store](#)
- some clinical IT systems (EMIS/SystemOne/Vision/MiDatabank/Ulysses) for healthcare professionals.

If there is no online access to report a suspected side effect to the Yellow Card Scheme, call 0800 731 6789 for free, Monday to Friday between 10am and 2pm. You can leave a message outside of these hours.

Please report all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.

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 may also be reported to the company:

Address: 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.

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