Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

7 August 2018

DDL_Esmya_Aug-2018-UPDATE

Dear Healthcare Professional,

Esmya (ulipristal acetate) for symptoms of uterine fibroids: restrictions to use and requirement to check liver function before, during and after treatment

I am writing to inform you of the restrictions to the use of Esmya for the symptoms of uterine fibroids following completion of an EU review to investigate the link between Esmya and cases of serious liver injury.

These restrictions replace the temporary safety measures, including no new patients to be prescribed Esmya, introduced in February 2018 while the review of the association between Esmya and liver damage was ongoing (see DDL_Esmya-Feb-2018-alert.pdf).

Summary

Rare but serious cases of liver injury, including cases of hepatic failure requiring liver transplantation, have been reported worldwide in women treated with Esmya for the symptoms of uterine fibroids. An EU review of the available data concluded that Esmya may have contributed to the onset of some of the 8 cases of serious liver injury and has now finalised with a number of measures to minimise this risk. In particular, more than one treatment course is now authorised only in women who are not eligible for surgery, and liver function monitoring is to be carried out in all women treated with Esmya (see below).

Restricted indication and new contraindication

- Esmya is now indicated for:
  - the intermittent treatment[1] of moderate to severe symptoms of uterine fibroids in women of reproductive age who are not eligible for surgery
  - one course of pre-operative treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age

- Esmya treatment is to be initiated and supervised by a physician experienced in the diagnosis and treatment of uterine fibroids
- Esmya is contraindicated in women with underlying liver disorders

Liver function monitoring

- *Before initiation of each treatment course*: perform liver function tests; do not initiate Esmya in women with baseline alanine transaminase (ALT) or aspartate aminotransferase (AST) more that 2-times the upper limit of normal [ULN]
- *During the first 2 treatment courses*: perform liver function tests every month
- *For further treatment courses*: perform liver function tests once before each new course and when clinically indicated
- *At the end of each treatment course:* perform liver function tests after 2–4 weeks
- Stop Esmya treatment and closely monitor women with ALT or AST more than 3-times ULN; consider the need for specialist hepatology referral

[1]Each treatment course should not exceed 3 months and should only be repeated after a break in treatment. See Summary of Product Characteristics for method of administration.

Discuss the risk of liver damage with Esmya with women and report any suspected adverse drug reactions

- Before initiating Esmya, discuss with women the rare risk of liver damage and the need for liver function testing before, during, and after treatment courses
- Pharmacists should provide the new patient card to women when dispensing Esmya; copies of this card were included in the letter sent by post from Gedeon Richter on 1 August 2018 and are available online by searching medicines.org.uk/emc for Esmya and selecting Risk Materials; this will only be required until packs with the pre-inserted patient card reach the market
- Advise women to seek urgent medical attention if they develop any symptoms or signs of liver injury (such as unusual tiredness, yellowing of the skin, darkening of the urine, nausea and vomiting)
- Report any suspected adverse drug reaction to Esmya on a Yellow Card without delay

ellaOne

The emergency contraceptive ellaOne also contains ulipristal acetate in a single dose of 30mg. No cases of serious liver injury have been reported with ellaOne since it was authorised in the EU in 2009 and there are no concerns or changes to its use at this time.

Background

Approximately 20,400 treatment courses of Esmya were dispensed in the UK between 1 October 2016 and 30 September 2017.[2] To date, we have received 1 suspected adverse drug reaction report of hepatitis, 1 of hepatic fibrosis, 1 of non-alcoholic fatty liver, and 8 of abnormal liver function tests associated with the use of Esmya in the UK.

The EU-wide review of Esmya was started in December 2017 following reports of serious liver injury in women using the medicine. Further information about the review can be found on the European Medicines Agency website http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Esmya_20/Opinion_provided_by_Committee_for_Medicinal_Products_for_Human_Use/WC500249905.pdf.

Yours sincerely,

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[2]Data derived from IQVIA MIDAS 10/2016-09/2017 by MHRA, January 2018. The usage estimate is based on the assumption that each treatment course was of 3 months' duration. The number of courses each woman takes may vary between 1 and 4 courses. The number of courses quoted is a broad estimation and is not therefore equivalent to the number of women who used Esmya.