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

Dear Healthcare Professional,

<MAHs> in agreement with the European Medicines Agency (EMA) and the <National Competent 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- **Ulipristal acetate 5 mg is temporarily withdrawn from the market during the ongoing review.**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 *<include the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system>.*

Company contact point

Local contact details to be added on a country by country basis

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Ulipristal acetate 5 mg-containing medicinal products
Marketing authorisation holder(s)	Various In cases where the DHPC concerns several marketing authorisation holders of the same active substance or is part of a class review, it is strongly encouraged that a single consistent message is sent to healthcare professionals in each EU Member State. All concerned marketing authorisation holders in each Member State are strongly encouraged to collaborate, so that a single DHPC is prepared and circulated in each Member State. The letter circulated in each Member State should cover all active substance-containing products authorised in that Member State. It is encouraged that the originator marketing authorisation holder (where available) in each Member State acts as the contact point for the national competent authority, on behalf of the other concerned marketing authorisation holders in the same Member State.
Safety concern and purpose of the communication	To inform prescribers and pharmacists of the suspension of products containing ulipristal acetate 5 mg due to a new case of an acute liver failure leading to transplantation reported with Esmya (ulipristal acetate)
DHPC recipients	Specialists in Obstetrics & Gynaecology, specialists in Hepatology & Gastroenterology, General Practitioners, Professional societies in gynaecology and in hepatology/gastroenterology, Pharmacists. Target groups should be further defined and agreed at national level, depending on national health care systems.
Member States where the DHPC will be distributed	All EU Member States where products are authorised/marketed

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	12 March 2020
Submission of translated DHPCs to the national competent authorities for review	16 March 2020
Agreement of translations by national competent authorities	18 March 2020
Dissemination of DHPC	23 March 2020