# Esmya review conclusions: EMA recommends new measures to minimise the risk of liver injury in treated women.

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## Information on Esmya

- Esmya (ulipristal acetate) is used to treat moderate to severe symptoms of uterine fibroids (benign tumours of the womb). The medicine has been shown to be effective at reducing bleeding and anaemia associated with uterine fibroids, as well as the size of the fibroids.
- Ulipristal acetate works by attaching to the receptors that the hormone progesterone normally attaches to, preventing progesterone from having its effect. Since progesterone may promote the growth of fibroids, by preventing the effects of progesterone ulipristal acetate reduces the size of the fibroids.

In Malta Esmya is authorised through the centralised procedure.

## Information about EMA's review conclusion on Esmya and PRAC's recommendations

The review of Esmya was initiated on 30th November 2017 at the request of European Commission under Article 20 of Regulation (EC) No 726/2004. The review of Esmya was carried out by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) which concluded that Esmya may have contributed to the development of some cases of serious liver injury. The EMA's recommended implemented measures are:

- The use of Esmya should be restricted to women not suffering from liver disease
- The use of Esmya for more than one treatment course should be restricted to women who are not eligible for surgery
- Liver tests should be performed before, during and after stopping the treatment
- Patients' card should be given to patients to inform them about the need of liver monitoring and to contact their doctor whether they would develop symptoms of liver injury
- Studies should be performed to determine the effects of Esmya on the liver and whether the new measures are effective in minimising the risks

The PRAC's recommendations have been endorsed by EMA's Committee for Medicinal Products for Human Use (CHMP) and will be sent to the European Commission for a final legal decision which will be issued in due course

## In Malta

### For Healthcare Professionals

Four cases of serious liver injury leading to hepatic transplantation and additional cases of hepatic injury have been reported in patients treated with Esmya (ulipristal acetate). Therefore, EMA after the review performed on Esmya, has made the following recommendations:

- Patients with underlying liver disorders should not be started with Esmya
- The indication for Esmya is restricted to the intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women of reproductive age: Esmya should only be used in women who are not eligible for surgical treatment. Esmya continues to be indicated for one course (lasting up to 3 months) of pre-operative treatment for moderate to severe symptoms of uterine fibroids in adult women of reproductive age
- Liver function tests should be performed before starting a treatment with Esmya, monthly during the first 2 treatment courses, and thereafter as clinically indicated. Liver testing should be performed again 2-4 weeks after stopping treatment
- Esmya should not be started if levels of alanine transaminase (ALT) or aspartate aminotransferase (AST) are more than 2 times the upper limit of normal (ULN).
- Treatment should be stopped in patients with ALT or AST levels more than 3 times ULN.

Healthcare professionals should advise their patients about the signs and symptoms of liver injury and the action to take should they occur. In case of signs or symptoms suggestive of such injury, treatment should be stopped. Patients should be investigated immediately including liver function testing.

Healthcare professionals prescribing Esmya in the EU will receive an additional letter with further details once a European Commission decision has been issued. A DHPC letter about the safety concern was disseminated to HCPs in Malta in February 2018. Archived DHPC letters are available online at http://www.medicinesauthority.gov.mt/dhpc

### Advice for Patients

- The medicine Esmya, used to treat uterine fibroids, has been reviewed because cases of serious liver problems have occurred in women taking the medicine, including four cases that resulted in liver transplantation
- Esmya will not be prescribed to you if you have liver problems

- A liver test will be performed before you start treatment and if the test is abnormal, treatment with Esmya will not be started
- You will also have liver tests during treatment and after treatment has stopped
- If no liver problems are detected, a single course of Esmya can be used in women who are about to have surgery for their fibroids; Esmya can be used for more than one course only in women who cannot have surgery
- A card will be included in the package of the medicine with information on the risk of liver injury and the need for liver monitoring
- You should stop treatment and contact your doctor immediately if you develop symptoms of liver injury (such as tiredness, yellowing of the skin, darkening of the urine, nausea and vomiting)
- If you have any questions or concern about your treatment, speak to your doctor or pharmacist

For more information, please see the European Medicines Agency's Esmya referral webpage

**Reporting Adverse Drug Reactions**

Healthcare professionals and patients are encouraged to maintain vigilance on Esmya. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form (available from: **http://www.medicinesauthority.gov.mt/adrportal**) and sent by mail to Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or email to postlicensing.medicinesauthority@gov.mt or to the marketing authorisation holder or their local representatives.

**Post-Licensing Directorate**
**Medicines Authority**

***Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.***

**Feedback Form**

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

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Malta Life Sciences Park

San Ġwann SĠN 3000