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# 衛生福利部食品藥物管理署　函

機關地址：11561 臺北市南港區昆陽街161-2號
傳　　真：02-2787-7498
聯絡人及電話：廖家麗 02-2787-7815
電子郵件信箱：liaochialee@fda.gov.tw

10688
台北市大安區安和路一段29號9樓

受文者：中華民國醫師公會全國聯合會

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附件：EMA警訊

主旨：有關「恩惜膜5毫克錠劑(Esmya)」藥品之臨床效益及風險再評估相關事宜，詳如說明段，請查照。

說明：

一、因國外接獲數件使用Esmya®（ulipristal acetate）藥品後發生嚴重肝損傷之不良反應通報。本署擬重新評估旨揭藥品之臨床效益及風險。另查，歐盟目前亦在評估該藥品之安全性(詳見附件一)。

二、貴學會倘有下列意見，請於107年6月6日前檢送至本署，並檢附相關文獻資料，逾期未能提具資料者，視同無意見。

(一)臨床效益：目前我國所核准該藥品之適應症是否為國內目前常規治療選擇或第一線用藥，是否有其他替代藥品或療法，倘限縮於沒有其他適當的治療選項下使用，是否合理。

(二)臨床風險：臨床使用經驗是否有該藥品導致嚴重肝損傷的不良反應相關案例？是否有預防或降低風險的方法？

(三)其他意見或建議。

正本：社團法人臺灣臨床藥學會、台灣消化系醫學會、台灣婦癌醫學會、台灣臨床腫瘤醫學會、台灣婦產科醫學會、中華民國醫師公會全國聯合會、台灣醫院協會、台灣藥物臨床研究協會、台灣內科醫學會、台灣社區醫院學會、中華民國基層醫療協會
副本：全國藥物不良反應通報中心

署長 吳秀梅

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

9 February 2018
EMA/152535/2018 – Corr. [1]

# Women taking Esmya for uterine fibroids to have regular liver tests while EMA review is ongoing

## No new patients should start treatment for the time being

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) is currently reviewing the benefits and risks with Esmya, following reports of serious liver injury, including liver failure leading to transplantation.

As a temporary measure while the review is ongoing, the PRAC has recommended regular liver monitoring for women taking Esmya for uterine fibroids.

All women taking Esmya should have a liver function test at least once a month during treatment. If the test is abnormal (liver enzyme levels more than 2 times the upper limit of normal), the healthcare professional should stop treatment and closely monitor the patient. Liver tests should be repeated 2 to 4 weeks after stopping treatment.

The PRAC is also recommending that no new patients should be started on Esmya and no patients who have completed a course of treatment should start another one for the time being.

A link between Esmya and cases of serious liver injury is under review. These recommendations are temporary measures to protect patients' health, pending the conclusion of the review of Esmya which started on 30 November 2017.

**Information for patients**

- Esmya, used to treat uterine fibroids, is being reviewed because cases of serious liver problems have occurred in women taking the medicine.
- As a precaution, while taking Esmya you will be required to have blood tests to check that your liver is working well. If the tests indicate that you have a liver problem, your treatment will be stopped.
- If you have nausea (feeling sick), vomiting, upper belly pain, lack of appetite, tiredness or yellowing of the eyes or skin, contact your doctor immediately as these could be signs of liver problems.
- If you were about to start treatment with Esmya or start a new course of treatment, your doctor will put your treatment on hold until EMA's review of the medicine is complete.

[1] Start of the procedure date on page 1 corrected from December 2017 to 30 November 2017.

30 Churchill Place • Canary Wharf • London E14 5EU • United Kingdom
**Telephone** +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
**Send a question via our website** www.ema.europa.eu/contact

- If your treatment is stopped, your doctor will check how well your liver is working 2 to 4 weeks after you stop taking Esmya.

**Information for healthcare professionals**

Following reports of liver injury and hepatic failure with Esmya, EMA has made the following temporary recommendations:

- Do not start new patients on Esmya or new treatment courses in patients who have already completed a previous one.
- Perform liver function tests at least once a month for all patients taking Esmya. If the patient develops transaminase levels more than 2 times the upper limit of normal, stop treatment and monitor the patient closely. Liver test should be repeated 2 to 4 weeks after stopping treatment.
- For any patient with signs or symptoms consistent with liver injury (such as nausea, vomiting, right hypochondrial pain, anorexia, asthenia, jaundice), check transaminase levels immediately. If transaminase levels are more than 2 times the upper limit of normal, stop treatment and closely monitor the patient.
- Advise your patients about the signs and symptoms of liver injury.

These recommendations are temporary measures, pending the conclusion of an ongoing EMA review of Esmya. Healthcare professionals prescribing Esmya in the EU will receive a letter with further details.

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**More about the medicine**

Esmya was authorised in the EU in 2012 for the treatment of moderate to severe symptoms of uterine fibroids, which are non-cancerous (benign) tumours of the womb, in women who have not reached the menopause. It is used for up to 3 months before women undergo surgery to remove the fibroids and can also be used long-term but with treatment breaks in other women.

The active substance in Esmya, ulipristal acetate, works by attaching to the targets on cells (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.

More information on Esmya can be found here.

Ulipristal acetate is also the active substance of a single-dose medicine authorised for emergency contraception, ellaOne. No cases of serious liver injury have been reported with ellaOne and there are no concerns with this medicine at this time.

**More about the procedure**

The review of Esmya was initiated at the request of European Commission on 30 November 2017, under Article 20 of Regulation (EC) No 726/2004.

The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations.

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On 8 February 2018, while the review was ongoing, the PRAC issue temporary recommendations.

The PRAC's final recommendations will be forwarded to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use, which will adopt an opinion. The final stage of the review procedure is the adoption by the European Commission of a legally binding decision applicable in all EU Member States.