Article 20 of Regulation (EC) No 726/2004 resulting from pharmacovigilance data

Procedure No: EMEA/H/A-20/1460/C/2041/0043

Esmya (INN: ulipristal acetate)

Divergent statement:

The following CHMP Members consider that even if the agreed PI changes and RMP update are implemented, the benefit risk ratio of Esmya is not favourable based on the following grounds:

Rare but very severe hepatic failures occurred in patients treated with Esmya. A causal relationship is far from excluded and is even likely in some cases. There are no elements to define a toxic mechanism or risk factors that could have predicted these events and that could be a basis for an efficient prevention strategy.

Esmya demonstrated a benefit in controlling symptoms (bleeding) in uterine fibroma. There is no convincing evidence that treatment with Esmya will avoid surgery or show a favourable Benefit/Risk balance in the long term. Regarding short term treatment (<3 months) in a pre-operative context, according to the experts from ad hoc expert group conclusions, available medical alternatives (such as GnRH agonists) demonstrated similar benefits without any relevant risk of hepatic failure and would be a preferable option for short term treatment for a pre-operative purpose.

The benefits established with Esmya in the broad modified indications accepted by the CHMP majority are limited as efficacy and safety have not been established with certainty in the proposed population. In pre-operative treatment, alternatives exist and Esmya is no longer considered as a suitable medicinal option. For intermittent treatment of fibroids, only a last line indication, to control severe symptoms of the disease when surgery is impossible and when other medical treatments are not an option, would have been acceptable in light of the severe risks observed.

The amendments adopted by the CHMP majority to the product information and RMP will unfortunately not prevent the hepatic risk and not limit these concerns.

Therefore, we consider that in the CHMP's proposed indications for Esmya, the risk (especially hepatic) continue to outweigh benefit leading to a negative B/R balance.

CHMP Member expressing a divergent opinion:

- Joseph Emmerich

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CHMP Member expressing a divergent opinion:

- Svein Rune Andersen