EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Caitlin Dean
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EMA/516514/2019
Stakeholders and Communication Division

Dear Ms Dean,

Thank you for your follow-up letter of 12 September 2019 addressed to the PRAC regarding the use of ondansetron in pregnant women with hyperemesis gravidarum (HG).

We fully understand the concerns expressed by your organisation and others regarding the burden HG poses to women and the limited treatment options. Please allow us to provide some additional clarifications to our letter of 12 September.

The recommendation not to use ondansetron in pregnancy by EMA's safety Committee PRAC only applies to its licensed indications and was based on new data on orofacial malformations and cardiac malformations when used in the first trimester of pregnancy (https://www.ema.europa.eu/en/documents/prac-recommendation/prac-recommendations-signals-adopted-8-11-july-2019-prac-meeting_en.pdf).

We understand that ondansetron is widely used to treat HG and that it is recommended in treatment guidelines. However, ondansetron is not authorised for use in HG and this use is therefore not reflected in the SmPC and considered off-label. A use of a medicine can only be reflected in the SmPC if this is requested by the company and subsequently assessed by the regulator. In case of ondansetron, the company did not apply for authorisation for HG.

In this context treatment guidelines are wider as they advise on clinical practice and may therefore provide more information, including on the use in indications that do not always reflect authorised uses as per the SmPC.

To ensure that the SmPC contains the latest scientific data to allow healthcare professionals and patients to take well informed decisions about the benefits and risks of authorised uses of the medicine, PRAC recommended to add information in section 4.6 of the SmPC on the magnitude of the risk of orofacial malformations. It further advised that the SmPC, which already warns that use of ondansetron in pregnancy is not recommended, should be updated to advise against using it for its authorised indications in the first trimester. By definition, neither the benefits nor the risks of off-label

use are covered by the SmPC, and the benefit-risk calculation for different uses can vary enormously. The principle that the risks to the unborn child when taking a medicine during pregnancy have to be weighed against the risks to the mother and child of not taking the medicine still apply. For the use of medicines outside their standard licensed indications this is a matter of clinical judgment and expertise based on an individual benefit-risk assessment.

PRAC's recommendation reflects the current knowledge, based on PRAC's assessment of published epidemiological studies and EMA will continue to monitor the safety of ondansetron through its routine monitoring activities and should any new data arise, EMA will take necessary regulatory action.

In order to help with gathering new information, EMA at the request of PRAC will collect data on the use of ondansetron in pregnancy in several EU member states.

We would also like to offer the possibility to schedule a teleconference with you and representatives of other organisations to clarify the issue further. Please let us know if you would be interested and we can schedule a call. Please kindly liaise with my colleague Justina Januskiene who can be contacted on the following email address: Justina.januskiene@ema.europa.eu.

Kind regards,

Sabine Straus PhD MSc

PRAC Chair