EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): perampanel

Procedure No. EMEA/H/C/PSUSA/00009255/201907

Period covered by the PSUR:21/07/2018 to 21/07/2019

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for perampanel, the scientific conclusions of CHMP are as follows:

Hepatotoxicity

In view of available data on hepatotoxicity from clinical trials, literature data, spontaneous reports with plausible temporality including in 12 serious cases a positive de-challenge and in 1 serious case a positive re-challenge, a causal relationship between perampanel and hepatotoxicity could not be excluded. The PRAC concluded that the product information of products containing perampanel should be amended accordingly.

Hormonal contraceptives

One case of pregnancy was reported where the patient was noted to be using a subcutaneous contraceptive device. Perampanel is a weak inducer of CYP3A4/5 and is known to reduce the exposure to levonorgestrel by 40% and thus impair the efficacy of the contraceptive method. This finding is reasonably relevant for all hormonal contraceptives containing progestins. Currently the Product information of perampanel, only mentions the possible lack of efficacy with progestatin-containing oral contraceptive whereas, all hormonal contraceptives, not only oral, but also implants, patches are concerned. The Summary of Product Characteristic (SmPC) and the package leaflet (PIL) should be amended accordingly.

Stevens - Johnson syndrome

Three cases of Stevens-Johnson syndrome (SJS) were retrieved during the period of this PSUR. One case did not bring enough information and carbamazepine was introduced concomitantly to perampanel. The second case had a confirmed diagnosis of SJS but the chronology was unclear with an unknown outcome. The last case had a suggestive time to onset for perampanel (9 days) and a positive dechallenge and was considered possibly related to perampanel (score of Alden: 3). This case provides sufficient data to warrant an update to the Summary of Product Characteristic (SmPC) and the package leaflet (PIL) to reflect the risk of SJS according to the guideline "Severe Cutaneous Adverse Reactions (EMA/PRAC/710714/2017).

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for perampanel the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing perampanel is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.