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Committee for Medicinal Products for Human Use (CHMP)

Ivemend

International non-proprietary name: fosaprepitant

Procedure No. EMEA/H/C/000743/PSUV/0022

Period covered by the PSUR: 26.03.2012 – 25.03.2013

Scientific conclusions and grounds recommending the variation to the terms of the Marketing Authorisation

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR for Ivemend, the scientific conclusions of PRAC are as follows:

During the process of evaluating a signal of encephalopathy, it was noted that more than 50% of the encephalopathy cases were due to a potential drug-drug interaction between aprepitant and ifosfamide. Due to this new signal, the MAH has initiated a cumulative review of cases in which ifosfamide was co-administered with aprepitant. The available scientific information suggests that drug-drug interactions may lead to altered ifosfamide metabolism through enzyme induction or competition. Aprepitant is a substrate, a weak-to-moderate (dose-dependent) inhibitor, and a mild/modest inducer of CYP3A4. As a moderate inhibitor of CYP3A4 at a dose of 125 mg/80 mg, aprepitant may increase plasma concentrations of concomitantly administered oral medications that are metabolized through CYP3A4. Accordingly, the MAH has opened a new signal evaluation for drug-drug interaction.

The post-marketing data and available data suggest a possible drug-drug interaction between ifosfamide and aprepitant that may contribute to the observed neurotoxicity.

Based on the presented data including review of literature, the Drug Interaction Section of the product will be revised to include information regarding a possible drug-drug interaction between aprepitant and ifosfamide.

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

Grounds recommending the variation to the terms of the Marketing Authorisation

On the basis of the scientific conclusions for Ivemend, the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing the active substance fosaprepitant is favourable subject to the proposed changes to the product information.

The CHMP recommends that the terms of the Marketing Authorisation should be varied.