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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): betaine anhydrous (centrally authorised product only)

Procedure No. EMEA/H/C/PSUSA/00000390/201602

Period covered by the PSUR: 01 March 2015 to 28 February 2016

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for betaine anhydrous (centrally authorised product only), the scientific conclusions of CHMP are as follows:

Based on an analysis by the Marketing Authorisation Holder of the most frequent off-label use with regard to dosing, the PRAC agreed that dose recommendations in section 4.2 of the Summary of Product Characteristic should be updated. Evaluation of data showed that there should be a distinction between different subtypes of homocystinurea. Whereas for patients with remethylation disorders higher than the recommended doses were used, patients with Cystathionine β-synthase (CBS) deficiency were slightly underdosed. Although overall betaine anhydrous is well tolerated there is the risk of hypermethioninaemia in CBS deficient patients, particularly when overdosed. Methionine levels should be closely monitored in these patients.

In addition, the recommended total daily dose in both adult and paediatric patients is 100 mg/kg/day given in 2 doses daily. However, the dose should be individually titrated according to plasma levels of homocysteine and methionine. In some patients doses above 200 mg/ kg/day were needed to reach therapeutic goals.

Therefore, in view of the data presented in the reviewed PSUSA, the PRAC considered that changes to the product information of medicinal products containing betaine anhydrous were warranted.

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 betaine anhydrous (centrally authorised product only) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing betaine anhydrous (centrally authorised product only) 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.