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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): anagrelide

Procedure No. EMEA/H/C/PSUSA/00000208/201609

Period covered by the PSUR: 14 September 2015 to 13 September 2016

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Scientific conclusions

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

During the reporting period, nine new cases were retrieved through the search with the SMQ for pulmonary hypertension, all serious. Pulmonary hypertension is part of the known safety profile for anagrelide, currently listed in section 4.8 of the SmPC as a 'rare' adverse reaction.

Based on the updated total of 35 cases of pulmonary hypertension retrieved from the clinical trials cumulatively, all assessed as unrelated to the underlying treated disease of essential thrombocythaemia, the reporting frequency for pulmonary hypertension from evaluable clinical trials was recalculated as 35/5578 = 0.0063 (0.63%), which corresponds to an 'uncommon' event. Considering the nine new cases suggesting a causal relationship with anagrelide together with the recalculated reporting frequency, a change in frequency from 'rare' to 'uncommon' is considered appropriate. The change should be implemented accordingly in the package leaflet.

Moreover, these new cases and the higher frequency of occurrence also raise the need for further information to be provided in section 4.4 of the SmPC, in order to alert healthcare professionals to this serious adverse reaction and the need for close monitoring of the patients for any symptom of pulmonary hypertension, including in patients with a medical history of pulmonary hypertension. The package leaflet should be updated accordingly.

As Xagrid and Thromboreductin contain the same active substance, with similar therapeutic schemes, the safety profile for this risk is expected to be similar, despite lower reporting with Thromboreductin and the PRAC therefore considered that the changes to the product information should be implemented for both products.

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 anagrelide the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing anagrelide 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.