EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

International non-proprietary name: bosentan

Procedure No. EMEA/H/C/PSUSA/00000425/201411

Period covered by the PSUR: 20 November 2013 – 19 November 2014

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Scientific conclusions

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

In the previous periodic safety update report (PSUR), 176 new cases of nasal congestion were reported, some of them with close time of onset after start of treatment by bosentan. The vasodilatation property of bosentan was suggested as a possible role of bosentan in the occurrence of the events. It is known that endothelin receptor type A / endothelin receptor type B (ETA and ETB) are localised in the nasal mucosa which suggest a potential effect of bosentan on nasal mucosal vessel. Nasal congestion is listed in section 4.8 of Summary of Product Characteristics (SmPC) of endothelin receptor antagonists (ERA) selective of ETA. When known, a positive dechallenge was reported in 48/58 cases where the drug was discontinued or interrupted, moreover a positive rechallenge was reported in 4 isolated cases. Furthermore, in the final report of the controlled study COMPASS-2 that has been completed during this period, it was noted that nasal congestion was reported more frequently on bosentan/sildenafil group compared to placebo/sildenafil group (5.0% vs 0% respectively).

The review of autoimmune hepatitis (AIH) provided by the Marketing Authorisation Holder (MAH), did not show evidence that bosentan might be an initiator of autoimmune processes or events of AIH including AIH. Despite this, the potential role of bosentan in unmasking or worsening of AIH in patient with autoimmune diseases remains unclear, but it could not be ruled out in some cases in this review.

Therefore, in view of available data regarding nasal congestion and autoimmune hepatitis, the PRAC considered that changes to the product information were warranted.

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 bosentan the CHMP is of the opinion that the benefit-risk balance of the medicinal products containing bosentan is favourable subject to the proposed changes to the product information

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