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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): plerixafor

Procedure No. EMEA/H/C/PSUSA/00002451/201612

Period covered by the PSUR: 16 December 2013 – 15 December 2016

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Scientific conclusions

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

The MAH presented, as requested in the previous PSUR, a cumulative review where a total of 64 cases (64 events) related to splenomegaly were identified, of which the following PTs were reported: 45 cases of abdominal pain, 8 cases of abdominal pain upper, 4 cases of splenomegaly, 3 cases of splenic rupture, 1 case of splenic haemorrhage, and 1 case of spleen disorder.

Of the 4 cases reporting splenomegaly, three cases had insufficient information, while one had a medical history significant for splenomegaly. Of the 3 cases reporting splenic rupture, one case was a duplicate, leaving 2 unique cases, both serious and considered related by the reporter. Both cases presented a short time to event (between 4 and 7 days after administration of Mozobil). However, both cases were confounded by G-CSF and underlying amyloidosis.

No cases of splenomegaly, splenic rupture, splenic haemorrhage or spleen disorder were reported in clinical trials, however, the effect of plerixafor on spleen size in patients has not been specifically evaluated in clinical studies. As reflected in section 4.4 of the SmPC, there is preclinical data suggestive of splenomegaly with Mozobil.

Based on the two reported cases of splenic rupture, it is difficult to establish a direct causal association with Mozobil given that in both cases it was coadministered with G-CSF, which is known for the potential to cause both splenomegaly and splenic rupture. Nevertheless, a causal association with Mozobil cannot be excluded. Given the existing pre-clinical findings, the fact that Mozobil is indicated in combination with G-CSF, and the seriousness of the event, it is agreed that an update to the SmPC (section 4.4 and 4.8) is warranted to reflect the occurrence of these cases.

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