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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): alemtuzumab

Procedure No. EMEA/H/C/PSUSA/00010055/201809

Period covered by the PSUR: 13 September 2017 to 12 September 2018

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Scientific conclusions

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

During the reporting period serious case reports were identified of pulmonary alveolar haemorrhage, myocardial infarction and stroke (haemorrhagic and ischaemic) and cervicocephalic (vertebral and carotid) arterial dissection which occurred with close temporal relationship to alemtuzumab infusion. Cases of myocardial infarction have previously been observed during use of alemtuzumab for the treatment of B-cell chronic lymphocytic leukaemia.

Based on 7 case reports of haemophagocytic lymphohistiocytosis in patients treated with alemtuzumab for multiple sclerosis, a causal association was established between alemtuzumab treatment and the occurrence of haemophagocytic lymphohistiocytosis. Two of the seven cases were fatal.

Fatal and life-threatening cases of auto-immune hepatitis and hepatic injury were identified. A causality could not be fully established based on the presented data, however, due to the seriousness of these events, a warning is warranted.

For temporally associated pulmonary alveolar haemorrhage, temporally associated stroke (haemorrhagic and ischaemic), temporally associated cervicocephalic arterial dissection and haemophagocytic lymphohistiocytocis, no cases were observed within MAH's clinical trials. Therefore, based on an estimate of the upper limit of the 95% CI interval in the safety population, the frequency of the ADRs was estimated to rare. For temporally associated myocardial infarction, 1 case was reported in observational studies and the frequency was estimated to rare.

Literature published in the reporting period emphasised that patients with ongoing thyroid disorders are at higher risk of developing severe thyroid adverse reactions. Therefore it was reinforced that in patients with ongoing thyroid disorder alemtuzumab should only be administered if the potential benefit justifies the potential risks.

Twelve apparently unconfounded post marketing cases of neutropenia had a temporal onset within 2 months of Lematrada infusion. All cases met the seriousness criteria of fatal, life-threatening, or Grade 3/Grade 4/severe intensity with TTO $\leqslant$ 2 months.

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