EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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/00010055/201703

Period covered by the PSUR: 13 September 2016 to 12 March 2017

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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:

Alemtuzumab acts through antibody-dependent cellular cytolysis and complement-mediated lysis following cell surface binding to T and B lymphocytes with a subsequent reduction in the level of circulating B and T cells increasing the risk for infections or worsening of existing infections. Based on the mechanism of action and the biological plausibility for worsening of active infections, it is recommended to add a contraindication to initiate alemtuzumab treatment in patients with severe active infection until resolution.

Based on data from the review period, a causal association is identified between listeriosis/listeria meningitis and alemtuzumab treatment prior and during the initiation of the treatment. A total of 26 serious events concerning listeriosis have been reported, among them a post-marketing fatal case was identified where a causal relationship with alemtuzumab could not be excluded. Moreover, an evaluation of time to onset of listeriosis was undertaken within this review. A case report mentioned that as in most other cases of listeriosis, symptoms started rapidly after the last alemtuzumab infusion, which suggests that patients could have been infected with the bacteria already prior to the alemtuzumab infusions. The incubation period of invasive listeriosis is found to be wide (median 8 days, range 1–67 days). For cases with involvement of the central nervous system (CNS) the period is more narrow (median 9 days, range 1–14 days) (Goulet et al. 2013). In another study, the median incubation period is 11 days and 90% occurs within 28 days. Based on this observation, and due to the wide incubation period of Listeria infectious agents which is usually two weeks, the PRAC recommends to add to the existing warning that possibly listeria contaminated food items should be avoided not only one month after, but also two weeks prior and during alemtuzumab infusion.

Based on data from the review period, a causal association is identified between pneumonitis and alemtuzumab treatment. In clinical studies, 6 of 1217 (0.5%) LEMTRADA-treated patients had pneumonitis of varying severity. Cases of hypersensitivity pneumonitis with fibrosis have occurred. Additional cases reported, majority in postmarketing setting, of which some occurred less than a month (n=18) after treatment with alemtuzumab, has prompted the marketing authorization holder to add information to warn about the possibility of developing pneumonitis in alemtuzumab treated patients.

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.