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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): fingolimod

Procedure No. EMEA/H/C/PSUSA/00001393/201902

Period covered by the PSUR: 01 March 2018 To 28 February 2019

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Scientific conclusions

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

Regarding the signal 'autoimmune haemolytic anaemia (AIHA)', the PRAC concluded that the cumulative review provided by the MAH as well as the plausible theoretical mechanism support a causal relationship between therapy with fingolimod and occurrence of AIHA:

- Four cases without identified cofounders and with supportive chronology and clinical course with improvement/recovery following discontinuation of fingolimod.
- One case with very suggestive chronology of the event with compatible outcome then de-challenge and re-challenge positive
- Fingolimod is an immunosuppressant and immunosuppression conditions are risk factors for dysimmunity.

Based on the noteworthy cases identified in post-marketing, AIHA should be added to the section of the adverse drug reactions in the SmPC and in the package leaflet.

For weight decreased, section 4.8 of SmPC and section 4 of the package leaflet should be updated to include this AE following the current PSUSA with the frequency common.

Regarding lymphoma, the MAH proposed to update the section 4.4 of the SmPC regarding the risk of lymphoma "There have been cases of lymphoma in clinical studies and the post-marketing setting. The cases reported were heterogeneous in nature, mainly non-Hodgkin's lymphoma, including B-cell and T-cell lymphomas. Cases of cutaneous T-cell lymphoma (mycosis fungoides) have been observed." and under the section 2 of the PL "A type of cancer of the lymphatic system (lymphoma) has been reported in MS patients treated with Gilenya". The section 4.8 of the SmPC regarding lymphomas specifies that cases of lymphoma include also a fatal case of Epstein-Barr virus (EBV) positive B-cell lymphoma. Detailed information of adverse reactions with no recommendation should not be included in this section.

Therefore, information relating to fatal case of Epstein-Barr virus (EBV) positive B-cell lymphoma and a precaution for use regarding the interruption of treatment if lymphoma is suspected, should be included in the PI.

For PML, section 4.4 of the SmPC and section 2 of the PL should be updated in order to highlight the importance of MRI finding.

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