23 June 2022
EMA/780791/2022
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): tofacitinib

Procedure No. EMEA/H/C/PSUSA/00010588/202111

Period covered by the PSUR: 06 November 2020 to: 05 November 2021

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Scientific conclusions

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

In view of the available data on hypoglycaemia from spontaneous reports, including 3 cases with a positive de-challenge with tofacitinib in patients with diabetes and 1 case were anti-diabetic medication adjusted in a patient with diabetes upon which the event of hypoglycaemia resolved (all four case with a plausible temporal relationship), data from literature including patients with diabetes who are using JAK inhibitors including tofacitinib were hypoglycaemia improved after discontinuation or dose reductions of the JAK inhibitor or of the antidiabetic drug, data from clinical trial(s) showing a small trend for hypoglycemia in patients with a medical history of diabetes, and in view of a plausible mechanism of action of the JAK/STAT pathway on the insulin resistance and/or increased sensitivity as described in literature, the PRAC considers a causal relationship between tofacitinib and hypoglycaemia in patients with diabetes after initiation of tofacitinib is at least a reasonable possibility and a warning is recommended with a proposal for action in case of hypoglycaemia in those patients. The PRAC concluded that the product information of products containing tofacitinib should be amended accordingly.

Furthermore, in view of the available data on retinal venous thrombosis from fifteen spontaneous reports and the previously established VTE risk, the PRAC considers a causal relationship between tofacitinib and retinal venous thrombosis is at least a reasonable possibility. Therefore, a warning in section 4.4 with a proposal for action in case of symptoms of retinal venous thrombosis occur and an update of the footnote under the ADR table in section 4.8 is recommended. The PRAC concluded that the product information of products containing tofacitinib should be amended accordingly.

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