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): baricitinib

Procedure No. EMEA/H/C/PSUSA/00010578/201902

Period covered by the PSUR: 12 August 2018 – 12 February 2019

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Scientific conclusions

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

An imbalance in reports of VTE with 0% (EAIR of 0,0) for placebo vs. 0,53% (EAIR of 1,3) for baricitinib 4-mg was noted in placebo-controlled trials. VTE reporting rate is increasing. In July 2019 VTE reporting rate was 0,13% compared to 0,09% in February 2019. As of 01 July 2019, 114 VTEs have been reported in 102 cases from post-marketing reports. Moreover, recurrent DVT and subsequent PE observed September 2018 in patient who continued treatment with baricitinib after the first DVT also confirm possible relationship between use of baricitinib and occurrence of VTE. Therefore, the PRAC requests the MAH to update section 4.4 of the SmPC to modify the wording on "Venous Thromboembolism" to indicate that if clinical features of DVT/PE occur, baricitinib treatment should be discontinued and to update section 4.8 of the SmPC to add the adverse reaction pulmonary embolism and deep vein thrombosis with a frequency not known.

Data from clinical studies shows that the incidence rate of urticaria and face oedema is higher in the baricitinib 4 mg arm [urticarial: 0.60; face oedema: 0.89] compared to placebo arm [urticarial: 0.29; face oedema:0.29]. From the 316 events included for review from post-marketing reports, rash (n=95) was the most frequently reported event. Swelling face (n=23) and urticaria (n=20) were also frequently reported. From the 316 events retrieved as of 13 May 2019, 78 were categorised as systemic/oedema and 38 were categorised as non-specific. Taking into account information provided by MAH, at least part of non-specific events were indeed systemic however due the limited information it is not possible to categorise them properly. Moreover positive dechallenge (e.g. one case categorised as systemic) and positive dechallenge and rechallenge (e.g. one case categorised as non-specific) also support the view that baricitinib may cause systemic events. Therefore, the PRAC requests the MAH to update of section 4.4 of the SmPC to add a warning on hypersensitivity and to update of Section 4.8 to add the adverse reactions "rash" with a frequency common and "swelling of the face, urticaria" with a frequency uncommon.

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