EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 June 2021
EMA/403012/2021
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): ibrutinib

Procedure No. EMEA/H/C/PSUSA/00010301/202011

Period covered by the PSUR: 13 November 2019 to 12 November 2020

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Scientific conclusions

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

In view of available data on hepatic events (cases of hepatitis B reactivation and cases of hepatitis E, which may be chronic, as well as hepatic failure, including fatal events) from spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge the PRAC considers a causal relationship between ibrutinib and hepatic events is at least a reasonable possibility. The PRAC concluded that the product information of products containing ibrutinib should be amended to add a recommendation to assess liver function and viral hepatitis status before initiating treatment with ibrutinib and to periodically monitor for changes in liver function parameters during treatment and, as clinically indicated, to perform viral load and serological testing for infectious hepatitis.

In view of available data on eye haemorrhage including high number of cases reporting events related to ocular haemorrhagic disorders (435 cases cumulatively), of which 32 cases positive dechallenge including 2 cases of a positive rechallenge (of which 1 rechallenge case of intraocular bleeding causing loss of vision), imbalance in clinical trial data and in view of a plausible mechanism of action since it is known that ibrutinib is associated with bleeding events and haemorrhage is an important identified risk for ibrutinib, the PRAC considers a causal relationship between ibrutinib and eye haemorrhage is established. Additionally, since in some of these cases loss of vision occurred (in at least 20 cases including one case with positive rechallenge), this information is also proposed to be added to the product information. The PRAC concluded that the product information of products containing ibrutinib 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 ibrutinib the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing ibrutinib 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.