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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): carfilzomib

Procedure No. EMEA/H/C/PSUSA/00010448/202007

Period covered by the PSUR: 18 July 2019 – 18 July 2020

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Scientific conclusions

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

Following the assessment of available data on bradycardia from clinical trials, literature, spontaneous reports including 2 cases with a close temporal relationship (within 1 day or less from latest carfilzomib infusion) and accompanying symptoms, which are suggestive of a possible infusion reaction, a positive re-challenge in one case, and in view of a plausible mechanism of action the PRAC concluded that a causal relationship between carfilzomib and bradycardia as a symptom of infusion related reaction is possible. Therefore, an update of the section 4.4 of the SmPC to add a warning on bradycardia as symptom of infusion related reaction was decided. The Package leaflet is updated accordingly.

Following the assessment of available data on ventricular tachycardia from clinical trials, literature, spontaneous reports, including 2 cases with a close temporal relationship, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between carfilzomib and ventricular tachycardia cannot be excluded. Therefore, an update of SmPC in section 4.4 to add a warning that reports of ventricular tachycardia have been reported in patients receiving carfilzomib and in section 4.8 to add ventricular tachycardia as an adverse event with frequency uncommon has been decided.

Following the assessment of available data from cumulative review of QT prolongation events showing the source distribution of reviewed serious events (of total 39 serious event: spontaneous (n = 17), PM NIS (n = 12), literature (n = 6), solicited (n = 2), MAH sponsored clinical trial (n = 1), and non-MAH sponsored clinical trial (n = 1)), an update of section 4.4 was decided to reflect the occurrence of QT prolongation also in the postmarketing setting in addition to the existing wording about relevant reports only in clinical studies

Following the assessment of available data from clinical trials, spontaneous reports, including 10 cases with a close temporal relationship (a positive rechallenge and dechallenge, and a potential class effect, the PRAC considers a causal relationship between carfilzomib and acute pancreatitis established. The PRAC Rapporteur concluded that an update of section 4.8 of the SmPC to add the acute pancreatitis with a frequency uncommon is necessary. The Package leaflet is updated 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 carfilzomib the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing carfilzomib 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.