EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 July 2018
EMA/565256/2018
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): ponatinib

Procedure No. EMEA/H/C/PSUSA/00010128/201712

Period covered by the PSUR: 14 December 2016 – 13 December 2017

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

Scientific conclusions

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

Cases of posterior reversible encephalopathy syndrome (PRES) have been reported in ponatinib treated patients. A cumulative review in previous PSUSA (EMEA/H/C/PSUSA/00010128/201606) identified 16 events of possible PRES from post-marketing sources. None of them were fatal. Among them, three cases reporting PRES were identified, of these one was confirmed and two indicated positive de-challenges; however, based on the case details provided it was considered that the evidence was not sufficiently strong to update the Summary of Product Characteristics (SmPC); PRES was included as a potential risk in the RMP and the MAH updated the Company Core Data Sheet (CCDS).

Hypertension including hypertensive crisis is a known complication with ponatinib treatment and may further contribute to the risk of PRES. Furthermore, inhibitors of Vascular Endothelial Growth Factor (VEGF) have previously been associated with PRES in the literature (Tlemsani et al. Target Oncol. 2011 Dec;6(4):253-8; Tirumani et al. RadioGraphics 2015; 35:455–474). Ponatinib has shown activity against the VEGFR families of kinases supporting a possible association between the drug and the event.

During the current reporting period, two new cases of PRES have been reported, adding to a cumulative total of 5 cases of PRES. One of the cases reported in the current reporting period was confirmed by Magnetic Resonance Imaging (MRI), included a possible temporal relationship and a positive de-challenge. Therefore, taken together the biological plausibility, the cases reported post-marketing and the seriousness of the events of PRES, the PRAC considered that changes to the product information of medicinal products containing ponatinib were warranted to reflect the risk of posterior reversible encephalopathy syndrome (PRES).

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