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Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

International non-proprietary name: crizotinib

Procedure No. EMEA/H/C/PSUSA/00010042/201502

Period covered by the PSUR: 26 August 2014 – 25 February 2015

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Scientific conclusions

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

Cumulatively, 50 cases reporting events of cardiac failure have been identified by the MAH: 35 from spontaneous sources including 4 cases reported after the data lock point (DLP), 6 from non-interventional studies, 3 from compassionate use programs and 6 from clinical trials.

Due to the high reporting rate of cases of cardiac failure, the seriousness of the adverse drug reaction (ADR) of cardiac failure reported (all but one were serious), the temporal relationship, cases of positive dechallenge and positive rechallenge in cases with no confounding cardiac disorders the level of evidence is considered sufficient to support at least a reasonable possibility of causal relationship between the ADR of cardiac failure and crizotinib. It was also noted that in the majority of cases with confounding cardiac disorders, crizotinib may have triggered cardiac disorders. Therefore, the crizotinib Product Information should be updated with the adverse reaction of cardiac failure with the frequency "common" based on frequency observed in clinical trials.

Therefore, in view of available data regarding cardiac failure the PRAC considered that changes to the product information were warranted.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds recommending the variation to the terms of the Marketing Authorisation

On the basis of the scientific conclusions for crizotinib the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing crizotinib is favourable subject to the proposed changes to the product information

The CHMP recommends that the terms of the Marketing Authorisation should be varied.