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): trametinib

Procedure No. EMEA/H/C/PSUSA/00010262/201511

Period covered by the PSUR: 30 May 2015 to 29 November 2015

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for trametinib, the scientific conclusions of CHMP are as follows:
Cumulatively, there are three reported cases of myocarditis in patients receiving trametinib in combination with dabrafenib. All three cases are reported as causally related to the trametinib/dabrafenib combination and were categorised as serious. One case was fatal and in the two non-fatal cases there was recovery after stopping the trametinib/dabrafenib combination. Based on the evidence presented the PRAC considered that causal relationship between myocarditis and the trametinib/dabrafenib combination is likely in each of the two non-fatal cases based on temporal relationship, positive de-challenge and the absence of compelling alternative causes. In addition, in the context of myocarditis being a potentially life-threatening event that can be misdiagnosed, the PRAC recommended that the existing warning on left ventricular ejection fraction (LVEF) reduction/Left ventricular dysfunction should be updated to include specific reference to these cases of myocarditis in order to raise awareness of the possibility of this adverse reaction amongst prescribers, and highlight that stopping treatment resolved the myocarditis.
Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing trametinib were warranted.
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 trametinib the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing trametinib 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.

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