EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 March 2017
EMA/395587/2017
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): dabrafenib

Procedure No. EMEA/H/C/PSUSA/00010084/201608

Period covered by the PSUR:27 August 2015 to 26 August 2016

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
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Scientific conclusions

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

Based on a total of 9 cases of gastrointestinal perforation cumulatively reported with dabrafenib monotherapy and considering that the trametinib SmPC has been updated to include gastrointestinal perforations for the combination therapy trametinib/dabrafenib and considering the potentially

life-threatening nature of these events, the PRAC considered that the dabrafenib SmPC should be updated to include gastrointestinal perforations as a new warning and as a new adverse drug reaction with an 'uncommon' frequency.

Based on a cumulative review of 'Gastrointestinal disorders (diarrhoea, colitis, and gastroinstestinal perforation)', taking into account that the trametinib SmPC has been updated to include colitis as a new warning and as a new adverse drug reaction for the combination therapy trametinib/dabrafenib and considering the potentially serious nature of colitis, the PRAC considered that the dabrafenib SmPC should be updated to include colitis reported with combination therapy as a new warning and as a new adverse drug reaction with an 'uncommon' frequency.

Based on a new reported case of myocarditis in a patient on dabrafenib and trametinib combination therapy with a positive dechallenge to combination therapy, considering that the trametinib SmPC has been updated with information on myocarditis and taking into account the potentially life-threatening nature of myocarditis, the PRAC considered that the dabrafenib SmPC should be updated to include 'myocarditis' as a new adverse drug reaction with a 'not known' frequency.

Dabrafenib was shown to be phototoxic in non-clinical studies being part of the authorisation application. Based on 33 cases of photosensitivity from the post-marketing setting, including one serious/severe case was reported with positive de- and re-challenge to dabrafenib/trametinib combination therapy, the PRAC considered that 'photosensitivity reaction' should be included as a new adverse drug reaction in the dabrafenib SmPC with a 'common' frequency.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing dabrafenib were warranted.

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

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Grounds for the variation to the terms of the marketing authorisation

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

The CHMP recommends that the terms of the marketing authorisation should be varied.

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