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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): pomalidomide

Procedure No. EMEA/H/C/PSUSA/00010127/201508

Period covered by the PSUR: 08 February 2015 - 07 August 2015

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Scientific conclusions

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

The PRAC considered that based on evidence from cases (compatible temporal relationship, unusual presentation is some cases), biological plausibility and potential class effect, there is a reasonable possibility of a causal association between pomalidomide and non-melanoma skin cancer (NMSC). Therefore, NMSC should be included in the existing warning regarding second primary malignancy in section 4.4 and in section 4.8 of the pomalidomide product information. The safety concern 'second primary malignancies' in the risk management plan (RMP) should be updated to include relevant information about NMSC.
In view of the case reports of viral reactivation (plausible temporal relationship, reported causality) and biological plausibility, a contributory role for pomalidomide in combination with dexamethasone in varizella-zoster virus and hepatitis B virus (HBV) reactivation is likely. These adverse reactions should therefore be included in the product information. Two of the five cases of hepatitis B reactivation resulted in acute hepatic failure. Communicating about the risk of hepatitis B reactivation in the current warning on hepatic disorders in section 4.4 of the SmPC is therefore recommended, with a statement advising caution in patients with a history of HBV infection, including monitoring for signs and symptoms of active HBV infection. The PRAC also recommends that hepatitis B virus status should be established before initiating treatment with pomalidomide. Furthermore, a direct healthcare professional communication (DHPC) should be distributed to relevant healthcare professionals to inform about the new risk minimisation measures, in agreement with the communication plan. In the RMP, the existing important identified risk of 'Infection' should be updated to include information about reactivation of HBV and VZV. Furthermore, the MAH committed to update the relevant sections of the healthcare professional's educational material in order to reflect the new recommendation.

The PRAC considered that taking into account strong biological plausibility and cases of gastrointestinal haemorrhage for which a causal association cannot be excluded that there is a reasonable possibility that pomalidomide is causally related to gastrointestinal haemorrhage. Therefore, gastrointestinal haemorrhage should be included in section 4.8 of the SmPC. Given the various types of haemorrhagic events from different system organ classes that can occur with pomalidomide and the seriousness of some of these events, haemorrhagic disorders should be included in the description of selected adverse reactions in section 4.8 of the SmPC, with a cross-reference from the relevant warning in section 4.4. The important identified risk 'thrombocytopenia and bleeding' in the RMP should be updated to include information on gastrointestinal haemorrhage.

Finally, the preferred term 'Pneumonia' in the tabulated list of adverse reactions of section 4.8 should be broadened to 'Pneumonia (bacterial, viral and fungal infections, including opportunistic infections)'. Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing pomalidomide 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 pomalidomide the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing pomalidomide 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.