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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): nintedanib (oncology indications)

Procedure No. EMEA/H/C/PSUSA/00010318/201611

Period covered by the PSUR: 22 May 2016 to 21 November 2016

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Scientific conclusions

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

Following the MAH's initial review of renal failure/acute kidney injury and the MAH's requested re-analysis of all available data, 57 cases of acute renal failure including fatal cases were retrieved, including 11 cases of dehydration associated with gastrointestinal adverse events and 5 cases of gastrointestinal AEs. However considering the importance of dehydration and electrolytes imbalance, the PRAC concluded that the current warning on diarrhoea should be amended to include that serious cases of diarrhoea leading to dehydration and electrolyte disturbances have been reported in the post-marketing, in line with the recent update to the Ofev (nintedanib) SmPC.

Following the MAH's initial review of bleeding and the MAH's requested re-analysis of all available data, 48 cases of haemorrhage reported including 20 serious cases of which 10 were fatal. Two fatal cases have been reporting during the period covered by the PSUR that included haemorrhagic events in which the role of Vargatef could not be ruled out. Cases of respiratory, gastrointestinal and central nervous system haemorrhage were the most frequently observed bleeding events in the post-marketing settings. The PRAC therefore concluded that the current warning in section 4.4 of the SmPC on haemorrhage should be updated to reflect that non-serious and serious bleeding events, some of which were fatal, were reported post-marketing and to include some guidance to prescribers on the need to consider dose adjustment, interruption or discontinuation of treatment as well as the most frequent bleeding locations reported post-marketing. Finally the PRAC concluded that the current adverse drug reaction 'haemorrhage' in section 4.8 of the SmPC should be updated to include a cross-reference to section 4.4 of the SmPC and that the description of the selected adverse event 'bleeding' in section 4.8 of the SmPC should also be updated.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing nintedanib (oncology indication) 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 nintedanib (oncology indications) the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing nintedanib (oncology indications) 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.