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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): alectinib

Procedure No. EMEA/H/C/PSUSA/00010581/201907

Period covered by the PSUR: 03/01/2019 To: 03/07/2019

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Scientific conclusions

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

Following the evaluation of the cumulative review and detailed analysis of GI perforation, ulceration, haemorrhage or obstruction cases, there were 17 AEs identified for alectinib in 14 patients from clinical trials and further 73 cases from post-marketing were identified within the company safety database. In all of them some risk factor was present, mostly some concomitant disease (such as diverticulitis, appendicitis, gastritis, gastroenteritis, metastases to intestine or ileus of intestine) or concomitantly used medications (such as bevacizumab, opioids, dexamethasone or other/unspecified corticosteroids).

The results from toxicology studies, in monkeys treated with alectinib, a dilatation of the large intestine was seen, and a decreased stool, no-faeces, and retention of GI contents were seen in both rats and monkeys at 60 mg/kg/day and were accompanied by very slight erosions/ulcers in the stomach, duodenum, caecum and colon.

The risk of GI perforation is currently not present in the SmPC for alectinib. The SmPC for crizotinib which also belongs to the ALK inhibitor class includes the GI perforation in sections 4.4 and 4.8.

The retrieved cases of GI perforation do not provide a clear causal association with alectinib treatment. However, considering the results from toxicology studies in monkeys and rats, the seriousness of the events of GI perforation which might lead to death and the importance of early recognition and prompt medical intervention, it is considered that the product information of alectinib should include the warning on possible risk of gastrointestinal perforation in patients who are at higher risk of development of such condition and recommended actions in the section 4.4 of SmPC and in the corresponding part of the Package leaflet.

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 alectinib the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing alectinib 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.