



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

## XALKORI

Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation

International non-proprietary name: crizotinib

Procedure No.: EMEA/H/C/002489/PSUV/0012

Period covered by the PSUR: 26/02/2013 - 25/08/2013



## **Scientific conclusions**

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

In view of available data regarding gastrointestinal perforations, the PRAC considered that changes to the product information were warranted. A total of ten cases were identified in the MAH pharmacovigilance database: Gastrointestinal perforation (1), Intestinal perforation (6), Large intestine perforation (2) and Diverticular perforation (1). Six of these ten patients may have alternative aetiologies for the gastrointestinal perforation including metastatic disease to the intestinal wall, pre-existing diverticulitis, prior abdominal surgical procedure with drainage tubes in place, radiation treatment and concomitant use of dexamethasone which is known to be associated with gastrointestinal perforation. For the remaining four patients, there was limited information or no specific aetiology was determined.

Based on the current data from crizotinib clinical studies (including compassionate use), the estimated incidence of gastrointestinal perforation among NSCLC patients receiving crizotinib treatment is approximately 0.20% (7/3,571). Three cases are not included in this calculation because they are from spontaneous report. Therefore the PRAC recommends the inclusion of gastrointestinal perforation as a warning and into the list of adverse drug reactions in the Xalkori Summary of Product Characteristics (SmPC) and in the package leaflet accordingly.

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

## **Grounds recommending the variation to the terms of the Marketing Authorisation**

On the basis of the scientific conclusions for Xalkori, the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing the active substance crizotinib is favourable subject to the proposed changes to the product information.

The CHMP recommends that the terms of the Marketing Authorisation should be varied.