10 November
EMA/94652/2017
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): nintedanib (respiratory indication)

Procedure No. EMEA/H/C/PSUSA/00010319/201604

Period covered by the PSUR: 16 Oct 20 15 to 15 Apr 2016

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Scientific conclusions

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

Following a cumulative review of all reported cases of DILI, a total number of 10 cases was identified in the MAH's safety database: 2 cases from clinical trials, 2 from compassionate use programme, 5 from observational studies and one case from spontanoues reporting. All 10 cases were reported as serious including 3 fatal cases. Out of the 10 cases, two from post-marketing were well described cases with significant elevation of liver enzymes (> 5 upper limit of normal (ULN)), positive dechallenge and exclusion of other possible cause of DILI. In 7 other cases, DILI could not be excluded as not sufficient information is available. Finally one case was excluded based on the low level of liver enzymes. A search in EudraVigilance was also performed by the PRAC Rapporteur which identified 5 additional cases, all reported after this PSUR's data lock point. One of the additional case is a well documented case from the literature which also described an extensive elevation of liver enzymes (ALT and ASAT eleveated 11.8 and 5.5 times the ULN respectively and a positive dechallenge excluded other possible causes of DILI. Liver enzyme and bilirubin elevation is a listed adverse reaction for Ofev and is well described in the SmPC and in the RMP. Based on the available evidence, the PRAC considered that DILI should be added to sections 4.4 and 4.8 of the SmPC.

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 (respiratory 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 (respiratory indication) the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing nintedanib (respiratory indication) 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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