EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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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

Procedure No. EMEA/H/C/PSUSA/00010318/201511

Period covered by the PSUR: 22/05/2015-21/11/2015

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR for nintedanib (oncology indications),
the scientific conclusions of CHMP are as follows:
A cumulative review of the Adverse Drug Reaction (ADR) “Gamma-glutamyltransferase (GGT) increased” was provided by the Marketing Authorisation Holder (MAH) in the current PSUR for Vargatef. In the overall population and in adenocarcinoma patients in the study 1199.13, Adverse
Events (AEs) of increased GGT were more frequent under treatment with nintedanib and docetaxel
than with docetaxel alone. The majority of AEs were of grade 1/2. The AEs were managed with dose
reduction. Permanent discontinuation of study medication was infrequently needed. AEs of increased
GGT were also reported under treatment with nintedanib monotherapy.
Review of cases revealed other factors which have probably contributed to the elevation of GGT, such
as concomitant medications which are known to be associated with elevations of liver enzymes and/or
bilirubin and concomitant conditions, e.g. tumor progression in the liver, gallbladder stone, cholestasis. In the majority of cases, elevation of GGT occurred in conjunction with elevations of
alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALKP).
Elevations of GGT were reversible in the majority of patients. On the basis of this cumulative analysis,
the PRAC is of the opinion that there is enough evidence leading to the conclusion that nintedanib
(oncology indications) treatment can result to increased GGT.
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 indications) were
warranted.
The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation

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 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 should be varied.

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