EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 April 2018
EMA/428932/2018
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): trabectedin

Procedure No. EMEA/H/C/PSUSA/00003001/201709

Period covered by the PSUR: 18 September 2016 to 17 September 2017

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

Scientific conclusions

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

Capillary leak syndrome (CLS) is a rare entity characterized by recurrent and unpredictable attacks of capillary leakage of plasma fluid and proteins throughout the endothelium. Capillary leak syndrome (CLS) is usually characterized by peripheral oedema, hypotension which is relatively well tolerated, oliguria with acute pre-renal failure. In some patients, a compartment syndrome can occur. CLS can be idiopathic (Clarkson's disease) or secondary to various conditions and treatments. Secondary CLSs are mostly due to malignant hematological diseases, viral infections, and treatments such as chemotherapies and therapeutic growth factors.

Based on an ad-hoc review of CLS cases performed by an External Independent Adjudication Committee (IAC), it was determined possible or probable trabectedin causality in 5 out of 6 fatal cases among 14 probable CLS cases. The Pharmacovigilance and Risk Assessment Committee (PRAC) considered the results of the IAC report highly credible. The 3 assessors are independent, have no conflict of interest, are all specialists on CLS, and they provided a relevant description of their methodology and criteria, a distinction between possible and probable CLS and for the probable CLS cases, that are fatal, an evaluation of trabectedin causality. Their finding of possible or probable trabectedin causality in 5 of 6 fatal cases among 14 probable CLS cases warrants an update of the SmPC within this procedure to reflect there are cases with a fatal outcome.

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