21 April 2017
EMA/CHMP/390382/2017
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): trabectedin

Procedure No. EMEA/H/C/PSUSA/00003001/201609

Period covered by the PSUR: 18 September 2015 – 18 September 2016

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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 a cumulative review of suspected CLS cases, there is evidence to suggest a casual association between CLS and the use of trabectedin. A cumulative review of the 102 suspected CLS cases performed by an independent experts committee concluded that CLS was considered as possible in 48 cases (defined as more information needed to exclude or confirm that diagnostic criteria were met); CLS was considered probable (defined as a very strong clinical suspicion) in 14 cases (all from clinical trial or solicited sources). Causality was assessed as doubtful in 3 of these cases and at least possible in the remaining 11 cases.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing trabectedin 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 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.

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