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Committee for Medicinal Products for Human Use (CHMP)

Evoltra

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

International non-proprietary name: CLOFARABINE

Procedure No. EMEA/H/C/000613/PSUV/0044

Period covered by the PSUR: 29 December 2012 – 28 December 2013

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Scientific conclusions

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

In clinical practice, clofarabine is widely used in combined regimen, especially in association with etoposide and cyclophosphamide, according to guidelines for treatment of ALL. This is an off-labelled use that is clinically justified by the fact that treatment with multidrug regimens, including clofarabine containing regimen, in paediatric patients with second relapse, is the only way to allow them to be eligible for allogeneic HSCT. This off-label use with clofarabine is an important identified risk, for which product labelling represents the risk minimization tool.

Therefore, in view of available data regarding Evoltra, the PRAC considers that the following changes to the Evoltra SmPC are warranted:

in section 4.2 “Posology and method of administration”, it should be specified that recommended dose of 52 mg/m2 should be used as monotherapy, in order to avoid using this dose in combination,

in section 4.4 “Special warnings and precautions for use”, a warning should be added regarding higher toxicity of clofarabine in association with other agents.

In addition, the PRAC agrees with the MAH’s proposal to add hyponatremia as a new ADR in section 4.8 “Undesirable effects” of the EU SPC, under the SOC “Metabolism and nutrition disorders” with a frequency “not known”.

Therefore, in view of available data regarding Evoltra and coadministration, as well as post marketing reports on hyponatraemia, the PRAC considered that changes to the product information were warranted.

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 Evoltra, the CHMP is of the opinion that the benefit-risk balance of the medicinal product containing the active substance clofarabine is favourable subject to the proposed changes to the product information.

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