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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): decitabine

Procedure No. EMEA/H/C/PSUSA/00009118/202005

Period covered by the PSUR: 2 May 2018 – 1 May 2020

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Scientific conclusions

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

1/ Differentiation syndrome

Following a Tracked Safety Issue created by FDA in February 2019 which led to an update of the US product information, the MAH performed a cumulative review of cases of differentiation syndrome with decitabine including cases reported in the safety database, literature data and disproportionality analysis. Overall, 3 cases reporting at least 3 criteria for differentiation syndrome have been identified. Moreover, among these 3 cases, 2 case reports published in the literature provided evidence of a possible causal association with decitabine administration.

Furthermore, there is a biological plausibility for this differentiation syndrome as decitabine is a DNA-hypomethylating agent that induces differentiation and apoptosis of leukemic cells, and differentiation syndrome typically occurs during induction therapy with differentiating agents while leukemic blasts are massively present.

In view of available data on differentiation syndrome from the literature and spontaneous reports and taking into account the plausible mechanism of action, the PRAC considers a causal relationship between decitabine and differentiation syndrome is at least a reasonable possibility. The PRAC concluded that the product information of products containing decitabine should be amended accordingly.

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