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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): azacitidine

Procedure No. EMEA/H/C/PSUSA/00000274/201505

Period covered by the PSUR: 19 May 2014 – 18 May 2015

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Scientific conclusions

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

Scientific conclusions and grounds for variation to the terms of the marketing authorisations

During the reporting interval, there were 3 new reports of pyoderma gangrenosum, and 13 reports have been received cumulatively. Taking into account all sources of information (studies, literature, spontaneous reports), 20 reports of azacitidine-associated pyoderma gangrenosum were retrieved from the safety database. Among these, there were 3 biopsy-confirmed cases with a positive rechallenge and three cases reporting a positive dechallenge, although only one was confirmed by biopsy. Overall, the cumulative data received to date, and in particular the 3 cases with a positive rechallenge, indicate that treatment with azacitidine is associated with the risk of pyoderma gangrenosum. Pyoderma gangrenosum should therefore be included as an adverse drug reaction in the summary of product characteristics of azacitidine with a frequency “uncommon”. The package leaflet should be updated accordingly.

Cumulatively, 16 cases of tumour lysis syndrome have been reported to date, of which 7 during post-marketing experience. The cumulative data indicates that, even though patients initiating azacitidine are at risk of developing tumour lysis syndrome, the overall risk appears to be low. This is further supported by the finding that no cases of tumour lysis syndrome have occurred in marketing authorisation holder-sponsored studies. Currently tumour lysis syndrome is addressed in section 4.8 of the summary of product characteristics (frequency: rare), and listed as important identified risk in the risk management plan. The PRAC endorsed the MAH proposal to include an additional warning on tumour lysis syndrome in section 4.4 of the summary of product characteristics.

Therefore, in view of the data presented in the reviewed PSUR(s), the PRAC considered that changes to the product information of medicinal products containing azacitidine 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 azacitidine the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing azacitidine 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.