18 May 2017
EMA/480962/2017
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): mercaptopurine

Procedure No. EMEA/H/C/PSUSA/00001988/201609

Period covered by the PSUR: 14 September 2013 – 1 September 2016

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Scientific conclusions

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

Patients receiving treatment with 6-mercaptopurine who develop myelosuppression are at increased risk of developing infections. Considering the spontaneous case reports of infections received and those published, including serious infections such as hepatitis B, varicella zoster and pneumocystis jirovecii pneumonia during the reporting period of this PSUSA, and the potential temporal relationship, the PRAC supported the MAH's proposal to update section 4.4 of the SmPC to include a warning regarding and to add 'bacterial and viral infections' and 'infections associated with neutropenia' as new adverse drug reactions with an 'uncommon' frequency in section 4.8 of the SmPC.

Based on recent publications, it can be concluded that the risk of induced leukopenia and alopecia from thiopurines is significantly increased in patients positive for the mutated nudix hydrolase 15 (NUDT15)R139 C variant. This genetic factor is often observed in patients with ancestry across broad areas of Asia, including Japanese, Korean and Chinese populations. Based on data derived from the published literature, the PRAC considered that there is currently sufficient available evidence to update sections 4.2 and 4.4 of the SmPC to include a new warning on the increased risk of severe toxicity in patients with inherited mutated NUDT15 gene treated with 6-mercaptopurine. There is currently no data available to support mandating physicians to initiate genetic testing prior to use of the product. However, the PRAC agreed to include a statement that genotypic testing of NUDT15 prior to initiating treatment may be considered.

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