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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): azathioprine

Procedure No. PSUSA/00000275/202412

Period covered by the PSUR: 6 years to 12 December 2024

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Scientific conclusions

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

Cardiac dysfunction (as part of hypersensitivity reactions)

In view of available data on cardiac dysfunction (as part of hypersensitivity reactions) from the literature, including in seven cases a close temporal relationship, a positive de-challenge and/or re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between azathioprine and cardiac dysfunction (as part of hypersensitivity reactions) is at least a reasonable possibility. The PRAC concluded that the product information of products containing azathioprine should be amended accordingly.

Cholestasis of pregnancy

In view of available data on cholestasis of pregnancy from the literature, spontaneous reports including in eight cases a close temporal relationship and a positive de-challenge, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between azathioprine and cholestasis of pregnancy is at least a reasonable possibility. The PRAC concluded that the product information of products containing azathioprine should be amended accordingly.

Pellagra / nicotinic acid deficiency

In view of available data on pellagra from the literature, including 8 literature cases with a close temporal relationship and a positive de-challenge, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between azathioprine and pellagra is at least a reasonable possibility. The PRAC concluded that the product information of products containing azathioprine should be amended accordingly.

Posterior reversible encephalopathy syndrome (PRES)

In view of available data on posterior reversible encephalopathy syndrome from the literature, spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between azathioprine and posterior reversible encephalopathy syndrome is at least a reasonable possibility. The PRAC concluded that the product information of products containing azathioprine should be amended accordingly.

Sialoadenitis

In view of available data on sialoadenitis from the literature, including 5 cases with a close temporal relationship, and a positive de-challenge and re-challenge, the PRAC considers a causal relationship between azathioprine and sialoadenitis is at least a reasonable possibility. The PRAC concluded that the product information of products containing azathioprine should be amended accordingly.

Tremor

In view of available data on tremor from the literature and spontaneous reports, including in some cases a close temporal relationship and a positive de-challenge and/or re-challenge, the PRAC considers a causal relationship between azathioprine and tremor is at least a reasonable possibility. The PRAC concluded that the product information of products containing azathioprine should be amended accordingly.

Drug-drug interaction between azathioprine and allopurinol

In view of available data on the interaction between azathioprine and allopurinol from spontaneous reports, the PRAC considers an amendment of the existing wording warranted. The PRAC concluded that the product information of products containing azathioprine should be amended accordingly.

Having reviewed the PRAC recommendation, the CHMP agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for azathioprine the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing azathioprine 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.