20 September 2018
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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): nitisinone

Procedure No. EMEA/H/C/PSUSA/00002169/201802

Period covered by the PSUR: 21 February 2017 to 20 February 2018

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Scientific conclusions

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

In an ongoing phase III clinical study (SONIA 2) to assess the effectiveness and safety of nitisinone in patients with alkaptonuria, ten of 69 nitisinone-treated patients have presented with signs of tyrosine-related ocular adverse events. In addition, two literature articles referred to patients using nitisinone at low doses for the treatment of alkaptonuria. These articles focused on the observation that keratopathy may be asymptomatic. The introduction of a low protein diet with low dose nitisinone was successful in controlling plasma tyrosine levels (below 600 µmol/L) and in controlling visual symptoms. The evidence was collected in the context of off-label use of nitisinone, i.e. alkaptonuria, which is characterised by high plasma tyrosine levels. Nevertheless, since tyrosine-related ocular adverse events are a known and listed feature in patients with HT-1 treated with nitisinone, the risks related to a delayed diagnosis of asymptomatic eye disorders may also apply in the approved indication. Therefore, the PRAC concluded that the current recommendation for specific examination before treatment should be modified to include regular examinations of the eyes also during treatment.

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