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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): deferasirox

Procedure No. EMEA/H/C/PSUSA/00000939/201810

Period covered by the PSUR: 01/11/2017 to: 31/10/2018

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## Scientific conclusions

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

Based on a cumulative review of overdose cases, early signs of deferasirox overdose seem to be of digestive type with AEs such as abdominal pain, nausea and vomiting. Furthermore, hepatic disorders manifesting with liver enzyme increase, jaundice with increased total and direct bilirubin, hepatic failure and one case of liver injury with liver enzyme increased associated with Fanconi syndrome (90 mg/kg once) were reported. Cases of renal disorders with positive dechallenge were retrieved. Cases of rash were also reported in context of overdose and section 4.4 of the SmPC mentions dose-dependence in the paragraph dedicated to rashes. In conclusion, an update of section 4.9 of the SmPC to adequately reflect data regarding overdose with deferasirox is considered necessary.

In addition, data made available during the interval support the contributory role of the dose administered and over-chelation in the occurrence of some toxicities (e.g. 'hyperammonaemia' occurring in a clinical context of renal/hepatic disorders, renal and hepatic failure disorders and metabolic acidosis) including in the paediatric population (renal and hepatic toxicities, including cases with acute tubular injuries, metabolic acidosis, hyperammonaemia and hearing and ocular toxicities). As a result, recommendations regarding over-chelation should be updated in the Product Information.

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