25 January 2024
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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): fenfluramine

Procedure No. EMEA/H/C/PSUSA/00010907/202306

Period covered by the PSUR: 25/12/2022 To: 24/06/2023

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Scientific conclusions

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

Given the known risk of VHD/PAH at higher doses of fenfluramine used in the past to treat adult obesity, the first probable case of pulmonary arterial hypertension in a child treated with lower doses of fenfluramine (10.12 mg/day) for Dravet syndrome (index case) is of particular importance. VHD/PAH represent very important potential risks of fenfluramine for the treatment of DS and LGS. Taking into account the serotonergic stimulation of cardiac valve tissue as a plausible mechanism of action and the known association between VHD/PAH and higher doses of fenfluramine used as an appetite suppressant, the PRAC considers that this single case warrants an update of the product information to provide clinicians with the most up-to-date evidence on this important risk. The product information of products containing fenfluramine should be amended accordingly.

In view of available data including 18 post-marketing reports of aggression/anger with a positive de-challenge and 19 post-marketing reports with a plausible onset latency a causal relation between fenfluramine and aggression is at least possible. Aggression was recently added to the ADR table for DS (variation EMEA/H/C/003933/II/018). The MAH proposes to add 'aggression' to the ADR table for LGS with the frequency unknown. However, as aggression was reported in 1.1 % in fenfluramine-treated participants in clinical trials, it should be assigned to the frequency category common.

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