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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): telotristat

Procedure No. EMEA/H/C/PSUSA/00010639/201902

Period covered by the PSUR: 28 August 2018 to 27 February 2019

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Scientific conclusions

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

Based on post marketing and clinical data it is recommended to update section 4.8 to include nausea as an adverse drug reaction in Section 4.8 under the SOC Gastrointestinal disorders with a frequency "very common". The adverse event was observed in clinical trials with frequency "very common" and is being reported from post-marketing setting.

It is also recommended that the MAH should add the ADR "intestinal obstruction" to the section 4.8 of the SmPC and section 4 of PL with the frequency "uncommon". A cumulative search identified 62 relevant cases some of which with a close temporal relationship with the initiation of treatment with telotristat. The majority of intestinal obstruction events were serious (56 cases) and 33 cases were medically confirmed. Some cases had more than one event of intestinal obstruction.

Finally, it is recommended to add depression and depressed mood to section 4.8 of the SmPC and section 4 of PL under Psychiatric disorders with frequency "common". Although patients with carcinoid syndrome may have a predisposition for depression, there were 38 post-marketing cases indicative of depression and depression-related events including two cases with positive dechallenge. Moreover, in the long-term safety study (LX1606.1-302-CS), the incidence of depression was 21% and there is a probable biological mechanism that telotristat reduces the production of serotonin that may lead to symptoms of depression.

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