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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): linaclotide

Procedure No. EMEA/H/C/PSUSA/00010025/201508

Period covered by the PSUR: 30-August- 2014 to 29 August-2015

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Scientific conclusions

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

During this PSUR reporting period case reports showed a close time relationship to treatment start and plausible underlying mechanism as well as a considerable number of cases with a positive de-challenge for "vomiting" so that at least a possible causal relationship to treatment was concluded.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing linaclotide were warranted to include "nausea" and "vomiting".

Since the international birth date (IBD) of linaclotide (30 August 2012), a number of cases of gastrointestinal bleeding were reported from post-marketing sources the majority of which are serious. The vast majority of the bleeding reports concern the lower part of the intestine. As haematochezia or rectal bleeding are associated with bowel movement in patients with constipation/haemorrhoids, increasing bowel movements by linaclotide treatment increases the risk for bleeding events.

Therefore, in view of the data presented in the reviewed PSURs, the PRAC considered that changes to the product information of medicinal products containing linaclotide were warranted to include lower gastrointestinal haemorrhage including haemorrhoidal haemorrhage and rectal haemorrhage" in section 4.8 and to amend the warning on diarrhoea in section 4.4 of the SmPC.

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