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EMA/173542/2020
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): semaglutide

Procedure No. EMEA/H/C/PSUSA/00010671/201905

Period covered by the PSUR: From: 01/12/2018 To: 31/05/2019

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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Scientific conclusions

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

Acute Pancreatitis

In line with the Article 5(3) procedure EMEA/H/A-5(3)/1369 in 2013 GLP1 cases of acute pancreatitis have been evaluated on a product-specific basis for semaglutide in this PSUR. The PRAC concluded that 'acute pancreatitis' should be added as a new ADR in section 4.8 of the SmPC, as well as wording describing cases observed e.g. in clinical trials, and in the Package Leaflet in order to align the semaglutide product information with the other GLP1-RA products. No data have been provided that indicate that semaglutide stands out from other GLP1-RAs regarding pancreatitis and therefore there is nothing at present that would justify an exclusion of semaglutide with regard to this class effect.

Diabetes ketoacidosis (DKA)

An EMA signal of DKA concerning the GLP-1 agonists dulaglutide, exenatide and liraglutide was adopted as a PRAC request (data cut-off 31 July 2018). MAHs of the GLP-1 agonists not involved in the concerned procedure, e.g. semaglutide, were recommended by PRAC to monitor and discuss the signal of DKA within their coming PSURs. Consequently, a cumulative review of DKA cases was performed by the MAH for semaglutide in the present PSUR. The assessment and analysis of this review do not indicate a causal association between treatment with semaglutide and DKA. This is in line with the findings for the GLP1 RA evaluated in the signal (EPITT 19237). However, it cannot be excluded that in some cases the event of DKA could be attributed to abrupt dose reduction or discontinuation of insulin while initiating semaglutide due to initial improvement of glycaemic control, thereby causing insulin deficiency.

Therefore, to provide further guidance for prescribers and patients in adopting a stepwise dose-reduction of insulin and/or close monitoring of blood glucose levels, and in line with the PRAC Recommendation of the EPITT 19237 signal, the SmPC sections 4.2 and 4.4 and the respective sections of the Package leaflet have been updated.

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