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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): naloxegol

Procedure No. EMEA/H/C/PSUSA/00010317/201803

Period covered by the PSUR: September 2017 to 15 March 2018

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

During the reporting period of this PSUR (16 September 2017 and 15 March 2018) a medication error report was received concerning a patient who started Targin (oxycodone/ naloxone) while on naloxegol. The patient experienced withdrawal symptoms and was hospitalised.

Naloxegol is a PEGylated derivative of naloxone. Naloxegol is a full neutral antagonist at the mu-opioid receptor and acts by binding to mu-opioid receptors in the gastrointestinal tract. Naloxone is a competitive antagonist of μ, δ and κ-opioid receptors and is most potent at the μ receptor. Given that both opioid antagonists interact with the same peripherally located mu-opioid receptors, there is a potential for an additive effect and an increased risk of opioid withdrawal.

PRAC agreed that changes to the naloxegol SmPC are warranted and recommends to update section 4.5 of the SmPC to add a warning against use of naloxegol with other opioid antagonists due to the potential for an additive effect of opioid receptor antagonism and an increased risk of opioid withdrawal. Package Leaflet is updated accordingly.

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