Annex I

Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisation(s)

Scientific conclusions

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

Sphincter of Oddi dysfunction can involve the biliary sphincter and/or the pancreatic sphincter which may lead to respectively a dilated common bile duct and/or a dilated pancreatic duct (McLoughlin et al. 2007, Afghani et al. 2017). Therefore, the current warning regarding hepatobiliary disorders in the SmPC of oxycodone requires modification, by removing "..raising intrabiliary pressure..". There is no need to change the package leaflet, since the package leaflet does not include a reference to raised intrabiliary pressure.

Dependence and addiction are important risks of oxycodone and remain of concern in the EU/EEA. The reporting rate for opioid use disorder (OUD)-related events for the period 2016 to 2023 increased by around 2-fold as compared with the period 2012 to 2015 and did not decrease in the current PSUSA period. From literature, several published studies confirm increasing use of opioid-containing medicines in the EU/EEA, although trends may vary across individual member states (e.g., Kalkman et al. 2019, Häuser et al. 2020, Pierce et al. 2021). There are signals of problematic chronic and/or high dose opioid use in EU (e.g., Ellerbroek et al. 2024, Schrader et al. 2024, Vincent et al. 2024). In a recent cross-sectional survey study in the Netherlands (e.g., Jansen-Groot Koerkamp et al. 2024), among general practitioners' and community pharmacists, the majority of respondents agreed that too many opioids are used in the treatment of chronic non-malignant pain and that there are concerns about the addictive potential of opioids. There is also evidence suggesting that in some EU/EEA countries there is increase in opioid-related harm (e.g., di Gaudio et al. 2021, Häuser et al. 2020, Pierce et al. 2021).

The PRAC concluded that the product information of medicinal products containing oxycodone should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh 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 oxycodone the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing oxycodone is unchanged subject to the proposed changes to the product information.

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

Annex II

Amendments to the product information of the nationally authorised medicinal product(s)

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike-through~~)

Summary of Product Characteristics

- Section 4.4

A warning should be amended as follows:

Hepatobiliary disorders

Oxycodone may cause dysfunction and spasm of the sphincter of Oddi, thus ~~raising intrabiliary pressure and~~ increasing the risk of biliary tract symptoms and pancreatitis. Therefore, oxycodone has to be administered with caution in patients with pancreatitis and diseases of the biliary tract.

Package Leaflet

- Section 2

A black box warning should be added directly under the subheading 'Tolerance, dependence and addiction', as follows:

Tolerance, dependence and addiction

This medicine contains oxycodone, which is an opioid. It can cause dependence and/or addiction.

This medicine contains oxycodone which is an opioid medicine. Repeated use etc..

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	November 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	06 January 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	27 February 2025