

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:

Further to a safety announcement by the FDA in 2016 about serotonin syndrome with the entire class of opioid pain medicines, a significant number of cases of serotonin syndrome associated with oxycodone and concomitant medications were identified, and an increased number of literature articles on serotonin syndrome in oxycodone users was also noted. A cumulative review conducted by the brand leader Mundipharma provided evidence of this risk of interaction between oxycodone and serotonergic drugs, leading to serotonin syndrome. Therefore an update of the product information is warranted.

The CMDh 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 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 reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing oxycodone are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

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 4.5

Concomitant administration of oxycodone with serotonin agents, such as a Selective Serotonin Re-uptake Inhibitor (SSRI) or a Serotonin Norepinephrine Re-uptake Inhibitor (SNRI) may cause serotonin toxicity. The symptoms of serotonin toxicity may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea). Oxycodone should be used with caution and the dosage may need to be reduced in patients using these medications.

Package Leaflet

- Section 2 - Interactions with other medicines

The risk of side effects increases, if you use antidepressants (such as citalopram, duloxetine, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, venlafaxine). These medicines may interact with oxycodone and you may experience symptoms such as involuntary, rhythmic contractions of muscles, including the muscles that control movement of the eye, agitation, excessive sweating, tremor, exaggeration of reflexes, increased muscle tension, body temperature above 38°C. Contact your doctor when experiencing such symptoms.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	26 January 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	27 March 2019