15 November 2018
EMA/532488/2019
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): dexmedetomidine

Procedure No. EMEA/H/C/PSUSA/00000998/201803

Period covered by the PSUR: 16 March 2017 to 15 March 2018

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Scientific conclusions and grounds for variation to the terms of the marketing authorisations

During the current reporting period 16 March 2017 – 15 Mar 2018, the market authorisation holder, Orion pharma undertook a cumulative review of all reports of the adverse reaction of hyperthermia Their review identified 172 reports, 91 of which were serious and 81 of which were non-serious. In approximately 50% of cases, positive dechallenges were reported. The time to recovery ranged from a short time after discontinuation of dexmedetomidine, to some days later. However, the majority were within 12 hours. Very high temperatures had been reported in a small number of the case reports, and that anti-pyretic agents or/external cooling were not effective. The adverse drug reaction (ADR) of hyperthermia is already highlighted in the Summary of Product Characteristics (SmPCs) therefore is subject to routine pharmacovigilance and routine risk minimisation, however the current warning in section 4.4 of the SmPC does not mention the lack of effect of cooling through other measures. Therefore the PRAC recommends a more prominent warning that dexmedetomidine should not be used in malignant hyperthermia-sensitive patients.

Orion pharma noted that case reports of overdose are frequently associated with ADRs of bradycardia, hypotension, over sedation, cardiac arrest, respiratory depression and hypertension so proposed to reinforce the existing warnings in section 4.9 of the SmPC and to include the adverse reaction of hypertension, and to redefine somnolence as respiratory depression. The PRAC endorsed this revision.