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 propofol, the scientific conclusions are as follows:

Propofol infusion syndrome (PRIS) is a rare but potentially lethal adverse effect of propofol which is reported in the propofol product information and in scientific literature but which is probably under-diagnosed in clinical use.

Based on literature review articles and on cases reported including two relevant cases with a fatal outcome in patients with known risk factors of PRIS, the PRAC considers that the product information of medicinal products containing propofol should be updated.

The information on PRIS included in section 4.4 of the SmPC of all propofol containing products should be updated to advice immediate discontinuation of propofol infusion and switch to an alternative sedative at the first sign of occurrence of PRIS symptoms (and not only decrease the dosage as currently mentioned).

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 propofol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing propofol 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 propofol 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 4.4

Prescribers should be alert to these events in patients with the above risk factors and ~~promptly consider decreasing or stopping the~~ **immediately discontinue** propofol ~~dosage~~ when the above signs develop.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	08 September 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	07 November 2018