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 thiopental, the scientific conclusions are as follows:

In this PSUR a number of serious adverse drug reactions reported in association with thiopental are consistent with potential events of anaphylaxis: anaphylactic reaction (n=4), anaphylactic shock (n=16), anaphylactoid reaction (n=3), anaphylactoid shock (n=1), rash (n=8), erythema (n=9), bronchospasm (n=16), circulatory collapse (n=4), shock (n=2). Further, during this interval, 148 cases of anaphylaxis in association with thiopental were reported in Eudravigilance. Causality assessment was precluded in all cases due to limited information and confounding by concomitant medication. However, case reports have previously been published where the causal relationship between anaphylaxis and the administration of thiopental was established via allergy testing (i.e. percutaneous skin tests, intradermal skin tests, co-precipitation test, passive transfer test, human basophil degranulation tests and leucocyte histamine release test). Considering the totality of the data, PRAC is of the view that there is sufficient evidence to substantiate a causal association and therefore anaphylactic reaction should be added to the product information with a frequency not known.

Therefore, in view of the data presented in the reviewed PSUR(s), the PRAC considered that changes to the product information of medicinal products containing thiopental, were 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 thiopental the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing thiopental 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 thiopental are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that such marketing authorisations are varied accordingly.

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 4.8

The following adverse reaction should be added under the SOC immune system disorders with a frequency not known: **anaphylactic reaction**

Package Leaflet

- Section 4

The following text should be placed at the top of section 4:

Tell your doctor right away if you notice any of the following symptoms - you may need urgent medical treatment:

Difficulty breathing, wheezing, rash, itching, hives and dizziness. This could be a severe allergic reaction (frequency not known, cannot be estimated from the available data).

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2016 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	28 January 2017
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	29 March 2017