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 bismuth subcitrate potassium / metronidazole / tetracycline, the scientific conclusions are as follows:

Respectively, one and two cases of meningitis were reported during the reporting period and cumulatively for bismuth subcitrate potassium/metronidazole/tetracycline combination; additionally two case reports for metronidazole have been published in the literature. Aseptic meningitis is also listed in the summary of product characteristics for metronidazole with a frequency not known. Therefore, considering the seriousness of drug induced aseptic meningitis and and in view of the data presented in the reviewed PSUR(s) bismuth subcitrate potassium / metronidazole / tetracycline and available for metronidazole, PRAC considered that changes to the product information of medicinal products containing bismuth subcitrate potassium / metronidazole / tetracycline, are 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 bismuth subcitrate potassium / metronidazole / tetracycline the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing bismuth subcitrate potassium / metronidazole / tetracycline 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 bismuth subcitrate potassium / metronidazole / tetracycline 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 4.8

The following adverse reaction(s) should be added under the SOC Nervous system disorders with a frequency not known: **Aseptic meningitis**

Package Leaflet

- Section 4

Not known (frequency cannot be estimated from the available data)

Aseptic meningitis: A group of symptoms together including: fever, nausea, vomiting, headache, stiff neck and extreme sensitivity to bright light. This may be caused by an inflammation of the membranes that cover the brain and spinal cord (meningitis).

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	10 March 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	09 May 2018