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 phenobarbital, the scientific conclusions are as follows:

In view of available data on **hyperammonaemia** in patients concomitantly treated with valproate and phenobarbital from clinical trials, literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC considers a causal relationship between hyperammonaemia in patients concomitantly treated with valproate and phenobarbital is at least a reasonable possibility. Therefore, the PRAC concluded that the PI of products containing phenobarbital should be amended accordingly.

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 phenobarbital the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing phenobarbital 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 phenobarbital 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~~)>

Section 4.5

Warnings should be added as follows:

Patients treated concomitantly with valproate and phenobarbital should be monitored for signs of hyperammonemia. In half of the reported cases hyperammonaemia was asymptomatic and does not necessarily result in clinical encephalopathy.

No updates to the Patient Information Leaflet (PIL) are deemed necessary, as valproate is already listed in the document.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	October 2020 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	29 November 2020
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	28 January 2021