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 baclofen (oral), the scientific conclusions are as follows:

In view of available data on tinnitus from the literature and spontaneous reports, including in cases with a close temporal relationship, and resolution with dose reduction, the PRAC considers that there is sufficient evidence of a causal relationship between baclofen (oral), in the context of overdose, and tinnitus. The PRAC concluded that the product information of products containing baclofen (oral) should be amended accordingly.

In view of available data on the risk of baclofen toxicity at a dose of 5 mg/day in patients with end stage renal failure undergoing chronic haemodialysis from the literature and spontaneous reports, including in some cases a close temporal relationship, a positive de-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between baclofen (oral) at a dose of 5mg/day and toxicity in this patient cohort is at least a reasonable possibility. The PRAC concluded that the product information of products containing baclofen (oral) 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 baclofen (oral) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing baclofen (oral) 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 baclofen (oral)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

A warning should be amended as follows:

Renal impairment

….

'Neurological signs and symptoms of overdose including clinical manifestations of toxic encephalopathy (e.g. confusion, disorientation, somnolence and depressed level of consciousness) have been observed in patients with renal impairment taking oral baclofen at doses of more than 5mg per day **and at doses of 5mg per day in patients with end-stage renal failure being treated with chronic haemodialysis.** Patients with impaired renal function should be closely monitored for prompt diagnosis of early symptoms of toxicity (See section 4.9 Overdose).' …..

- Section 4.9

The following adverse reaction should be added as a symptom of baclofen (oral) overdose:

Tinnitus

Package Leaflet

Section 3 "How to take baclofen"

Signs of overdose are:

Ringing in the ears

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	June 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	8 August 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	7 October 2021