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 use, for muscle spasticity indication), the scientific conclusions are as follows:

In view of available data on encephalopathy and generalised slowing on electroencephalogram (EEG) from the literature and spontaneous reports, including in cases with a close temporal relationship, positive de-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between baclofen and encephalopathy as well as generalised slowing on EEG is at least a reasonable possibility. The PRAC concluded that the product information of products containing baclofen (oral use, for muscle spasticity indication) should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for baclofen (oral use, for muscle spasticity indication) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing baclofen (oral use, for muscle spasticity indication) is unchanged subject to the proposed changes to the product information.

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

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 added as follows:

Encephalopathy

Cases of encephalopathy have been reported in patients receiving baclofen at therapeutic doses, which were reversible after treatment discontinuation. Symptoms included somnolence, depressed level of consciousness, confusion, myoclonus and coma.

If signs of encephalopathy are observed, baclofen should be discontinued.

- Section 4.8

The following adverse reaction should be added under the SOC Nervous system disorders with a frequency not known.

SOC Nervous system disorders: **Encephalopathy**

- Section 4.9

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

"**Encephalopathy**"

"**Generalised slowing on EEG**"

…

Symptoms: Prominent features are signs of central nervous depression **or encephalopathy:** somnolence, depressed level of consciousness, respiratory depression, coma and tinnitus.

Also liable to occur are**:** confusion, hallucinations, agitation, convulsion, abnormal electroencephalogram (burst suppression pattern and triphasic waves, **generalised slowing on EEG**)**,** accommodation disorder, impaired pupillary reflex; generalised muscular hypotonia, myoclonia**,** hyporeflexia or areflexia; convulsions; peripheral vasodilatation, hypotension or hypertension, bradycardia or tachycardia, or cardiac arrhythmia; hypothermia; nausea, vomiting, diarrhoea, salivary hypersecretion; increased hepatic enzymes, sleep apnoea, rhabdomyolysis.

Package Leaflet

Section 2 "What you need to know before you take baclofen"

Warnings and Precautions:

There have been reports of reduction in brain function (encephalopathy) in some patients taking <medicinal product> at prescribed doses, which resolved after stopping the medication. Symptoms include increased sleepiness, new onset of drowsiness, confusion, muscle jerks or coma. If you experience any of these symptoms, seek medical attention immediately. Your physician will decide whether baclofen has to be discontinued.

- Section 4 "Possible side effects"

Not known: the frequency cannot be estimated from the available data

- Reduction in brain function (encephalopathy)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	May 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	14 July 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	12 September 2024