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 tiagabine, the scientific conclusions are as follows:

In view of available data on

- memory troubles in a context of overdose from spontaneous reports including in 2 cases a close temporal relationship with a positive de-challenge,

- memory troubles that occurred at recommended doses from spontaneous reports including in some cases a close temporal relationship and a positive de-challenge,

the PRAC considers a causal relationship between tiagabine and amnesia is at least a reasonable possibility. The PRAC concluded that the product information of products containing tiagabine should be amended accordingly.

In view of detailed available data on dyskinesia reported in a context of overdose from a clinical trial and spontaneous reports including in some cases a close temporal relationship, the PRAC considers a causal relationship between tiagabine and dyskinesia in a context of overdose is at least a reasonable possibility. The PRAC concluded that the product information of products containing tiagabine 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 tiagabine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing tiagabine 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 tiagabine 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 should be added under the SOC Nervous system disorders with a frequency "not known": **amnesia**

Post marketing data:

Post-marketing reports have shown that {X} use has been associated with new onset seizures and status epilepticus in patients without epilepsy treated by tiagabine for unapproved indication (see section 4.4).

During post-marketing experience, there have been reports of vision blurred, vomiting, ataxia, abnormal gait, speech disorder, hostility, insomnia, dermatitis bullous, vesiculobullous rash**,** ~~and~~ muscle twitching **and amnesia. In case reports, amnesia occurred within days after initiation or dose increase of tiagabine and was reversible upon discontinuation of tiagabine or dose decrease.**

- Section 4.9

The symptoms of overdose should be amended as follows:

Symptoms most often accompanying {X} overdose, alone or in combination with other medicinal products, have included seizures, including status epilepticus, in patients with and without underlying seizure disorders, mute and withdrawn appearance of the patient, **amnesia,** coma, spike wave stupor, encephalopathy, somnolence, **dyskinesia**, myoclonus, tremors, ataxia or incoordination, dizziness, impaired speech, hostility, agitation, vomiting, and respiratory depression has been seen in the context of seizures.

From post-marketing experience, there have been no reports of fatal overdoses involving {X} alone (doses up to 720 mg), although a number of patients required intubation and ventilatory support as part of the management of their status epilepticus.

In case of overdose, standard symptomatic treatment is recommended. Hospitalisation can be recommended in case of severe overdoses.

Package Leaflet

- 3. How to take {X}

[…] **If you take more** {X} **than you should**

The most common symptoms of overdose with {X} are seizures, mute (silent) and withdrawn, **loss of memory,** coma, difficulty coordinating movements, sleepiness, dizziness, confusion, impaired speech, agitation, tremors, **abnormal involuntary movements (dyskinesia)**, involuntary contraction of muscles, vomiting and hostility.

If you have taken too many tablets or if a child has taken any, immediately contact your doctor or the nearest hospital. […]

- 4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects are generally mild to moderate. Most occur during the first few months of the treatment and are often short-lived. These may include:

Frequency unknown (exact frequency cannot be estimated from the available data)

temporary loss of memory

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	February 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	10 April 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	9 June 2022