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 (fos)carbidopa / (fos)levodopa, the scientific conclusions are as follows:

In view of available data on seizures associated with decreased levels of vitamin B6 from clinical trials, the literature, and spontaneous reports including 5 well-documented literature cases, 2 post-marketing cases with positive dechallenge and 2 cases with positive rechallenge, and in a view of a plausible mechanism of action, the PRAC considers that a causal relationship between (fos)carbidopa/(fos)levodopa and seizures associated with decreased levels of vitamin B6 is at least a reasonable possibility.

The PRAC concluded that the product information of products containing (fos)carbidopa/(fos)levodopa 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 (fos)carbidopa / (fos)levodopa the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing (fos)carbidopa / (fos)levodopa 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. Special warnings and precautions for use

Text applicable for medicinal products containing carbidopa/levodopa

Treatment with carbidopa/levodopa can lead to vitamin B6 deficiency, which may increase the risk of seizures, particularly in patients receiving higher doses, and/or those with poor nutritional status. Monitoring of pyridoxine (vitamin B6) levels and vitamin B6 supplementation should be considered in patients receiving high-dose carbidopa/levodopa and those presenting with clinical manifestations suggestive of vitamin B6 deficiency.

Text applicable for medicinal products containing foscarbidopa/foslevodopa

Treatment with foscarbidopa/foslevodopa can lead to vitamin B6 deficiency, which may increase the risk of seizures, particularly in patients receiving higher doses, and/or those with poor nutritional status. Monitoring of pyridoxine (vitamin B6) levels and vitamin B6 supplementation should be considered in patients receiving high-dose foscarbidopa/foslevodopa and those presenting with clinical manifestations suggestive of vitamin B6 deficiency.

Section 4.8. Undesirable effects

The following adverse reaction should be added under the SOC 'Metabolism and nutrition disorders' with a frequency 'common':

Vitamin B6 deficiency

Package Leaflet

Section 2. Warnings and precautions

Text applicable for medicinal products containing carbidopa/levodopa

Treatment with high doses of carbidopa/levodopa may lead to low levels of vitamin B6, which can increase the risk of seizures. If you are receiving high doses of this medicine, your doctor may perform blood tests to check your vitamin B6 levels. Tell your doctor if you experience signs of low levels of vitamin B6, such as pale skin, weakness or breathlessness (anemia), nerve pain or tingling in the hands and feet (polyneuropathy), or seizures.

Text applicable for medicinal products containing foscarbidopa/foslevodopa

Treatment with high doses of foscarbidopa/foslevodopa may lead to low levels of vitamin B6, which can increase the risk of seizures. If you are receiving high doses of this medicine, your doctor may perform blood tests to check your vitamin B6 levels. Tell your doctor if you experience signs of low levels of vitamin B6, such as pale skin, weakness or breathlessness (anemia), nerve pain or tingling in the hands and feet (polyneuropathy), or seizures.

Section 4. Possible side effects

Common: may affect up to 1 in 10 people:

Having too little vitamin B6

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	June 2026 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	10 August 2026
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	8 October 2026