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 carbidopa / levodopa, the scientific conclusions are as follows:

Serious cases of urinary tract infections (UTI) in relation to carbidopa/levodopa use have been reported, including reports with positive dechallenge and multiple cases with fatal outcome. A retrospective, observational study from Germany found significantly increased risk of UTIs for carbidopa/levodopa compared to benserazide/levodopa. Plausible mechanisms could include the known adverse drug reactions (ADRs) of urinary retention and urinary incontinence, which could subsequently increase the risk for UTI, and a possible role of carbidopa in immunosuppression of T cells. Thus, update of Section 4.8 of the SmPC (and the corresponding section 4 in the package leaflet) to add the ADR of "Urinary tract infection (UTI)", is warranted, in order to raise awareness of physicians on occurrence of UTI in association to carbidopa/levodopa use.

The wording applies strictly to carbidopa/levodopa combination, as the exact mechanism is not elucidated and it cannot be established if the causal relationship of this ADR is in connection to one of the substances, both or combination

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 carbidopa / levodopa the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing carbidopa / levodopa 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 carbidopa / levodopa 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

Under SOC Infections and Infestations: **Urinary tract infections**

frequency: **very common**

Package Leaflet

Section 4 Possible side effects

Urinary tract infections

frequency: **very common**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	May 2023 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	9 July 2023
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	7 September 2023