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 ciclosporin (systemic use), the scientific conclusions are as follows:

In view of available data on risk of hearing impairment from the literature, spontaneous reports, including in some cases a positive de-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between **high level of ciclosporin and hearing impairment** is at least a reasonable possibility.

The PRAC concluded that the product information of products containing ciclosporin 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 ciclosporin (systemic use) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing ciclosporin (systemic use) 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 ciclosporin (systemic use) 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

"***hearing impairment***" should be added under the SOC "Ear and labyrinth disorders" with a frequency "not known", and the following text as footnote to the ADR table: "***Hearing impairment has been reported in the post-marketing phase in patients with high levels of ciclosporin***".

Package Leaflet

- Section 4, under the sub-heading 'Not known: Frequency cannot be estimated from the available data.'

[…]
Hearing impairment.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	September 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	31 October 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	29 December 2022