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 the literature, and spontaneous reports the PRAC considers that cyclosporin is not compatible with breast-feeding. The PRAC concluded that the product information of products containing ciclosporin 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 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 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 4.6**

...

Breast feeding

Ciclosporin enters breast milk usually in low amounts, but maternal milk levels may be variable. ~~Mothers receiving treatment with Sandimmun should not breast-feed because of the potential of Sandimmun to cause serious adverse drug reactions in breast-fed newborns/infants. A decision should be made whether to abstain from breastfeeding or to abstain from using the medicinal drug, taking into account the benefit of breastfeeding for the newborn/infant and the importance of the medicinal product to the mother.~~
~~Limited data showed that the milk to maternal blood concentration ratio of ciclosporin was in the range of 0.17 to 1.4. Based on the infant milk intake, the highest estimated ciclosporin dose ingested by fully breastfed infant was approximately 2% of maternal weight-adjusted dose.~~ **With typical maternal ciclosporin blood levels, a fully breastfed infant would usually receive no more than about 2% of the mother's weight-adjusted dosage. In most breastfed infants, ciclosporin was not detectable in blood, however, in a few cases blood levels ranging from detectable to therapeutic have been measured, even when ciclosporin milk levels were low. Follow-up of breastfed infants have not identified any adverse effects, however the long-term risks of even small amounts of exposure are still unknown.**

Ciclosporin is not recommended during breastfeeding due to the potential for adverse reactions in the infant.

Package Leaflet

- **Section 2**

Pregnancy and breast-feeding
...

Tell your doctor if you are breast-feeding. Breast-feeding is not recommended during treatment with ciclosporin. This is because ciclosporin, the active substance, passes into breast milk. This may affect your baby.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	September 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	2 November 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	1 January 2026