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 cisatracurium, the scientific conclusions are as follows:

In view of available data on breastfeeding (influence on the breastfed infant and time to abstain from breastfeeding) from the literature and based on the pharmacokinetic profile, the PRAC concluded that the product information of products containing cisatracurium should be amended accordingly.

In view of available data on anaphylactic shock from the literature and spontaneous reports including cases with a close temporal relationship, the PRAC considers that a causal relationship between cisatracurium and anaphylactic shock is established. The PRAC concluded that the product information of products containing cisatracurium 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 cisatracurium the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) cisatracurium 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 cisatracurium 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 4.6

The following wording should be added:

Lactation

It is not known whether cisatracurium or its metabolites are excreted in human milk.

A risk to the breastfed infant cannot be excluded. However, due to the short half-life, an influence on the breastfed infant is not to be expected if the mother restarts breast-feeding after the effects of the substance have worn off. As a precaution breast-feeding should be discontinued during treatment and it is recommended to abstain from next breastfeeding for five elimination half- lives of cisatracurium, i.e. for about 3 hours after the last dose or the end of infusion of cisatracurium.

- Section 4.8

The following adverse reaction should be added under the SOC Immune system disorders with a frequency very rare:

Post-marketing data

Anaphylactic reaction, **Anaphylactic shock**

Anaphylactic reactions of varying degrees of severity have been observed after the administration of neuromuscular blocking agents**, including anaphylactic shock**. Very rarely, severe anaphylactic reactions have been reported in patients receiving cisatracurium in conjunction with one or more anaesthetic agents.

Package Leaflet

- Section 2

Pregnancy and breastfeeding

An adverse impact of cisatracurium on the breastfed child cannot be excluded, however it is not expected if breastfeeding is restarted after the effects of the substance have worn off. Cisatracurium is quickly eliminated from the body. Women should abstain from breastfeeding for 3 hours after the treatment discontinuation.

- Section 4

Allergic reactions (affects less than 1 in 10,000 people)

If you have an allergic reaction, tell your doctor or nurse straight away. The signs may include:

- sudden wheeziness, chest pain or chest tightness
- swelling of your eyelids, face, lips, mouth or tongue
- a lumpy skin rash or 'hives' anywhere on your body
- a collapse **and shock**.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	March 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	9 May 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	8 July 2021