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 metoclopramide, the scientific conclusions are as follows:

Based on the available data, the observed reactions of visual disturbances and in particular oculogyric crisis is considered to be important clinical manifestations of listed adverse reactions such as extrapyramidal reactions and dystonia. In the EudraVigilance database there are 478 ICSRs of oculogyric crisis for metoclopramide (data not checked for duplicates). In a few of the EU SmPCs oculogyric crisis and visual disturbances are listed, however in most EU SmPCs visual disturbances and oculogyric crisis are not mentioned in section 4.8. As visual disturbances and oculogyric crisis are important clinical manifestations of dystonia that could be mistaken for other diseases such as epilepsy or encephalitis, the LMS considers that these reactions should be included in the product information as examples of the clinical manifestations of dystonia to ensure that physicians and patients are alert to the possibility that these reactions could affect the eyes.

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

Update of section 4.8 of the SmPC to add visual disturbances and oculogyric crisis with a frequency uncommon. The Package leaflet is updated accordingly.

The following changes to the product information of medicinal products containing the active substance metoclopramide are recommended (new text **underlined and in bold**, deleted text ~~strike through~~):

Summary of Product Characteristics

- Section 4.8

The following adverse reaction(s) should be added under the SOC "Nervous system disorders" with a frequency Uncommon: Dystonia **(including visual disturbances and oculogyric crisis)**

Package Leaflet

Section 4:

Uncommon: Visual disturbances and involuntary deviation of the eye ball

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	08 September 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	07 November 2019