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 loperamide, loperamide / simeticone, the scientific conclusions are as follows:

Based on review of literature and spontaneous reporting, the PRAC considered that a causal relationship between QRS complex prolongation and loperamide, loperamide/simeticone, cannot be excluded and therefore recommends that this is added to sections 4.4 and 4.9 of the SmPC within the cardiac events.

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 loperamide, loperamide / simeticone the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing loperamide, loperamide / simeticone 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 loperamide, loperamide / simeticone 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 4.4

A warning should be revised as follows:

Cardiac events including QT interval **and QRS complex** prolongation, torsade de pointes have been reported in association with overdose. Some cases had a fatal outcome (see section 4.9). Patients should not exceed the recommended dose and/or the recommended duration of treatment.

- Section 4.9

A warning should be revised as follows:

In individuals who have ingested overdoses of loperamide ~~HCl~~, cardiac events such as QT interval **and QRS complex** prolongation, torsade de pointes, other serious ventricular arrhythmias, cardiac arrest and syncope have been observed (see section 4.4). Fatal cases have also been reported.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	16 March 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	15 May 2019