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:

Scientific conclusions and grounds for variation to the terms of the marketing authorisations

In view of available data on acute pancreatitis from the literature, spontaneous reports including in 9 a positive de-challenge and 1 re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between loperamide and loperamide/simeticone and acute pancreatitis is at least a reasonable possibility. The PRAC concluded that the product information of products containing loperamide and loperamide/simeticone 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 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 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

The following adverse reaction(s) should be added under the SOC Gastrointestinal disorder with a frequency “not known”:

acute pancreatitis

Package Leaflet

- Section 4:

Get medical help at once:

(...)

Not known (frequency cannot be estimated from the available data)

Upper abdominal pain, abdominal pain that radiates to back, tenderness when touching the abdomen, fever, rapid pulse, nausea, vomiting, which may be symptoms of inflammation of the pancreas (acute pancreatitis).

If you get any of these, stop using the medicine and get medical help at once.

(...)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position :	14 March 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	12 May 2022