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 magnesium hydroxide, the scientific conclusions are as follows:

Based on literature reviewed during the reporting period, magnesium excretion may be insufficient to balance intestinal magnesium absorption in renal impaired patients. As children are a vulnerable population and at higher risk of developing hypermagnesemia, especially if they suffer from renal impairment or dehydration, PRAC considered to include a warning in section 4.4 of the summary of products characteristics (SmPC) regarding the risk of hypermagnesemia in children in the product information (PI) of magnesium hydroxide containing products with an approved indication in children. Hypermagnesemia in adults with renal impairment has been also described in literature as an adverse drug reaction (ADR) and therefore an update of section 4.8 of the SmPC to include hypermagnesemia is also recommended. In addition, abdominal pain should be included in section 4.8 of the SmPC as an ADR based on cases retrieved from Eudravigilance and also taking into account that the mode of action of magnesium hydroxide underlines a possible interaction within the gastrointestinal-tract. Further, an analysis of drug-drug-interactions (DDI) of outpatient prescriptions in infants and newborns found that interactions between aspirin and aluminium / magnesium hydroxide were most common, with potential reducing effects on serum salicylate. As salicylates are widely used in adults, the conclusion of this analysis should be considered for further patient groups and therefore, PRAC recommended updating section 4.5 of the SmPCs to include the interaction between magnesium hydroxide containing products and salicylates. The package leaflet is updated 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 magnesium hydroxide the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing magnesium hydroxide 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 magnesium hydroxide 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 Special warnings and precautions for use

[A warning should be added in those SmPCs with an approved indication for children as follows]

Paediatric population

In young children the use of magnesium hydroxide can produce a hypermagnesemia, especially if they present renal impairment or dehydration.

- Section 4.5 Interaction with other medicinal products and other forms of interaction

[The following text should be added as follows]
Urine alkalinisation secondary to administration of magnesium hydroxide may modify excretion of some drugs; thus, increased excretion of salicylates has been seen.

- Section 4.8 Undesirable effects

[The following adverse reaction should be added under the SOC Gastrointestinal disorders with a frequency not known]

Abdominal pain

[The following adverse reaction should be added under the SOC Metabolism and nutrition disorders with a frequency very rare]

Hypermagnesemia. Observed after prolonged administration of magnesium hydroxide to patients with renal impairment.

Package leaflet

- Section 2

[The following text should be added if applicable due to an approved indication in children]

Children

In small children use of magnesium hydroxide may cause hypermagnesemia particularly if they have renal impairment or dehydration.

[The following text should be added as follows]

Other medicines and magnesium hydroxide

Some medicines may be affected by magnesium hydroxide or they may affect how well magnesium hydroxide will work. Tell your doctor or pharmacist if you are already taking: - salicylates

- Section 4

[The following adverse reactions should be added with a frequency not known]

- Abdominal pain

[The following adverse reactions should be added with a frequency very rare]

- Hypermagnesemia. This was seen after prolonged administration to patients with renal impairment."

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2017 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	2 September 2017
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	1 November 2017