# 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 lanthanum, the scientific conclusions are as follows:

In view of available data on risk of lanthanum deposition in the gastrointestinal tract from the literature and also spontaneous reports, and in view of a plausible mechanism of action, the PRAC considers that a causal relationship between lanthanum and lanthanum deposition in the gastrointestinal mucosa is established. The PRAC concluded that the product information of products containing lanthanum 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 lanthanum the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing lanthanum 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 lanthanum 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**

*For chewable tablets and oral powder*

- Section 4.4 Special warnings and precautions for use

A warning should be amended as follows:

Tissue deposition of lanthanum has been shown with lanthanum in animal studies. In 105 bone biopsies from patients treated with lanthanum carbonate, some for up to 4.5 years, rising levels of lanthanum were noted over time (see section 5.1). Cases of lanthanum deposition in gastrointestinal mucosa, mainly after long term use, have been reported. **Lanthanum deposition in gastroduodenal mucosa is demonstrated endoscopically as whitish lesions of different sizes and shapes. Also, various pathological features were identified in gastroduodenal mucosa with lanthanum deposition, such as chronic or active inflammation, glandular atrophy, regenerative changes, foveolar hyperplasia, intestinal metaplasia and neoplasia.** ~~The clinical significance of this finding is yet unknown.~~ The use of lanthanum carbonate in clinical studies beyond 2 years is currently limited. However, treatment of subjects with lanthanum carbonate for up to 6 years has not demonstrated a change in the benefit/risk profile.

- Section 4.8

The following adverse reaction should be added under the SOC Investigations with a frequency unknown:

SOC Investigations

**Product residue present[1]**

**[1]See Lanthanum deposition in gastrointestinal mucosa warning in section 4.4 Special warnings and precautions for use**

**Package Leaflet**

2. What you need to know before you take [product name] (lanthanum)

Warning and precautions

.....
If you need to have an x-ray, please inform your doctor that you are taking [product name] (lanthanum) as it may affect the results.

**If you need to have a gastrointestinal endoscopy, please inform your doctor that you are taking [product name] (lanthanum) because the endoscopist might detect lanthanum deposits in the digestive tract.**

4. Possible side effects

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

**Product residue present in digestive tract**

## Annex III

## Timetable for the implementation of this position

## Timetable for the implementation of the agreement

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|---|---|
| Adoption of CMDh position: | October 2021 CMDh meeting |
| Transmission to National Competent Authorities of the translations of the annexes to the position: | 26 November 2021 |
| Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder): | 27 January 2022 |