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 dexlansoprazole, lansoprazole, the scientific conclusions are as follows:

In view of available data on tubulointerstitial nephritis (TIN) from the literature and spontaneous reports, including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge, and in view of a plausible mechanism of action, the PRAC considers that a causal relationship between dexlansoprazole or lansoprazole (and other proton pump inhibitors) and TIN, which can progress to other forms of kidney injury, is at least a reasonable possibility. The PRAC concluded that the product information of medicinal products containing the active substance dexlansoprazole or lansoprazole 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 dexlansoprazole, lansoprazole the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing dexlansoprazole, lansoprazole 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 dexlansoprazole, lansoprazole 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 added as follows:

Renal impairment

Acute tubulointerstitial nephritis (TIN) has been observed in patients taking [active substance] and may occur at any point during [active substance] therapy (see section 4.8). Acute tubulointerstitial nephritis can progress to renal failure.

[Active substance] should be discontinued in case of suspected TIN, and appropriate treatment should be promptly initiated.

- Section 4.8

The following adverse reaction(s) should be added or amended, as applicable, under the SOC Renal and urinary disorders with a frequency "rare":

Tubulointerstitial nephritis **(with possible progression to renal failure)**

Package Leaflet

- Section 2

Under sub-section "Warnings and precautions" the following should be added:

When taking [active substance], inflammation in your kidney may occur. Signs and symptoms may include decreased volume of urine or blood in your urine and/or hypersensitivity reactions such as fever, rash, and joint stiffness. You should report such signs to the treating physician.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	09/2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	30 October 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	29 December 2022