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 racecadotril, the scientific conclusions are as follows:

In view of available data on drug reaction with eosinophilia and systemic symptoms (DRESS) and anaphylactic shock from the spontaneous reports and the literature, including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge, the PRAC considers a causal relationship between racecadotril and drug reaction with eosinophilia and systemic symptoms (DRESS) and racecadotril and anaphylactic shock is at least a reasonable possibility. The PRAC concluded that the product information of products containing racecadotril should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for racecadotril the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing racecadotril is unchanged subject to the proposed changes to the product information

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

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**)

Summary of Product Characteristics

- Section 4.4

A warning should be added as follows:

Severe cutaneous adverse reactions (SCARs):

Severe cutaneous adverse reactions (SCARs) including drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported in association with racecadotril treatment. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of DRESS appear, racecadotril should be withdrawn immediately and an alternative treatment considered. If the patient has developed DRESS with the use of racecadotril, treatment with racecadotril must not be restarted in these patients at any time.

- Section 4.8

Summary of safety profile:

Severe cutaneous adverse reactions (SCARs) including drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with racecadotril treatment (see section 4.4).

Table of ADRs

(…..)

The following adverse reaction(s) should be added under the SOC Skin and subcutaneous tissue disorders with a frequency not known:

- **Drug reaction with eosinophilia and systemic symptoms (DRESS)**

The following adverse reaction(s) should be added under the SOC Immune System disorders with a frequency not known:

- **Anaphylactic shock**

Package Leaflet

- Section 2 - What you need to know before you use racecadotril

DO NOT TAKE racecadotril:

- **If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking racecadotril**

Warnings and precautions - Take special care with racecadotril:

Serious skin reactions including drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with racecadotril treatment. Stop using racecadotril and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

- Section 4 – Possible side effects

Stop using racecadotril and seek medical attention immediately if you notice any of the following symptoms:

- **Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome)**
- **Breathing difficulty, swelling, lightheadedness, fast heartbeat, sweating and a feeling of loss of consciousness which are symptoms of a sudden, severe allergic reaction**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	14 December 2023
Transmission to National Competent Authorities of the translations of the annexes to the position:	01 February 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	28 March 2024