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 bacillus clausii multi-antibioresistant spores, the scientific conclusions are as follows:

PRAC considers a causal relationship between bacillus clausii multi-antibioresistant spores and bacteremia and sepsis is at least a reasonable possibility. Therefore, the inclusion of a warning in section 4.4 is justified by the need to inform HCPs and patients of the possibility of serious conditions related to Bacillus Clausii infection in patients with compromission of immune system and severely ill, and guide the clinical judgement accordingly. The existing wording on bacteraemia in section 4.8 will be further revised with the inclusion of septicemia and sepsis.
PRAC considers that the product information of products containing bacillus clausii multi-antibioresistant spores should be amended accordingly.
The benefit/risk balance of bacillus clausii multi-antibioresistant spores remains unchanged.

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 bacillus clausii multi-antibioresistant spores the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing bacillus clausii multi-antibioresistant spores 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 bacillus clausii multi-antibioresistant spores 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:

Bacteraemia/sepsis

Post-marketing cases of bacteraemia, septicaemia and sepsis have been reported in patients being immunocompromised or severely ill, and in preterm infants. In some critically-ill patients, the outcome was fatal. <Product name> should be avoided in these patient groups (see section 4.8).

- Section 4.8

A cross reference should be added to the existing undesirable effect, as follows:

Infections and infestations: bacteraemia**, septicaemia and sepsis** (in immunocompromised **or severely ill** patients) **(see section 4.4)**

Package Leaflet

Section 2. What you need to know before you take <*product name*>

Warnings and precautions

Talk to your doctor before taking <*product name*>:

- if your doctor informed you that your immune system may be weakened (reduced body natural defences) (see section 4).

- before giving <Product name> to a pre-term infant.

- Section 4

Unknown frequencies side effects (may affect less than 1 in 10,000 people):

In case of reduced body's defence mechanisms **or serious illness** and you are taking <product name>, Bacillus clausii may be found in your blood **and may lead to a serious blood infection (see section 2).**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	07/2020 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	21 September 2020
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	5 November 2020