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 ivermectin (systemic use), the scientific conclusions are as follows:

In view of available data on severe cutaneous adverse reactions from spontaneous reports and considering that these adverse reactions are already included in section 4.8 of the SmPC and section 4 of the PIL, the PRAC considers that, as these may be fatal or life-threatening, a warning needs to be added. The PRAC concluded that the product information of products containing ivermectin (systemic use) 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 ivermectin (systemic use) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing ivermectin (systemic use) 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 ivermectin (systemic use) 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**)

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 Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be life-threatening or fatal, have been reported in association with ivermectin treatment (see section 4.8).

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, ivermectin should be withdrawn immediately and an alternative treatment considered. If the patient has developed a severe cutaneous adverse reaction such as SJS or TEN with the use of ivermectin, treatment with ivermectin must not be restarted at any time.

Package Leaflet

- Section 2:

Do not take ivermectin:

- If you are allergic to ivermectin or any of the other ingredients of this medicine (listed in section 6). Signs of an allergic reaction to a medicine can include skin rash, difficulty breathing or fever.
- **If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking ivermectin**

Warnings and precautions

Talk to your doctor before taking ivermectin.

Serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported in association with ivermectin treatment. Stop using ivermectin and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

- Section 4:

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

- **reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome, toxic epidermal necrolysis).**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	17 February 2023
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	19 May 2023