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 permethrin, the scientific conclusions are as follows:

Based on a comprehensive review of “paraesthesia”, including spontaneous reports and literature, paraesthesia was identified as a plausible side effect of permethrin-containing products and therefore the PRAC agreed that the product information be updated accordingly.

In addition, based on a review of the risk of hypersensitive reactions in patients with a previous history of hypersensitivity reactions to chrysanthemums including literature references and post marketing reports as well as the plausibility of a pharmacological mechanism, the PRAC considers that this information should be added in section 4.4 of the SmPC.

Finally, based on a case report during the current PSUR interval suggesting a systemic intoxication and taking into account the recommendation of an Article 45 of Regulation (EC) No1901/2006 procedure finalised in 2013, the PRAC considers that section 4.4 of the SmPC should be amended to inform of the limited experience available with permethrin in children aged 2 months to 23 months and the need for close medical supervision. The Package Leaflet is updated 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 permethrin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing permethrin 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 permethrin are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that 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~~)

1. Paraesthesia

- **Permethrin 5% cream**

SmPC Section 4.8 Undesirable effects

The following adverse reaction should be added under the SOC 'Nervous system' with the frequency 'Common':

"Paraesthesia".

Package Leaflet Section 4. Possible side effects

Common: may affect up to 1 in 10 people

sensations on the skin (paraesthesias) such as tingling, pricking, skin burning sensation

- **Permethrin 1% and 0.43% cutaneous solutions**

SmPC Section 4.8 Undesirable effects

The following adverse reaction should be added under the SOC 'Nervous system' with the frequency 'Not known':

"Paraesthesia".

Package Leaflet Section 4. Possible side effects

Not known: frequency cannot be estimated from the available data

sensations on the skin (paraesthesia) such as tingling, pricking, skin burning sensation

2. Hypersensitivity reactions to chrysanthemums

The following warning should be present in the product information of all permethrin-containing medicinal products:

SmPC Section 4.4 Special warnings and precautions for use

In the case of hypersensitivity to chrysanthemums or other compositae, treatment should only be given if strictly indicated. In such cases treatment should be switched to a chemically different agent.

Package Leaflet Section 2. Warnings and precautions

Talk to your doctor or pharmacist before using X:

- **If you are known to be allergic to chrysanthemums or other compositae - you should only use X after speaking to your doctor.**

3. Limited experience with permethrin in children

The following warning should be present in the product information of all permethrin-containing medicinal products not already containing information regarding medical supervision for the treatment in very young children:

- **Permethrin 5% cream**

SmPC Section 4.4 Special warnings and precautions for use

Paediatric population

Only limited experience is available with X in children aged 2 months to 23 months. Therefore treatment must be given only under close medical supervision in this age group.

Package Leaflet Section 2. Warnings and precautions

Children up to 23 months of age
Do not use X in newborns and infants less than 2 months of age, unless your doctor tells you so. There is no adequate experience in infants and toddlers. Treatment to children up to 23 months of age should only be given under close medical supervision.

- **Permethrin 0.43% cutaneous solution**

SmPC Section 4.4 Special warnings and precautions for use

Paediatric population

Only limited experience is available with X in children aged over 2 months up to 3 years. Therefore, treatment must be performed only under close specialist supervision in this age group.

Package Leaflet Section 2. Warnings and precautions

Children up to 3 years
Do not use X in newborns and infants less than 2 months of age, unless your doctor tells you so. There is no adequate experience in infants and toddlers. Treatment to children up to 3 years of age should only be given under close medical supervision.

- **Permethrin 1% cutaneous solution**

SmPC Section 4.4 Special warnings and precautions for use

Paediatric population

Only limited experience is available with X in children aged over 6 months up to 3 years. Therefore, treatment must be performed only under close specialist supervision in this age group.

Package Leaflet Section 2. Warnings and precautions

Children up to 3 years
Do not use X in newborns and infants less than 6 months of age, unless your doctor tells you so. There is no adequate experience in infants and toddlers. Treatment to children up to 3 years of age should only be given under close medical supervision.

Annex III

Timetable for the implementation of this position>

Timetable for the implementation of this position

Adoption of CMDh position:	April 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position :	9 June 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	8 August 2018