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 ibuprofen / pseudoephedrine, the scientific conclusions are as follows:

Based on review of literature data, the PRAC considered that a causal relationship between the use of ibuprofen / pseudoephedrine and the occurrence of severe skin reactions such as acute generalised exanthematous pustulosis (AGEP) could not be excluded and therefore requests an update of the product information of all ibuprofen / pseudoephedrine containing products in this regard. The Summary of Product Characteristics should be updated to insert a warning on the risk of severe skin reactions such as acute generalized exanthematous pustulosis and to list this adverse drug reaction with the frequency not known. The Package Leaflet should be 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 ibuprofen / pseudoephedrine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing ibuprofen / pseudoephedrine 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 ibuprofen / pseudoephedrine 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~~)

Summary of Product Characteristics

- Section 4.4

A warning should be added as follows:

Severe Skin reactions

Severe skin reactions such as acute generalized exanthematous pustulosis (AGEP) may occur with pseudoephedrine-containing products. This acute pustular eruption may occur within the first 2 days of treatment, with fever, and numerous, small, mostly non-follicular pustules arising on a widespread oedematous erythema and mainly localized on the skin folds, trunk, and upper extremities. Patients should be carefully monitored. If signs and symptoms such as pyrexia, erythema, or many small pustules are observed, administration of <invented name> should be discontinued and appropriate measures taken if needed.

- Section 4.8

The following adverse reaction should be added under the SOC Skin and subcutaneous tissue disorders with a frequency unknown:

- Severe skin reactions, including acute generalized exanthematous pustulosis (AGEP)

Package Leaflet

- Section 2

Warnings and precautions

If you develop a feverish generalised erythema associated with pustules, stop taking <invented name> and contact your doctor or seek medical attention immediately. See section 4.

- Section 4

Frequency “Not known”

Sudden onset of fever, reddening of the skin, or many small pustules (possible symptoms of Acute Generalized Exanthematous Pustulosis - AGEP) may occur within the first 2 days of treatment with <invented name>. See section 2.

Stop using <invented name> if you develop these symptoms and contact your doctor or seek medical attention immediately.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	February 2018 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position :	07 April 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	06 June 2018