# 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 mesalazine, the scientific conclusions are as follows:

In view of available data from the literature and spontaneous reports including in some cases a close temporal relationship and a positive de-challenge, the Lead Member State considers a causal relationship between mesalazine and Severe Cutaneous Adverse Reactions including Stevens-Johnson-Syndrome and Toxic Epidermal Necrolysis is at least a reasonable possibility. The Lead Member State concluded that the product information of products containing mesalazine 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 mesalazine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing mesalazine 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 mesalazine 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:

**Severe cutaneous adverse reactions**

**Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in association with mesalazine treatment.**

**Mesalazine should be discontinued, at the first appearance of signs and symptoms of severe skin reactions, such as skin rash, mucosal lesions, or any other sign of hypersensitivity.**

- Section 4.8

The following adverse reaction(s) should be added under the SOC Skin and subcutaneous tissue disorders with a frequency unknown: Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN)

Section 4.8 Summary of safety profile:

**Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in association with mesalazine treatment (see section 4.4).**

Table of ADRs

Skin and subcutaneous tissue disorders SOC: Frequency: unknown

**Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)**

**Package Leaflet**

Section 2 - What you need to know before you use <medicine>

TELL YOUR DOCTOR BEFORE USING mesalazine:

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

Warnings and precautions - Take special care with mesalazine:

**Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis have been reported in association with mesalazine treatment. Stop using mesalazine**

**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 mesalazine 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**

## Annex III

## Timetable for the implementation of this position

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| Adoption of CMDh position: | 10/2020 CMDh meeting |
| Transmission to National Competent Authorities of the translations of the annexes to the position: | 29/11/2020 |
| Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder): | 20/01/2021 |