

**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 on urine discolouration from spontaneous reports and in view of a plausible mechanism of action, the PRAC considers a causal relationship between mesalazine and urine discolouration after contact with sodium hypochlorite is at least a reasonable possibility.

In view of available data on DRESS from spontaneous reports, the PRAC considers a causal relationship between mesalazine and DRESS is at least a reasonable possibility.

The PRAC 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:

**Mesalazine may produce red-brown urine discoloration after contact with sodium hypochlorite bleach (e.g., in toilets cleaned with sodium hypochlorite contained in certain bleaches)**

A warning should be added as follows:

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARs), including **Drug reaction with eosinophilia and systemic symptoms (DRESS)**, 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:

**Drug reaction with eosinophilia and systemic symptoms (DRESS)**

Summary of safety profile

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

#### Package Leaflet

Section 2 - What you need to know before you use mesalazine

Warnings and precautions

**Mesalazine may produce red-brown urine discoloration after contact with sodium hypochlorite bleach in the toilet water. It concerns a chemical reaction between mesalazine and bleach and is harmless.**

Warnings and precautions - Take special care with mesalazine:

Serious skin reactions including **Drug reaction with eosinophilia and systemic symptoms (DRESS)**, Stevens-Johnson syndrome (**SJS**), and toxic epidermal necrolysis (**TEN**) 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

Serious 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, **widespread rash, fever and enlarged lymph nodes**.

These serious skin rashes can be preceded by fever and flu-like symptoms.

**Annex III**

**Timetable for the implementation of this position**

### Timetable for the implementation of this position

Adoption of CMDh position:	October/2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	28 November 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	26 January 2023