

**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 metronidazole / neomycin / nystatin, the scientific conclusions are as follows:

In view of available data on risk of fixed-drug eruption and risk of vulvovaginal discomfort from the literature, spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and in view of a plausible mechanism of action, the Lead Member State considers a causal relationship between metronidazole / neomycin / nystatin and fixed-drug eruption, as well as vulvovaginal discomfort in cases of incomplete dissolution of the tablet, is at least a reasonable possibility. The PRAC concluded that the product information of products containing metronidazole / neomycin sulfate / nystatin should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

### **Grounds for the variation to the terms of the marketing authorisation(s)**

On the basis of the scientific conclusions for metronidazole / neomycin / nystatin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing metronidazole / neomycin / nystatin is unchanged subject to the proposed changes to the product information

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

## **Annex II**

**Amendments to the product information of the nationally authorised medicinal products**

**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 4.2

After a thorough hand wash, wet the tablet by soaking in water for 2 to 3 seconds. In order to dissolve well at the vaginal level, the tablet requires a minimum of hydration at the local level. In case of vaginal dryness, it is possible that the tablet does not disintegrate completely, **potentially causing vulvovaginal discomfort**. After moistening, the tablet should be introduced deep into the vagina, preferably in an extended position. The easiest way to do this is to lie on your back with your knees bent and spread. Then lie down for about 15 minutes.

- Section 4.8

The following adverse reaction(s) should be added with a frequency "**not known**", under the SOC:

- "***Skin and subcutaneous tissue disorders***" ~~*Cutaneous and mucosal signs: allergy (urticaria, pruritus), hot flashes, glossitis with a sensation of dry mouth;*~~ **Fixed drug eruption: cases of recurrence of fixed drug eruption have been reported with metronidazole by vaginal route in patients with previous occurrence of this reaction with oral administration of metronidazole.**
- "***Gastrointestinal disorders***": **glossitis with a sensation of dry mouth;**

### Package Leaflet

- Section 3

#### Method and route of administration

Vaginal route.

After thoroughly washing your hands, wet the tablet by dipping it in water for 2 to 3 seconds. **In case of vaginal dryness, the tablet may not disintegrate completely, potentially causing vulvovaginal discomfort.**

After soaking the tablet, insert it deep into the vagina, preferably while lying down. The easiest way to do this is to lie on your back with your knees bent and apart.

Then remain lying down for about fifteen minutes.

- Section 4:

frequency **not known (frequency cannot be estimated from the available data):**

- **A distinctive cutaneous allergic reaction known as fixed drug eruption, that may look like round or oval patches of redness and swelling of the skin, blistering (hives), itching.**

**Annex III**

**Timetable for the implementation of this position**

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Adoption of CMDh position:	April 2026 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	7 June 2026
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	6 August 2026