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 sumatriptan, naproxen / sumatriptan, the scientific conclusions are as follows:

Breastfeeding

Two lactation studies (Wojnar-Horton et al. 1996, and Amundsen et al. 2021), reported average relative infant doses (RID) values of respectively, 3.5% (95% CI 0.3 - 6.7%) and 1.8% (range: 0.8% - 3.8%), following administration of single dose of sumatriptan, including a single dose of 6 mg (s.c. injection), 20 mg (nasal spray), or 50 or 100 mg (tablets).

Breast pain

In view of available data on breast pain from spontaneous reports, a supporting plausible mechanism via vasoconstrictive effect of sumatriptan, and clinical trial data suggesting a higher incidence of breast pain in the sumatriptan group compared with placebo, the PRAC considers a causal relationship between sumatriptan and breast pain in breastfeeding and non-breastfeeding women established and concludes that the product information of products containing sumatriptan and naproxen/sumatriptan should be amended to include breast pain as ADR accordingly. Based on trial data (incidence breast pain of 0.049%), frequency category of PT 'breast pain', is rare ($\geqslant$1/10,000 to<1/1,000). In addition, the PRAC is of the opinion that HCPs and in specific breastfeeding women should be made aware of the possibility of breast pain and/or nipple pain after sumatriptan use and how long this pain takes and proposes to reflect this in section 4.6 and the corresponding PIL.

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 sumatriptan, naproxen / sumatriptan the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing sumatriptan, naproxen / sumatriptan 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 product(s)

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike through~~)

The following changes to the product information of medicinal products containing the active substance **sumatriptan** as **mono-**product are recommended (new text **underlined and in bold**, deleted text ~~strike through~~):

Summary of Product Characteristics

- Section 4.6

[…]

Breastfeeding

*~~It has been demonstrated that following subcutaneous administration, s~~**S**umatriptan is secreted into breast milk**, with average relative infant doses of < 4% following administration of a single dose of sumatriptan.** Infant exposure can be minimised by avoiding breast feeding for 12 hours after treatment, during which time any breast milk expressed should be discarded.*

There have been reports of breast pain and/or nipple pain following sumatriptan use in breastfeeding women (see section 4.8). The pain was usually transient and disappeared in 3 to 12 hours.

Package Leaflet

Section 2

Pregnancy and breast-feeding

[…]

Don't breast-feed your baby for 12 hours after <taking> <using> [Trade name]. *If you express any breast milk during this time, discard the milk and don't give it to your baby.*

Some breastfeeding women report breast and/or nipple pain after use of sumatriptan. The pain is usually temporary and disappears in 3 to 12 hours.

The following changes to the product information of medicinal products containing the active substances **sumatriptan / naproxen** are recommended (new text **underlined and in bold**, deleted text ~~strike through~~):

Summary of Product Characteristics

- Section 4.6

[…]

Breastfeeding

Both active components of [invented name], sumatriptan and naproxen sodium have been reported to be excreted in human breast milk. ***Sumatriptan is excreted into breast milk with average relative infant doses of < 4% following administration of a single dose of sumatriptan.*** *Because of the*

possible adverse effects of these drugs on neonates, use of [invented name] in nursing mothers should be avoided. Any breast milk expressed for at least 12 hours after treatment should be discarded.

Package Leaflet

- Section 2

<No changes proposed>

The following changes to the product information of medicinal products containing the active substance **sumatriptan**, for all products (**sumatriptan mono-product and sumatriptan / naproxen combination**), are recommended (new text **underlined and in bold**, deleted text ~~strike through~~):

Summary of Product Characteristics

- Section 4.8

The following adverse reaction should be added under the SOC Reproductive system and breast disorders with a frequency rare:

Breast pain

Package Leaflet

- Section 4

Other rare side effects include:
[…]
● Breast pain

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	May 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	6 July 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	4 September 2025