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 mifepristone, the scientific conclusions are as follows:

In view of available data on acute generalised exanthematous pustulosis (AGEP) from the literature, including in 2/2 cases a close temporal relationship, the PRAC considered a causal relationship between mifepristone and AGEP is at least a reasonable possibility. Therefore, the PRAC concluded that the product information (PI) of products containing mifepristone should be amended accordingly, updating

sections 4.4 and 4.8 of the SmPC, respectively, to add a warning on severe cutaneous adverse reactions, and the adverse reaction acute generalised exanthematous pustulosis (AGEP) with a frequency unknown. 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 mifepristone, the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing mifepristone 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 mifepristone 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:

Exelgyn/Nordic Group:

Severe cutaneous adverse reactions, including toxic epidermal necrolysis and acute generalised exanthematous pustulosis, have been reported in association with mifepristone (see section 4.8). In patients who experience severe cutaneous adverse reactions, treatment with mifepristone should be immediately discontinued. Re-treatment with mifepristone is not recommended.

Amring/Linepharma:

Severe cutaneous adverse reactions, including toxic epidermal necrolysis and acute generalised exanthematous pustulosis, have been reported in association with mifepristone (see section 4.8). In patients who experience severe cutaneous adverse reactions, re-treatment with mifepristone is not recommended.

- Section 4.8

Exelgyn/Nordic Group and Amring/Linepharma:

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

Acute generalised exanthematous pustulosis

Package Leaflet

Section 2

The following warning should be added under Warning and precautions:

Exelgyn/Nordic Group:

Serious skin reactions including toxic epidermal necrolysis and acute generalized exanthematous pustulosis have been reported in association with [product name] treatment. Stop using [product name] and seek medical attention immediately if you notice any of the symptoms described in section 4. If you get a serious skin reaction you should not use mifepristone again in the future.

Amring/Linepharma:

Serious skin reactions including toxic epidermal necrolysis and acute generalized exanthematous pustulosis have been reported in association with [product name] treatment. Seek medical attention immediately if you notice any of the symptoms described

in section 4. If you get a serious skin reaction you should not use mifepristone again in the future.

Section 4 Possible side effects

Exelgyn/Nordic Group:

The following should be added to the list of serious side effects requiring medical attention:

- **Reddish patches on the trunk, the patches are target-like macules or circular, 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 (toxic epidermal necrolysis, frequency: rare).**
- **A red, scaly widespread rash with bumps under the skin and blisters accompanied by fever. The symptoms usually appear at the initiation of treatment (acute generalised exanthematous pustulosis, frequency: not known).**

Amring/Linepharma:

Contact your doctor or go to the nearest hospital department immediately if you experience any of the following symptoms:

…

- **Reddish patches on the trunk, the patches are target-like macules or circular, 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 (toxic epidermal necrolysis, frequency: rare or very rare).**
- **A red, scaly widespread rash with bumps under the skin and blisters accompanied by fever. The symptoms usually appear at the initiation of treatment (acute generalised exanthematous pustulosis, frequency: not known).**

Rare (may affect up to 1 in 1,000 people) and very rare (may affect up to 1 in 10,000 people) side effects:

…

- ~~toxic epidermal necrolysis~~

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	27 January 2021
Transmission to National Competent Authorities of the translations of the annexes to the position:	13 March 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	12 May 2021