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 / misoprostol the scientific conclusions are as follows:

In view of available data on cardiovascular events (cardiac arrest, myocardial infarction and/or spasm of the coronary arteries and severe hypotension) from the literature, spontaneous reports including some cases with a close temporal relationship and in view of a plausible mechanism of action, the Lead Member State in the PSUSA procedure of the oral formulation of misoprostol (gynaecological indication – termination of pregnancy) considers a causal relationship between misoprostol (gynaecological indication – termination of pregnancy) and cardiovascular events is at least a reasonable possibility. It was concluded that the product information of products containing misoprostol (gynaecological indication – termination of pregnancy) should be amended accordingly.

For the PSUSA of the vaginal formulation of mifepristone/ misoprostol with the same indication (gynaecological indication - termination of pregnancy) the Lead Member State considers that the warning on cardiovascular events (cardiac arrest, myocardial infarction and/or spasm of the coronary arteries and severe hypotension) reported following us of misoprostol in the product information, section 4.4, of products containing mifepristone / misoprostol should also be amended to reflect the new information.

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 mifepristone / misoprostol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing mifepristone / misoprostol 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~~)

Summary of Product Characteristics

- Section 4.4

A warning should be amended as follows:

Rare but serious cardiovascular accidents **(cardiac arrest, myocardial infarction and/or spasm of the coronary arteries and severe hypotension)** have been reported following **use of misoprostol.** ~~administration of prostaglandin analogue~~. For this reason, women with risk factors for cardiovascular disease **(e.g. age over 35 years with chronic smoking, hyperlipidemia, diabetes)** or established cardiovascular disease should be treated with caution.

Package leaflet

2. What you need to know before you take <name of the product>

Warnings and precautions

Talk to your doctor before taking <name of the product>

- if you are at increased risk of cardiovascular disease. Risk factors include being aged over 35 years and a cigarette smoker or having high blood pressure, high blood cholesterol levels or diabetes

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	10 March 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	9 May 2024