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 misoprostol (gynaecological indication - labour induction), the scientific conclusions are as follows:

Based on a prospective study by Auffret et al. (2016) the PRAC considers that misoprostol use in early pregnancy was associated with specific patterns of foetal malformations in a likely non-dose-dependent manner and therefore recommends updating the Product Information by adding a warning in the section 4.6 of the SmPCs for misoprostol-containing products indicated for labour induction about the risk of teratogenicity in relation to exposure during early pregnancy.

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 misoprostol (gynaecological indication - labour induction)the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing misoprostol (gynaecological indication - labour induction)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 misoprostol (gynaecological indication - labour induction)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 4.6

A warning should be added as follows:

Pregnancy

[Product] is used for labour induction at a low misoprostol dosage for a short period of time at the very end of pregnancy. When used at that time of pregnancy, there is no risk of foetal malformations. [Product] should not be used at any other time during pregnancy: a three-fold increased risk of foetal malformations (including Moebius syndrome, amniotic band syndrome and central nervous system anomalies) has been reported in pregnancies exposed to misoprostol in first trimester.

Package Leaflet

- Section 2

Pregnancy

[Product] is used to help start labour from week [product-specific number of weeks] of pregnancy. When used at that time of pregnancy, there is no risk of birth defects for your baby. However, you should not use [product] at any other time during pregnancy because misoprostol can then cause birth defects.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	16 March 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	15 May 2019