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 betamethasone, the scientific conclusions are as follows:
In view of the literature reports of pheochromocytoma crisis indicating a close temporal relationship, including two describing a positive rechallenge, which suggest that administration of betamethasone may precipitate pheochromocytoma crisis, considering the literature reports of pheochromocytoma crisis in association with other corticosteroids suggesting a class effect, and the serious and potentially life-threatening nature of the condition, the PRAC Lead Member State concluded that the product information of products containing betamethasone should be amended accordingly.

In view of the literature data indicating an increased risk of neonatal hypoglycaemia following antenatal use of betamethasone the PRAC Lead Member State concluded that the product information of products containing betamethasone should be amended 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 betamethasone the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing betamethasone 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 betamethasone 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

For systemic (oral and parenteral) betamethasone products:

- Section 4.4

A warning should be added as follows:

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

For parenteral betamethasone products:

- Section 4.6

A warning should be added as follows:

Studies have shown an increased risk of neonatal hypoglycaemia following antenatal administration of a short course of betamethasone to women at risk for late preterm delivery.

Package Leaflet

For systemic (oral and parenteral) betamethasone products:

Section 2

Warnings and precautions

Talk to your doctor <or> <pharmacist> <or nurse> before <taking> <using> X

…

If you have pheochromocytoma (a tumour of the adrenal gland)

For parenteral betamethasone products:

Section 2
What you need to know before you <take> <use> X
Pregnancy <and> <,> breast-feeding <and fertility>
…
Newborn babies of mothers who received X near the end of pregnancy may have low blood sugar levels after birth.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	September CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	31 October 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	30 December 2021