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 dexamethasone, the scientific conclusions are as follows:

In view of available data on hypertrophic cardiomyopathy in preterm infants from the literature, and spontaneous case reports showing a close temporal relationship, a positive de-challenge (observed after withdrawal and/or dose reduction) and in view of a plausible mechanism of action, the Lead Member State considers a causal relationship between dexamethasone and hypertrophic cardiomyopathy in premature infants is at least a reasonable possibility. The Lead Member State concluded that the product information of products containing dexamethasone for parenteral use should be amended accordingly.

In view of the literature data indicating an increased risk of neonatal hypoglycaemia following antenatal use of dexamethasone the PRAC Lead Member State concluded that the product information of products containing dexamethasone for parenteral use 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 dexamethasone the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing dexamethasone 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 dexamethasone 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~~)>

For parenteral dexamethasone products:

Summary of Product Characteristics

- *Section 4.4*

A warning should be added as follows:

Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy was reported after systemic administration of corticosteroids including dexamethasone to prematurely born infants. In the majority of cases reported, this was reversible on withdrawal of treatment. In preterm infants treated with systemic dexamethasone diagnostic evaluation and monitoring of cardiac function and structure should be performed (section 4.8).

- *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 corticosteroids including dexamethasone to women at risk for late preterm delivery.

- *Section 4.8*

The following adverse reaction should be added under the SOC Cardiac Disorders with a frequency not known:

hypertrophic cardiomyopathy in prematurely born infants (see section 4.4).

Package Leaflet

Section 2. What you need to know before you are given <name of the product>

Warnings and precautions

If dexamethasone is given to a prematurely born baby, monitoring of heart function and structure is needed.

Package Leaflet

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.

Section 4. Possible side effects

Frequency 'Not known': ***Thickening of the heart muscle (hypertrophic cardiomyopathy) in prematurely born babies, that generally returns to normal after stopping treatment.***

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	October 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	28 November 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	27 January 2022