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 dexamfetamine, the scientific conclusions are as follows:

Based on available data from the literature on exposure during pregnancy, including 2 cohort studies, the PRAC considers that updates to the section 4.6 of the SmPC and 2 of the PL are warranted to describe the current information from use of lisdexamphetamine, amphetamine and dextroamphetamine during 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 dexamfetamine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing dexamfetamine 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 dexamfetamine 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

There is a limited amount of data from the use of dexamfetamine in pregnant women.

Data from a cohort study of in total approximately 5570 pregnancies exposed to amphetamine in the first trimester do not suggest an increased risk of congenital malformation. Data from another cohort study in approximately 3100 pregnancies exposed to amphetamine during the first 20 weeks of pregnancy, suggest an increased risk of preeclampsia, and preterm birth.

Children of mothers who are dependent on amfetamine have been shown to be at an increased risk of premature birth and reduced birth weight.

Moreover, these children may develop withdrawal symptoms like dysphoria, including hyperexcitability and pronounced exhaustion.

(...)

Package Leaflet

- Section 2

2. What you need to know before you take [TRADENAME]

Pregnancy, breast-feeding and fertility

~~<Tradename> may affect an unborn baby.~~

Available data from the use of [Tradename] during the first three months of pregnancy do not indicate increased risk of congenital malformation in the child, but may increase the risk for pre-eclampsia (a condition usually occurring after 20 weeks of pregnancy characterized by high blood pressure and protein in the urine) and preterm birth. Newborns exposed to amphetamine during pregnancy may experience withdrawal symptoms (changes in behavior including excessive crying, unstable or irritable mood, hyperexcitability and pronounced exhaustion).

(...)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	April 2020 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	14/06/2020
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	13/08/2020