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 leuprorelin (depot formulations), the scientific conclusions are as follows:

In view of available data on Idiopathic intracranial hypertension from the literature, clinical trials and spontaneous reports including as documented for some cases, a positive de-challenge, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between leuprorelin (depot formulations) and Idiopathic intracranial hypertension (pseudo tumor cerebri) as at least a reasonable possibility. The PRAC concluded that the product information of products containing leuprorelin (depot formulations) 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 leuprorelin (depot formulations) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing leuprorelin (depot formulations) 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 leuprorelin (depot formulations) 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

Leuprorelin (depot formulations) adult and paediatric indications

- Section 4.4

A warning should be added as follows:

Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (pseudotumor cerebri) has been reported in patients receiving leuprorelin. Patients should be warned for signs and symptoms of idiopathic intracranial hypertension, including severe or recurrent headache, vision disturbances and tinnitus. If idiopathic intracranial hypertension occurs, discontinuation of leuprorelin should be considered.

- Section 4.8

The following adverse reaction should be added under the SOC Nervous system disorders with a frequency Not known:

Idiopathic intracranial hypertension (pseudotumor cerebri) (see section 4.4)

Package Leaflet

Section 2:

Warnings and precautions

Talk to your doctor:

Leuprorelin (depot formulations) for both adult and paediatric indications

If you (or your child) suffer from a bad or recurrent headache, problems with your eyesight and ringing or buzzing in the ears contact your doctor immediately.

Leuprorelin (depot formulations) for adult indications only

- **If you suffer from a bad or recurrent headache, problems with your eyesight and ringing or buzzing in the ears contact your doctor immediately.**

Section 4: Possible side effects

Not known: frequency cannot be estimated from the available data

Idiopathic intracranial hypertension (increased intracranial pressure around the brain characterised by headache, double vision and other visual symptoms and ringing or buzzing in one or both ears)

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	March 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	9 May 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	7 July 2022