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 levonorgestrel / ethinylestradiol, ethinylestradiol (combination pack), the scientific conclusions are as follows:

In view of available data on Drug induced Liver injury (especially elevation of transaminases) from the literature, spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and re-challenge and in view of a plausible mechanism of action, the PRAC considers a causal relationship between levonorgestrel / ethinylestradiol, ethinylestradiol and elevation of hepatic enzymes is at least a reasonable possibility. The PRAC concluded that the product information of products containing for levonorgestrel / ethinylestradiol, ethinylestradiol (combination pack) should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions levonorgestrel / ethinylestradiol, ethinylestradiol (combination pack) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing levonorgestrel / ethinylestradiol, ethinylestradiol (combination pack) is unchanged subject to the proposed changes to the product information

The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

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 4.8

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

- **Transaminases increased**

Package Leaflet

4. Possible side effects

[…]

Not known: frequency cannot be estimated from the available data

- loss of consciousness
- baldness
- pains in arms or legs
- **liver enzymes increased (transaminase elevation).**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	September 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	3 November 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	2 January 2025