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, the scientific conclusions are as follows:

Intra-uterine devices:

Based on literature articles identified in the reporting interval of this PSUSA-procedure and as a precautionary measure, concomitant use of **menstrual cups** should be handled with caution in women using Levonorgestrel-containing intra-uterine devices. Instead, sanitary pads should be preferred in order to minimize the risk to inadvertently pull the strings when removing the cup. Therefore, an update of the package leaflet is considered necessary.

"Dizziness" is currently labelled in the product-information of oral levonorgestrel-containing hormonal contraceptives (Progestin-only pills). For levonorgestrel-containing intra-uterine devices, one MAH retrieved 2549 reports mentioning **dizziness** independently from the insertion/removal procedure cumulatively including 716 medically confirmed cases. Cases with a positive dechallenge and one case describing a positive de- and rechallenge with an at least possible or probable causal association have been identified. Although dizziness is frequent in the general population, the time to onset was in half of the cases less than 1 months after the insertion of the LNG-IUD (but independently from the insertion itself) and therefore plausible associated with the LNG-IUD. Since changes in blood pressure, which is already labelled, or hormonal disturbances might result in dizziness, a causal relationship for dizziness independently from the removal/insertion procedure is at least a reasonable possibility. Therefore, the MAHs for LNG-IUDs are requested to include "dizziness" in the product information.

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 levonorgestrel the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing levonorgestrel 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 levonorgestrel 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~~)

Intra-uterine devices:

Summary of Product Characteristics

- Section 4.8

The following adverse reaction should be added under the SOC "vascular disorders", with a frequency "common" for LNG-IUDs with 52 mg or 19.5 mg levonorgestrel and "uncommon" for LNG-IUDs with 13.5 mg levonorgestrel
"dizziness"

Package Leaflet

Section 2:

Warnings and precautions

[…] Use of sanitary pads is recommended. If tampons **or menstrual cups** are used, you should change them with care so as not to pull the threads of [product name].

Section 4 should be amended with the adverse event **"dizziness"** with a frequency "common" for LNG-IUDs with 52 mg or 19.5 mg levonorgestrel and "uncommon" for LNG-IUDs with 13.5 mg levonorgestrel.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2020 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	15/03/2020
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	14/05/2020