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 chlormadinone acetate / ethinylestradiol, the scientific conclusions are as follows:

In view of available data on risk of elevated liver enzymes from clinical trials, the PRAC considers a causal relationship between concomitant use of sofosbuvir/velpatasvir/voxilaprevir with ethinylestradiol and elevated liver enzymes is at least a reasonable possibility. The PRAC concluded that the product information of products containing chlormadinone acetate/ethinylestradiol 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 chlormadinone acetate / ethinylestradiol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing chlormadinone acetate / ethinylestradiol 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 chlormadinone acetate / ethinylestradiol 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 4.3

The contraindication/s should be amended as follows:

Ethinylestradiol 0.02 mg and chlormadinone acetate 2 mg film-coated tablet is contraindicated for concomitant use with the medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir**,** ~~or~~ medicinal products containing glecaprevir/pibrentasvir **or sofosbuvir/velpatasvir/voxilaprevir** (see ~~sections 4.4 and~~ section 4.5).

- Section 4.4

~~ALT elevations~~

~~During clinical trials with patients treated for hepatitis C virus infections (HCV) with medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin, transaminase (ALT) elevations higher than 5 times the upper limit of normal (ULN) occurred significantly more frequently in women using ethinylestradiol-containing medications such as combined hormonal contraceptives (CHCs). Additionally, also in patients treated with glecaprevir/pibrentasvir ALT elevations were observed in women using ethinylestradiol-containing medications such as CHCs (see sections 4.3 and 4.5).~~

- Section 4.5

An interactions should be added as follows:

During clinical trials with patients treated for hepatitis C virus infections (HCV) with medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin, transaminase (ALT) elevations higher than 5 times the upper limit of normal (ULN) occurred significantly more frequently in women using ethinylestradiol-containing medications such as combined hormonal contraceptives (CHCs). Additionally, also in patients treated with glecaprevir/pibrentasvir or sofosbuvir/velpatasvir/voxilaprevir, ALT elevations were observed in women using ethinylestradiol-containing medications such as CHCs (see section 4.3).

~~Concomitant use with medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir, with or without ribavirin, or glecaprevir/pibrentasvir **or sofosbuvir/velpatasvir/voxilaprevir** may increase the risk of ALT elevations (see sections 4.3 and 4.4).~~

Therefore, ethinylestradiol 0.02 mg and chlormadinone acetate 2 mg film-coated tablet -users must switch to an alternative method of contraception (e.g., progestagen-only contraception or non-hormonal methods) prior to starting therapy with th**e**~~is~~**e** combination drug regimen**s**. Ethinylestradiol 0.02 mg and chlormadinone acetate 2 mg film-coated tablet can be restarted 2 weeks following completion of treatment with th**e**~~is~~**e** combination drug regimen**s**.

Package Leaflet

2. What you need to know before you use [brand name]

Do not <take> <use> X<:>

Do not use <trade name> if you have hepatitis C and are taking the medicinal products containing ombitasvir/paritaprevir/ritonavir, dasabuvir, glecaprevir/pibrentasvir **or** **sofosbuvir/velpatasvir/voxilaprevir** (see also in section Other medicines and <trade name>).

Other medicines and [trade name]

<Tell your <doctor> <or> <pharmacist> if you are <taking> <using>, have recently <taken> <used> or might <take> <use> any other medicines.>

Do not use <trade name> if you have Hepatitis C and are taking the medicinal products containing ombitasvir/paritaprevir/ritonavir, dasabuvir, glecaprevir/pibrentasvir **or** **sofosbuvir/velpatasvir/voxilaprevir**, as ~~this~~ these products may cause increases in liver function blood test results (increase in ALT liver enzyme).

Your doctor will prescribe another type of contraceptive prior to start of the treatment with these medicinal products.

<trade name> can be restarted approximately 2 weeks after completion of this treatment. See section "Do not use <trade name>"

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2022 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	5 September 2022
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	3 November 2022