19 September 2024
EMA/64142/2025
Committee for Medicinal Products for Human Use (CHMP)

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): estradiol / nomegestrol acetate

Procedure No. EMEA/H/C/PSUSA/00002182/202401

Period covered by the PSUR:
27/01/2021 To: 26/01/2024

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Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for estradiol / nomegestrol acetate, the scientific conclusions of PRAC are as follows:

In view of available data from clinical trials on drug-drug interaction between ethinylestradiol and Direct acting antiviral agents used in hepatitis C treatments, which lead to significant liver's enzyme elevation, especially the newly added contra-indication between ethinylestradiol and sofosburvir/velpatasvir/ voxilaprevir adopted during the PSUSA procedure for chlormadinone/ethinylestradiol and extended to all ethinylestradiol-containing products by a CMDh decision , considering also the previous recommendations that extrapolated drug-drug-interactions between ethinylestradiol and anti–hepatitis C virus combinations (Viekirax (ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin) and Maviret (Glecaprevir/ pibrentasvir)) to estradiol-containing products , , and in view of a plausible mechanism of action, the PRAC considers that an interaction between estradiol/nomegestrol and sofosburvir/velpatasvir/voxilaprevir leading to hepatic function disorders is at least a reasonable possibility. Product information updates are proposed to reflect this interaction with Vosevi (4.4 and 4.5). In addition, the existing mention of DDI between Viekirax and nomegestrol/estradiol, should be corrected, as during Viekirax's development the studied regimen was ombitasvir/paritaprevir/ritonavir and dasabuvir with or without ribavirin and not ombitasvir/paritaprevir/ritonavir with or without dasabuvir.

The PRAC concluded that the product information of products containing nomegestrol/estradiol should be amended accordingly. This recommendation should also apply to all estradiol-containing products especially core SPC for HRT.

Having reviewed the PRAC recommendation, the CHMP 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 for estradiol / nomegestrol acetate the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing estradiol / nomegestrol acetate is unchanged subject to the proposed changes to the product informatio

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