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 ethinylestradiol / gestodene (transdermal application), the scientific conclusions are as follows:

During the PSUR period, 32 cases corresponding to 44ADRs related to skin reaction outside the application site were reported. Despite lack of information in the cases, one serious case of rash erythematous has been reported with a plausible time to onset (24h) and a positive dechallenge (recovered after patch withdrawal). Moreover, 7 cases of pruritus generalized were reported. In 3 cases, the reactions occurred during the application of lisvy. The outcome of these cases is unknown. Concomitantly to 'pruritus generalized' other ADRs were reported: Application site pruritus (6), Erythema (6), Application site erythema (5), Application site rash (3), Hypersensitivity (2), Rash (2), Application site hypersensitivity (1), Application site vesicles (1), Drug hypersensitivity (1), Off label use (1), Product adhesion issue (1). The concomitantly reported reactions suggest the possibility that in some cases generalized pruritus could have been the symptom of hypersensitivity.

Of note, Application site reactions were frequently reported during clinical trials. Skin reactions outside the application site are continuously reported (post-marketing source): cumulatively 78 ADRs corresponding to 58 cases were reported. The skin reactions outside application site are also described with other patch including a hormonal contraceptive.

For these reasons, the MAH proposal to add the skin reactions such as erythema, pruritus and skin irritation in the Lisvy and associated names product information is endorsed by PRAC.

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 ethinylestradiol / gestodene (transdermal application) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing ethinylestradiol / gestodene 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 ethinylestradiol / gestodene (transdermal application) 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 **<u>underlined and in bold</u>**, deleted text ~~strike through~~)>

Summary of Product Characteristics

- Section 4.8:

The following adverse reaction(s) should be added under the SOC Skin and subcutaneous tissue disorders with a frequency not known: **<u>skin reactions such as erythema, pruritus and skin irritation outside the application site</u>**

Package Leaflet

- **<u>Not known: cannot be estimated from the available data</u>**

<u>skin reactions such as skin redness, skin itching and skin irritation outside the application site</u>

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	October 2017 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	25 November 2017
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	24 January 2018