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Agreed approach post pilot on PSUSA ARs section 6 (other considerations)

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19th Industry Stakeholder Platform – Operation of EU Pharmacovigilance

Background

- PRAC **pilot (June 2023 - June 2024) where section 6 "other considerations" was removed from PSUSA ARs** [1]

- Analysis of the pilot including reported cases where assessors found difficulties with removal of section 6 → **New approach agreed at July 2024 PRAC and CMDh** [2]

[1] Minutes of PRAC meeting on 10-12 May 2023 (item 12.10.5) & Minutes of PRAC meeting on 23-26 October 2023 (item 12.10.5)

[2] Minutes of the PRAC meeting on 8-11 July 2024 (item 12.10.5) & CMDh minutes - July 2024 (item 6.6.1)

New approach since July 2024 – Key messages

- **Section 6 is permanently removed** from all PSUSA AR templates

- Request for **follow-up measures** and **RMP updates for NAPs** are maintained in the PSUSA AR template
- **Non-compliance** of previous EU regulatory decisions and **lack of harmonisation safety related in the PI** are **permanently discontinued**.

⚠ ***New:***

- Cases of **extrapolation of PSUSA outcome from mono-component to FDC or vice-versa**, where **evidence was reviewed** within the PSUSA, are to be included in the PSUSA AR (see next slide)
- **New DDIs** when the **interacting product is a NAP** will be highlighted to **CMDh** (see next slide)

Extrapolation

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Extrapolation of PSUSA outcome from Mono to FDC (or vice-versa), when evidence reviewed in the PSUSA:

- **Note** to be included in the PSUSA AR that the PSUSA outcome is relevant to the FDC/mono-component
- When extrapolation to CAP → the EMA PL will contact the MAH of the CAP so that the MAH can take appropriate regulatory action
- When extrapolation to NAP/MRP/DCP → CMDh will publish this information in their meeting minutes to enable NAP/MRP/DCP MAHs to take appropriate regulatory action

New DDIs (when interacting product is a NAP/MRP/DCP):

- CMDh will **prompt concerned MAHs** of the interacting NAP, via their **published minutes**, so that these MAHs can take appropriate regulatory action

Steps taken following agreement on the approach

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- **All PSUSA AR templates** (CAPs only, mix CAP/NAPs and NAPs only) were updated to reflect the new agreed approach

- CMDh revised in Sep 2024 their **Pharmacovigilance Q&A (Q10)** [1] for the cases of extrapolation of PSUSA outcome from mono-component to FDC or vice-versa & for new DDIs when the interacting product is a NAP

[1] CMDh_257_2012_Rev_25_2024_09_clean_-_QA_on_PhV.pdf (question 10)

Examples in practice since July 2024

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Dydrogesterone / estradiol - PSUSA/00001276/202312 (July 2024)

- PRAC recommended meningioma updates in SmPC 4.3 and 4.4/PL sections accordingly [1] & relevance of the PSUSA outcome for dydrogesterone

- **CMDh published minutes** [2] (July 2024)

6.2.1.4. Dydrogesterone / estradiol - PSUSA/00001276/202312

The CMDh, having considered the PSUR on the basis of the PRAC recommendation and the PRAC assessment report, agreed by consensus on the variation of the marketing authorisations of medicinal products containing dydrogesterone / estradiol.

Management of the risk of meningioma and the recommendations in the PSUSA are also relevant for medicinal products containing dydrogesterone as mono-component. In particular, PRAC recommends to update section 4.4 of SmPC (and corresponding sections of the PL) and that the contra-indication already present in section 4.3 should be adapted.

Concerned MAHs are reminded to keep the product information of their products up to date with the current scientific knowledge and should submit an appropriate variation application (as detailed in Q/A 3.3 on variations, http://www.hma.eu/20.html), unless duly justified.

[1] dydrogesterone-estradiol: CMDh scientific conclusions and grounds for the variation, amendments to the product information and timetable for the implementation - PSUSA/00001276/202312

[2] CMDh minutes - July 2024 (item 6.2.1.4.)

Examples in practice since July 2024

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Estradiol- Nomegestrol acetate ZOELY - PSUSA/00002182/202401 (Sep 2024)

- PRAC recommended updates in SmPC section 4.4 and 4.5 to amend the interaction between DAAs and estradiol-nomegestrol/ PL sections accordingly [1] & relevance of PSUSA outcome to estradiol

- **CMDh published minutes** [2] (Sep 2024)

8.3.9. Information on PRAC recommendations for PSUSAs for CAPs/NAPs / FR

Following the PRAC review of data on safety and efficacy for products containing the active substance estradiol/nomegestrol acetate (procedure PSUSA/00002182/202401, including CAPs and NAPs), the PRAC concluded that the risk-benefit balance of medicinal products containing nomegestrol/estradiol remains unchanged but recommends that the terms of the marketing authorisations should be varied.

The PRAC recommended changes in sections 4.4 and 4.5 of the SmPC (and corresponding sections of the PL) to amend the interaction between direct acting antiviral agents (DAAs) used in hepatitis C treatments and estradiol.

The proposed recommendations in the PSUSA are also relevant for all medicinal products containing estradiol. Concerned MAHs are reminded to keep the product information of their products up to date with the current scientific knowledge and should consider submission of an appropriate variation (as detailed in Q/A 3.3 on variations, http://www.hma.eu/20.html).

[1] Minutes of the PRAC meeting on 2-5 September 2024 (item 6.2.1)

[2] 2024_09_CMDh_minutes.pdf (item 8.3.9)

Any questions?

Further information

[Insert relevant information sources or contact details as applicable.]

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