Harmonization of Labeling Across Products with Same Active Moiety in the EU

Procedures in Regard to Entire Product Information Texts

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Decision providing procedures

- Dir 2001/83/EC, Article 30(1): divergent decisions of Member States for the same product
- Dir 2001/83/EC, Article 30(2): by CMDh's own choice selection of product information for harmonization
- PhVWP and CMDh Best Practice Guide for Work Sharing concerning the Assessment of PSURs (Update expected)
- Replaced by:
  - Dir 2001/83/EC, Article 107(e): A single assessment of PSURs for all medicinal products containing the same active substance(s)
  - Dir 2001/83/EC, Article 107(g): agreement cannot be reached in case of a single assessment of PSURs that recommends any action concerning more than one marketing authorization (except centralized procedures)

Article 30(1)

- If two or more applications submitted in accordance with Articles 8, 10, 10a, 10b, 10c and 11 have been made for marketing authorization for a particular medicinal product, and if Member States have adopted divergent decisions concerning the authorization of the medicinal product or its suspension or revocation,
- a Member State, the Commission or the applicant or the marketing authorization holder
- may refer the matter to the CMDh for the application of the procedure laid down in Articles 32, 33 and 34.

Article 30(2)

- In order to promote harmonization of authorizations for medicinal products authorized in the Community, Member States shall, each year, forward to the coordination group
- a list of medicinal products for which a harmonized summary of product characteristics should be drawn up.

Selection criteria

- Significant differences in core parts of the SmPC (Sections 4.1 – 4.4)
  - E,g list of contra-indications
- Exclusivity /,patent expiry dates
  - Closer to expiry comes first
- Extent of the use of the product
  - More widely used comes first
- Number of MS where the product is authorised
  - More MS involved – higher priority

Decisions proposed in 2010

Product Name	Active Substance	MAH
Flolan	epoprostenol	GSK
Sandimmun/Neoral	ciclosporin	Novartis
Targocid	teicoplanin	Sanofi Aventis
Rocephin	ceftriaxone	Roche

PSUR workshare procedure (old)

- Due to differences in SmPCs across Europe a document against which PSURs can be assessed is required.
- For the purpose of work sharing the reference safety information will be the Core Safety Profile (CSP).
- This document will be used to determine if new safety information should be added to all SmPCs in the EU.

PSUR workshare procedure (old)

Applicant	Agency
Innovator PSUR	Agency (P-RMS) Assessment Report including CSP based on reference safety information like SmPC, CCSI or CCDS
Generic PSURs (Optional)	
Implementation of the CSP via variation (Ib) within 4 months	Regular Update of the CSP according PSUR cycle

PSUR workshare procedure (old)

9. In the Core Safety Profile (CSP) principle paper, it is mentioned that *"the MAH should highlight to the P-RMS and P-CMS where there is disharmony for certain statements/warnings in SmPCs across the EU"*. What does it mean?

- The same safety information can be included in different sections of the SmPCs (ex: contraindications in a SmPC may be warnings in another SmPCs).
- Therefore the MAH should indicate to P-RMS and to P-CMS these discrepancies.
- In the proposed CSP, the information should be included in the section which best reflects the Company Core Safety Information (CCSI).

PSUR workshare procedure (old)

10. How should be presented the reference safety information (RSI) for PSURs based on EU HBD?

- The RSI (usually CCDS or CCSI) should still be used for preparation of the PSUR.
- For companies who do not have a CCSI or CCDS, the RSI should be the common safety information that is included in all current Summary of Product Characteristics (SmPCs) of the product, as authorised in Member States at the time of data lock point together with a summary of the other safety information that is not included in the RSI.

PSUR workshare procedure (old)

11. There are differences between our national SmPCs. Which SmPC/RSI will be sued as part of the PSUR WS assessment?

- Due to differences in national SmPCs, assessment based on SmPCs will not be possible. The assessment of PSURs under the WS agreement is based on the Core Safety Profile (CSP) (cf. CSP paper).

12. Where a medicinal product has several indications which cover different populations, is it possible to produce several CSPs?

- Yes, this is possible. However it needs to be discussed and agreed with the P-RMS and P-CMS before the start of the PSUR WS procedure. Several CSPs can be submitted, when judged necessary.

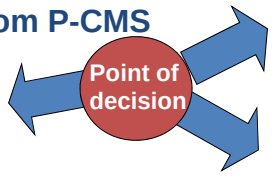
Article 107(e)

- In case at least one centrally authorized product is involved the PRAC will appoint the rapporteur
- In case no centrally authorized product is involved CMDh will appoint a reference member state
- Conditions:
  - Harmonized reference date
  - Harmonized frequency of reporting
- Procedure:
  - Rapporteur or reference member state will draft a preliminary report, seek comments from member states and forward the draft to the PRAC for adoption

PSUR workshare procedure (new)

Day 40 Preliminary draft WS-PSUR AR

Day 70 Comments from P-CMS



Day 74 LoQ to MAHs

Clock stop

Day 75 Draft WS-Final PSUR AR

Day 95 Final WS-PSUR AR + CSP

Day110 Adoption by PRAC

Day150 Referral according Article 107(g) by Commission

In case of divergences harmonization to be initiated

In case of significant actions hand over to PRAC

Article 107(g)

- The CMDh need to agree, considering the report of the Pharmacovigilance Risk Assessment Committee, on the maintenance, variation, suspension or revocation of the marketing authoriz7ations concerned, including a timetable for the implementation of the agreed position within 30 days after receipt of the report of the PRAC.
- If no agreement can be reached by consensus, the position of the majority of member states will be forwarded to the Commission to decide whether a referral shall be initiated.

Challenges

- Totally different way of the decision making process
  - The authority to decide on changes of the authorzation status is assigned to the PRAC
  - The proposal for recommendations wll be worked out by reference member state or rapporteur
  - CMDh and CHMP shall follow the decision adopted by the PRAC
  - Member states are requested to execute the decision
  - In case of disagreement the Commission shall apply for a referral according article 33 and 34 of the Directive
- The condition of harmonized data lock points and harmonized submission frequency of PSURs may contradict all efforts
- Experience need to be gained whether possible advantages of reducing workload can be achieved.

Summary

- The harmonisation efforts will be concentrated on safety information
- Based on SmPC, CCDS, CCSI or existing CSP a single assessment will be possible for products with harmonized data lock point as well as frequencies of PSURs submission
- Clear priority for the competence of the PRAC
- CHMP and CMDh have been put in the second line
- National competent authorities will have to execute the adopted decisions