EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

GVP V update

4th industry stakeholder platform - operation of EU pharmacovigilance legislation

Risk Management Plan (RMP) activities updates session

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Disclaimer

GVP Module V is a work in progress.

The orientations presented in this presentation may change following consultation of EMA Committees and the public consultation.

Guideline on good pharmacovigilance practices: Module V – Risk management systems

Published June 2012

Almost 3 years of PRAC experience for RMP assessment

New process for RMP assessment (CHMP & PRAC joint assessment)

Comments from:

- Assessors and rapporteurs
- Industry: on guidance (e.g. AESGP, EFPIA and EGA) and RMP template (pilot project)

-> Need for 2.0 update


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BEWARE OF THE DOGMA
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Eight major areas of focus for the GVP V update

1. Defined the purpose of the RMP (prospective planning, fit-for-purpose, reducing the size in the life cycle of the product)
2. Provided clarity on risk definitions, aligned with ICH E2E and E2C
3. Evidence based risk identification -> reshaped module SVII
4. Provided guidance on post-authorisation removal of safety concerns
5. Provided detailed guidance on requirements for all types of initial MAAs (GVP V and RMP template)
6. Data driven RMP updates! RMP submission is required only at initial MAA and/or when SS, PhV or RM activities change
7. Provided further PASS guidance on imposed & required studies
8. Cleaned annexes; clarified role and content

1. Planning document – not a historical record

- ✓ Focus on prospective planning
- ✓ Discuss safety findings; do not duplicate data assessed elsewhere
- ✓ Focus on correct identification of risks and missing information with the view to minimising or further characterising them
- ✓ Delete data from old RMP template not relevant for post-marketing planning
- ✓ Limit duplication of data presented in other modules of eCTD
- ✓ Make use of electronic format -> include links to support discussion

2. Risk definitions

- ✓ Keep aligned to ICH E2E and ICH E2C definitions
- ✓ Consider seriousness, frequency, patient and benefit/risk impact to define importance
- ✓ Provide clarity on what is an important risk and what is not
- ✓ Focus on strength of association between an event and the drug
- ✓ Present and discuss the scientific evidence of (causal) association
- ✓ Evidence based stepwise discussion of events observed in (pre-)clinical development -> risks -> important risks or missing information
- ✓ Support guidance with examples for specific circumstances

3. Risk presentation – Module SVII

- ✓ Bring together all elements to consider in one discussion (from scattered around the RMP): EU requirements, class effects, medication errors, off-label use, populations not studied, pre-clinical data, interactions, risks for biologicals and ATMPs)
- ✓ Structure guidance on stepwise discussion to identify the important risks and missing information
- ✓ Approach risks in consistent way, but allow flexibility for MAH proposals / assessment
- ✓ Keep scientific standards for identifying safety concerns, but encourage focus on further characterisation and minimisation activities when product gathers additional real-life, post-marketing data on safety (i.e. slimmer RMP in time, not heavier)
- ✓ Bring Missing Information to the table (as it will require activities in the PhV Plan)

4. Use data available, but plan for the future

Consider the life cycle of the product:

- ✓ Cast the net wide to capture potential safety concerns at approval
- ✓ Require only activities that can make a difference (minimise risks or further characterise them)
- ✓ Allow important risks or missing information to be changed once the scientific evidence changes (e.g. at first renewal, with first PSUR after renewal), for example:
  - Important potential risk -> important identified risk
  - Important potential risk -> removed (data does not confirm concern)
  - Important potential risk -> removed (data confirms concern but the now identified risk is not considered sufficiently important to remain in the list of safety concerns in the RMP)
  - Important identified risk -> removed (when risk is well characterised after sufficient use and risk minimisation activities are part of routine clinical practice)
  - Missing information -> removed (PASS results)

5. Requirements for initial MA applications

- ✓ Replaced table with detailed description
- ✓ Expanded guidance regarding modified requirements for generic medicines (considering data on CMDh website http://www.hma.eu/464.html)
- ✓ Addressed all types if initial MAAs: informed consent, hybrids, fixed combinations, well established use, herbal products, new products with substances authorised for more than 10 years.
- ✓ Detailed guidance on requirements for parts and modules: what is needed when
  - ✓ Further guidance to be included in the RMP template for the MAHs. i.e. when a section is required and when there is a limited scope or can be omitted

6. RMP updates

- ✓ Data driven; not procedure type driven
- ✓ RMP submission only when there is an impact on the safety specifications, PhV or risk minimisation plans
- ✓ Reduce assessors' and MAHs' administrative burden by reducing the number of potentially unnecessary RMP submissions
- ✓ Make the MAHs responsible and empower them to consider prospectively the planning needs following the submission of new data
- ✓ Addressed the submission of the RMPs in parallel procedures by allowing flexibility for submission and proposals for deferred RMP submissions

7. PASS

- ✓ Keep in the PhV Plan only the studies required/requested by the PRAC/CHMP
- ✓ Included further guidance on types of studies (Category 1, 2, and 3)
- ✓ Addressed the issue of PASS required by regulatory authorities outside EU
- ✓ Included in annexes an overview of all relevant ongoing and completed studies.
- ✓ Also included in annexes the protocols of all the studies in the PhV Plan:
  a. Protocols of proposed studies, submitted for assessment with this RMP
  b. Updates of previously approved protocols, submitted for assessment with this RMP
  c. Protocols previously approved by the Competent Authority

8. Refocus the annexes

- ✓ On what is needed for the RMP assessment
- ✓ Removed duplicates (e.g. SmPC); make use of electronic format (links when possible)
- ✓ Overview of on-going and completed pharmacoepidemiological study programme
- ✓ Overview of protocols for all studies in the PhV Plan (until study report is submitted and assessed – plan for the future)
- ✓ Clarified life cycle of risk minimisation key messages and examples of educational materials, and NCA role in assessing additional risk minimisation materials
- ✓ Strengthened the wording on sharing of materials across products with same substance

Next steps

- DIA RMP Information Day – 30 June
- Update in parallel: RMP template for industry
- PRAC, CHMP, CMDh endorsement
- Public consultation planned for autumn 2015: GVP V and RMP template (at the same time and in parallel)
- Receive Industry and other stakeholders' feedback

Thank you for your attention

Further information

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