European Risk Management Plans

Issues and concerns from the generics sector

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Risk Management Plans

- Module V of the GVP guidelines
- Required for all new submissions
  - From July 2012
- May be required for established products at any time in their life cycle
  - e.g. domperidone following Article 31 referral on QTc prolongation

Risk Management Plans

- RMP template issued October 2012
  - Modular format
  - Interchangeable with PSUR
  - Revised July 2013
- Risk proportionate
  - Some sections not required for a new generic MAA
  - But are required for an updated generic RMP
  - Based on proposed SmPC

Risk Management Plans

- Part I Product(s) Overview
- Part II Safety Specification
  - Module SI: Epidemiology of the indication(s) and target population(s)
  - Module SII: Non-clinical part of the Safety Specification
  - Module SIII: Clinical trial exposure
  - Module SIV: Populations not studied in clinical trials
  - Module SV: Post-Authorisation Experience
  - Module SVI: Additional EU requirements for the Safety Specification
  - Module SVII: Identified and potential risks
  - Module SVIII: Summary of the safety concerns
- Part III Pharmacovigilance Plan
- Part IV Plans for post-authorisation efficacy studies
- Part V Risk minimisation measures (including evaluation of the effectiveness of risk minimisation measures)
- Part VI Summary of the RMP
- Annexes

Not required for a new generic MAA

Risk Management Plans

- Summaries of RMPs to be published on EMA & NCA websites
  - But not yet
- Generic RMP should follow the innovator's
- To include a lay summary
- Risk minimisation activities include, e.g.:
  - Physician educational materials
  - Patient educational materials
  - Patient registries

Risk Management Plans

- Updates
  - As specified in the MA
  - Along with PSURs & renewals
  - Following Type II safety variations
  - Type 1B variation

How to follow the innovator

- GVP Module V (V.C.3.1.a):
  - ***New applications involving generic medicinal products.***
  - RMP module SVIII should be based on the safety concerns of the reference medicinal product …
- But:
  - Innovator's RMP not in the public domain
  - EPAR not available/may not include current safety concerns

How to follow the innovator

- Solution, freedom of information request
- But:
  - Receipt from UK MHRA 1 month after request
  - But up to 6 months after request to EMA
  - Dutch CBG/MEB will not release
  - Heavily redacted, e.g. educational materials

How to follow the innovator

- Solution, use sections 4.3 and 4.4 of SmPC
- But:
  - Which safety concerns to be selected?

How to follow the innovator

- GVP Module V (V.B.11.2):
  - ***Educational material***
  - …applicants/[MAHs] for the same active substance may be required by the competent authority to have educational material with as similar as possible layout, content, colour and format to avoid patient confusion.
- But:
  - Innovator's educational not in the public domain

How to follow the innovator

- GVP Module V (V.B.3.2):
  - ***Competent authorities***
  - …ensuring that [MAHs] of generic and/or similar biological medicinal products make similar changes to their risk minimisation measures when changes are made to those of the reference medicinal product..
- How is this communicated?

Assessment

- Multiple RMPs for same active
- Inconsistencies in assessment
  - Between agencies
  - Within agencies

National assessment of risk minimisation materials

- Generic materials should follow those of the reference medicinal product
- At assessment, significant changes are being requested
- Are the innovator's materials subsequently being revised?
- Impact on patient safety?

Distribution of risk minimisation materials

- Multiple versions to prescribers
- Which version does the patient receive?

Revision to the GVP module

- NCAs and EMA aware of industry concerns
- Consultation in progress on the module and the RMP template

DR. REDDY'S

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EU RMPs - issues & concerns of the generics sector, October 2014