Stakeholder Meeting, 7th June 2013

Considerations on the assessment of safety data originating from patient support programmes

Qun-Ying Yue; MPA, Sweden; PRAC member

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Disclaimer

- **The views presented in this presentation are those of the author and should not be understood or quoted as being made on behalf of the EMA and/or its scientific committees.**

- **Views are presented solely to aid the discussion and should not be interpreted as adopted guidance.**

Background

- The mandate of the PRAC shall cover all aspects of the risk management of the use of medicinal products for human use including
  - **the detection, assessment, minimisation and communication relating to the risk of adverse reactions,**
  - having due regard to the therapeutic effect of the MP for human use,
  - the design and evaluation of PASS and pharmacovigilance audit.
- PRAC tasks common to both centrally and non-centrally authorised products:
- (i) For Union procedures triggered for safety reasons: PRAC recommendation.
- (ii) For PSUR single assessment: PRAC shall issue a recommendation.
- (iii) For imposed PASS protocols: the PRAC shall issue a letter of endorsement or objection.
- (iv) For imposed PASS study results: the PRAC shall issue a recommendation.
- (v) For signals: the PRAC shall issue a recommendation.
- (vi) For EURD and frequency of PSURs submission: PRAC shall be consulted.
- (vii) For list of MP requiring additional monitoring: PRAC shall be consulted.
- (viii) For “for cause” pharmacovigilance inspections: PRAC shall issue an advice.

Pharmacovigilance data

- **High quality data collection is a prerequisite for signal detection and assessment.**

- **PSPs are not a single well defined entity but a range of activities**

- **The fundamental legal obligations apply regardless of the juxtaposition of activities involved in any given PSP**

Individual Case Safety Reports from PSPs

- **If Individual Case Safety Reports (ICSRs) come from PSPs on an ongoing basis as 15 day reports - what are the issues?**

- **If ICSRs come from PSPs as boluses of data (because they were derived from studies or post hoc data analsys, or as corrective action following non-compliance)?**

(Hypothetical) Scenario

- **Medical impact analysis for unreported adverse reactions cases from Patient Support Programmes**

- **Structured analysis /assessment**
  1. **Fatal cases**
  2. **Risks in the RMP or reactions subject to ongoing monitoring/review in PSURs**
  3. **Other important adverse reactions**

(Hypothetical) Scenario

Assessment on B/R impact analysis

Uncertainties - cases poorly documented, limited value for signal/risk assessment

- ***Number of PSPs and number of patients included***
- ***Follow up if sufficient details available (for patient or reporter)***
- ***Cases contain limited information (medical history, time to onset, indication and cause of death).***
- ***Reports from non health care professionals***
- ***Limited information precludes meaningful causality assessment***
- ***Potential impact on BR profile cannot be completely assessed.***

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health • quality • registration • regulations • reliability • risk/benefit • safety • scientific • standardisation • transparency • vigilance • approvals • authorisation • clinical trials • communication • competence • cosmetics • dialogue • directives • efficacy • environment • evaluation • approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health •

(Hypothetical) Scenario
Conclusions and recommendations on B/R impact analysis

Scenario 1 - No further action is required

- **No issues identified that have impact on ongoing monitoring activities**
- **not warrant an update to PI or RMP.**
- **Overall B/R unchanged and positive.**
- **Monitor certain issues in subsequent PSURs / Continued routine pharmacovigilance.**

- ***Reactions are covered in PI.***
- ***Low number of cases (vs total number in database);***
- ***Isolated reactions; non-serious cases***
- ***No new or changing safety signals can be identified***

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health • quality • registration • regulations • reliability • risk/benefit • safety • scientific • standardisation • transparency • vigilance • approvals • authorisation • clinical trials • communication • competence • cosmetics • dialogue • directives • efficacy • environment • evaluation • approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health •

(Hypothetical) Scenario

Conclusions and recommendations on B/R impact analysis

Scenario 2 - Further requests needed:

- procedures for ensuring adequate processing and follow-up of cases from PSPs to ensure case quality, to allow a reasonable causality assessment.
- approach to identify relevant reactions from the database
- measures taken to better document cases.

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health • quality • registration • regulations • reliability • risk/benefit • safety • scientific • standardisation • transparency • vigilance • approvals • authorisation • clinical trials • communication • competence • cosmetics • dialogue • directives • efficacy • environment • evaluation • approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health •

Reflections
- Role for PSP reports in signal detection

Further questions (1):

- **What influence do the reports originating from the PSPs have on the overall safety data for signal detection?**
  - **Some products have PSPs and others do not. How do reports originating from PSPs impact on the ability to identify potential safety issues in signal detection?**
  - **How to integrate PSPs in the routine monitoring of safety of medicinal products?**
  - **How to improve the quality of data to help signal detection and safety issue assessment?**

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health • quality • registration • regulations • reliability • risk/benefit • safety • scientific • standardisation • transparency • vigilance • approvals • authorisation • clinical trials • communication • competence • cosmetics • dialogue • directives • efficacy • environment • evaluation • approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health •

Reflections
- Role for PSP reports in signal detection

Further questions (2):

- **Relative value of ICSRs quality versus ICSRs quantity**
  - **What about the quality of the reports?**
  - **What are the challenges for causality assessments for the PSPs reports?**
  - **Causality assessment is essential for signal detection.**
  - **Improved quality of reports from PSPs is essential for assessors.**

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health • quality • registration • regulations • reliability • risk/benefit • safety • scientific • standardisation • transparency • vigilance • approvals • authorisation • clinical trials • communication • competence • cosmetics • dialogue • directives • efficacy • environment • evaluation • approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health •

Reflections
- Role for PSP reports in signal detection

Further questions (3):

- **The impact of data not being collected or included into global PV systems is an 'unknown unknown' and this makes things difficult for assessors and inspectors.**
- **The impact of the data available may be different.**
- **QPPV/pharmacovigilance should have oversight of what arrangements marketing departments and service providers are putting in place for these programmes (and collection of safety data from the programmes).**

Reflections
- Role for PSP reports in signal detection

Further questions (4):

- **How to best arrange the signal detection with the knowledge that there are PSP ongoing for a product?**
- **Can a signal detected from spontaneous reports be ascertained with cases originating from PSPs?**
- **Can a signal with rare events be identified from reports originating from PSPs?**
- **Do we need to wait for new spontaneous reports to react?**
- **Minimum quality of reports is required for safety surveillance of medicinal products, which allow for early identification of safety issues.**

Reflections - Role for PSPs in Risk Management Plans

- **Generation of safety data is largely a by-product of PSPs rather than the objective.**
- **If there is a need to demonstrate safety or investigate/ characterise a risk, presumably the preferred option is a well designed study with a clear research question, analysis plan etc.**
- **PSPs should not be used as the principal way to collect safety information in the frame of RMPs.**

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health • quality • registration • regulations • reliability • risk/benefit • safety • scientific • standardisation • transparency • vigilance • approvals • authorisation • clinical trials • communication • competence • cosmetics • dialogue • directives • efficacy • environment • evaluation • approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health •

In summary - Role for reports of suspected adverse reactions originating from PSPs

- **The impact of the data available from PSP may be different.**
- **Causality assessment is essential to report true cases of suspected adverse reactions to competent authorities**
- **Improved quality of reports from PSP is expected.**
- **PSPs should not be the principal mechanism to collect safety information in the frame of RMPs.**
- **Safety concerns should be addressed in the context of well-defined studies with protocols.**

LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health • quality• registration • regulations • reliability • risk/benefit • safety • scientific • standardisation • transparency • vigilance • approvals • authorisation • clinical trials • communication • competence • cosmetics • dialogue • directives • efficacy • environment • evaluation • approvals • authorisation • clinical trials • communication • competence • cosmtics • dialogue • directives • efficacy • environment • evaluation • guidelines • harmonisation • health economics • herbals • homeopathics • information • inspection laboratory analysis • market surveillance • medicinal products • medical devices • narcotics • public health •