Format and content of electronic periodic safety update reports
(Technical contribution to EC implementing measure)

First Stakeholders Forum on the implementation of the new Pharmacovigilance legislation, 15 April 2011

Presented by Almath Spooner, Irish Medicines Board
Legal basis for changes to PSURs

Directive 2010/84/EU, Article 107b

PSURs shall contain:

a) summaries of data relevant to the benefits and risks of the medicinal product, including results of all studies with a consideration of their potential impact on the marketing authorisation;

b) a scientific evaluation of the risk-benefit balance of the medicinal product, which shall be based on all available data, including data from clinical trials in unauthorised indications and populations.

c) All data relating to the volume of sales of the medicinal product and any data in possession of the marketing authorisation holder relating to the volume of prescriptions, including an estimate of the population exposed to the medicinal product.
Objective of the PSUR

1. To provide a tool for post marketing evaluation of the risks and benefits of a medicinal product based on the available data at a defined time point in the lifecycle of the product.

2. In the context of lifecycle benefit risk management and based on the assessment of the PSUR, to consider whether any action concerning the marketing authorisation for the medicinal product is necessary.

18/04/2011
Format and content

Format and content needs to be compatible with the objective of benefit-risk evaluation reporting.

- European Commission Implementing Measure implements Article 108(f) the format and content of electronic periodic safety update reports and risk management plans).

The development of the EC Implementing Measure will take account of the work on international harmonisation specifically the ICH E2C (R2) Guideline.
Rationale for scope and content

Minimising risks and optimising benefits throughout the lifecycle of a medicinal product will promote and protect public health and enhance patient safety by avoiding unnecessary risks to patients.

It is recognised that the benefit-risk profile may change throughout the lifecycle of the product as post marketing data on safety or clinical effectiveness emerge.

It is therefore important to periodically evaluate the benefit-risk profile of a medicinal product in the populations exposed in order to contribute to effective and ongoing benefit-risk management.

18/04/2011
Rationale for Scope and Content (2)

Reflective of technological and scientific developments:

- PSUR shall contain cumulative data whilst retaining focus on new information.
- Detailed listings of individual cases shall not be routinely included as these will be available for analysis in the EudraVigilance database to support single EU assessments.
- Focus is on structured evaluation rather than data presentation.
Scope of a single PSUR

It is envisaged, that unless otherwise specified in the MA or in the list published by the EMA, that a single PSUR will be prepared for all products containing the same active substance authorised to one MAH, irrespective of indications, routes of administration, dosage forms and regimens, with a single Data Lock Point for all aspects of product use.
PSUR Structure

A PSUR shall have a modular structure which will be laid down in the relevant Implementing Measure.

Modular structure intended to provide flexibility and to optimise functionality of its elements.
PSUR Structure – Introductory sections

- Introduction
- Worldwide Marketing Authorisation
- Actions taken in the Reporting Period for Safety reasons
- Changes to Reference Safety Information
- Accurate estimation of population exposed
PSUR structure – Data analysis by source

• Summary of data from studies:
  Interventional
  Non interventional
  Non clinical data
  Literature

• Summary of data from Marketing Experience
Key changes to the structure of the PSUR (1)

1) Risk Evaluation Module:
   • Safety Specification
   • Signals (newly identified, ongoing or closed in the reporting period).
   • Newly identified (or new information on) important risks
   • Effectiveness of risk minimisation

18/04/2011
Key changes to the structure of the PSUR (2)

2) Benefit evaluation

- Important Efficacy/Effectiveness information
- Strength of the evidence and limitations of the data
- Newly identified Efficacy/Effectiveness information
Key changes to the PSUR structure (3)

3) Integrated benefit/risk analysis for approved indications
   • Introduction (perspective).
   • Importance of benefits and risks
   • Discussion of the benefit-risk balance
1. During the transitional phase (i.e. until 12 months after the establishment of the functionalities of the PSUR repository has been announced by the Agency), marketing authorisation holders shall submit the periodic safety reports to the Agency and all Member States in which the medicinal product has been authorised or according to the submission requirements of Members States which shall be published on the Agency website.
2. Following establishment of the PSUR repository, the obligation on the part of the marketing authorisation holder will be to submit electronic periodic safety update reports only to the Agency.

   Further changes to technical requirements for submission of electronic PSURs shall be published by the Agency and shall take account of pre-standards and standardisation work.
Detailed Guidance

Pursuant to Article 108a (a) of Directive 2010/84/EU, the Agency shall publish detailed guidance on PSUR submission and evaluation in Good Vigilance Practices and this shall include reference to international consensus guidelines, and standards, where available.
PSUR Summary

- Post marketing evaluation tool for bringing together available evidence on effectiveness and harms in clinical use.
- It should aim to clearly identify limitations of evidence and uncertainty.
- This post marketing evaluation of the benefits and risks of a medicinal product should support ongoing risk management.
- PSUR assessment will inform regulatory decisions in the post marketing period.

18/04/2011
Questions welcome to
almath.spooner@imb.ie
Georgy.genov@ema.europa.eu
Peter.arlett@ema.europa.eu