EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Good Pharmacovigilance Practices (GVP) and Requirements for Marketing Authorisation Holders

SME Meeting, 26 April 2013

Presented by: Priya Bahri

GVP - Scope and objective

- Self-standing guidance on pharmacovigilance processes with legal basis
- Compliance with legal tasks and responsibilities
- Addressed to EU marketing authorisation holders, competent authorities in Member States and Agency
- Replaces Volume 9A

Notice: “Shall” and “should”

GVP Webpage on EMA website

Go to:

Home >

Regulatory >

Human medicines >

Pharmacovigilance >

Good pharmacovigilance practices

Link:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c

GVP - Structure

- 2 types of chapters:
  - Modules → Major processes
  - Considerations → Product- or populations-specifics
- within chapters:

A – Introduction

B – Structures and processes

C – Operation of the EU network

GVP Annexes

A I Definitions (Rev 1 final; Rev 2 with vaccine definitions)

A II Templates (PSUR Cover page (public 25 Apr), DHPC)

A III List of other valid phv guidance developed under previous legislation

A IV List of phv ICH Guidelines

A V Abbreviations

+ Links to relevant guidance developed outside GVP, e.g. on referrals

GVP Chapters
Final

M I PhV Systems and their Quality Systems

M II Rev 1 PhV System Master File

M III Inspections

M IV Audits

M V Risk Management Systems

M VI Individual Case Safety Reports

M VII Periodic Safety Update Reports

M VIII Rev 1 Post-Authorisation Safety Studies (Rev 1 public 25 Apr)

M IX Signals

M X Additional monitoring (public 25 Apr)

M XV Safety communication

GVP Chapters
Public consultation

M VII Rev 1 Periodic Safety Update Reports (public 25 Apr)

M XVI Risk minimisation measures (public end of Apr)

P.I Vaccines

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GVP Module I: Pharmacovigilance systems and their quality systems

Presented by: Priya Bahri

Pharmacovigilance (phv) system

= A system used by an organisation

to fulfil its legal tasks and responsibilities in relation to pharmacovigilance and

designed to monitor the safety of authorised medicinal products and

detect any change to their risk-benefit balance

3 columns of quality systems as per EC Implementing Regulation

- Management of human resources
- Compliance management
- Record management

QPPV

= MAH's qualified person responsible for pharmacovigilance in the EU

- Natural person
- Resides and operates in the EEA
- At the MAH's disposal permanently and continuously
- Back-up procedures in the case of absence of QPPV
- Additional national phv contact persons possible (reporting to QPPV)

MAH's responsibilities towards QPPV

- Name and contact details to be submitted by MAH (changes acc to Variation Reg and guidance)
- Job description and hierarchical relationships
- Sufficient authority to influence the performance of the quality system and the pharmacovigilance activities (inc contracts, acquisition)
- Authority over Pharmacovigilance System Master File (notification of changes)
- Provide QPPV with all relevant information, inc from compliance monitoring, quality reviews, audits, inspections
- Provide QPPV with access to all relevant information (inc CTs and contractors)
- Training

Compliance management for MAHs - General: Ensure

- Continuous monitoring of phv data, examination of options for risk minimisation/prevention, taking appropriate measures
- Evaluation of all risk information concerning inside and outside MA use
- Timely submission of accurate and verifiable data on serious and non-serious adverse reactions to CAs
- Effective communication with CAs
- Update of product information in the light of scientific knowledge
- Appropriate communication to healthcare professionals and patients

Compliance management for MAHs – EU-specific: Ensure

- Submission of adverse reaction data to EudraVigilance
- Monitoring of the use of terminology
- Retention of documents (as long as phv system exists =5 y; as long as MA exists + 10 y; unless longer requirements apply)
- Update of product information in the light of information on the European medicines web-portal

Description of MAH phv system

→ Pharmacovigilance System Master File: GVP M II

- Option of delegation of activities, but not responsibilities → contractual arrangements

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GVP Module V: Risk management systems

Presented by: Priya Bahri

Risk management system

A set of pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to a medicinal product, including the assessment of the effectiveness of those interventions

Risk management plan (RMP):

A detailed description of the risk management system

Main news

- RMP will be required for all new MA applications
- RMP should be proportionate to risks
- Post-authorisation studies may be condition of MA
- Summary of the RMP to be made public
- Requirement to monitor the effectiveness of risk minimisation
- Newly defined contents and format of a RMP

Risk management plan

- Safety profile (known and potential risks and missing data)
- Indicate how to characterise it further
- Measures to prevent or minimise the risks (RMM)
- Assessment of effectiveness of RMM
- Document post-MA obligations
- Indicate the applicability of CT efficacy to use in medical practice
- Document the need for studies on effectiveness and long term efficacy

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GVP Module VI: Management and reporting of adverse reactions

Presented by: Priya Bahri

Collection and reporting - Individual case safety reports

- Adverse reaction = Response to a suspected medicinal product which is noxious and unintended
- No reporting of events, but of suspected reactions:
  - Spontaneous reports imply suspicion (unless stated otherwise by primary reporter)
  - Solicited reports should have a causality assessment by primary source or sender (MAH/NCA)
- 4 minimum criteria need to be present in ICSR:
  - 1 or more primary source(s), 1 patient, 1 or more suspected medicinal product(s), 1 or more reaction(s)
- Validation criteria

Interim reporting modalities

Serious ICSRs: 15 days time frame

- occurring in EU from MAH to NCA on whose territory suspected adverse reactions occurred
- occurring outside EU from MAH to
  - EudraVigilance and
  - NCAs of Member States where medicinal product is authorised, if required.
- NCAs to MAH ICSRs which were reported directly to NCA

Non-serious ICSRs: 90 days time frame

- If required, MAHs shall report all non-serious ICSRs occurring in EU to NCA on whose territory suspected adverse reactions occurred.

Final reporting modalities

Serious ICSRs: 15 days time frame

- From MAH to EudraVigilance
- From NCAs to EudraVigilance those ICSRs which were reported directly to NCA

Non-serious ICSRs: 90 days time frame

- From MAH to EudraVigilance
- From NCAs to Eudravigialance those ICSRs which were reported directly to NCA

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GVP Module VII: Periodic safety update reports

Presented by: Priya Bahri

Objective of a PSUR

- To present a comprehensive and critical analysis of the risk-benefit balance taking into account new information in the context of cumulative data
  - Should **not** be used to provide initial notification of significant new safety information, or provide the means by which new safety issues are detected, or new efficacy data are submitted
- CAs assess PSURs to determine whether there are new risks or whether risks have changed or whether there are changes to the risk-benefit balance

Main news

- New focus on summary information and integrated risk-benefit evaluation
- Waiver for generics, well-established use, homeopathic and traditional herbals, unless:
  - the MA provides for the submission of PSURs as a condition
  - PSURs are requested by a competent authority
    - Concerns related to pharmacovigilance
    - Lack of PSURs relating to an active substance
- Public assessment reports

PSUR submission requirements

- Submission every 6 months until launch
- Every 6 months during the first 2 years following the initial placing on the market, once a year for the following 2 years and at 3-yearly intervals thereafter
- According to a condition of the MA
- According to the List of European Union References Dates (EURD)
- PSURs also need to be submitted upon request from a CA

PSUR submission timelines

- MAHs should submit PSURs according to the following timelines:
  - Within 70 days of the data lock point (DLP) for PSURs covering intervals up to 12 months
  - Within 90 days of the DLP for PSURs covering intervals more than 12 months

Emerging safety issues

- Information which may influence the benefit/risk evaluation has to be notified immediately to concerned NCAs and the Agency (P-PV-emerging-safety-issue@ema.europa.eu)
- Concerns e.g.:
  - Major safety findings from studies;
  - Signals of significant hazard to public health, inc related to use outside MA, misinformation in product information, supply of raw material;
  - Withdrawal, non-renewal, revocation, suspension of marketing authorisation or urgent safety restriction outside EU
- Indicate points of concern and actions proposed

Advice

Pharmacovigilance helpdesk:

p-pv-helpdesk@ema.europa.eu

Questions?