EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Post-authorisation safety studies and the EU PAS Register

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Content of the presentation

1. PASS: definition and objectives (a reminder)
2. Obligations and recommendations
3. The EU PAS Register
4. Guidance for PASS protocol submission

Post-authorisation safety study :definition

Any study relating to an authorised medicinal product conducted with the aim of identifying, characterising or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures.

Objectives of a PASS:

- to quantify potential or identified risks
- to evaluate risks of a medicinal product used in patient populations for which safety information is limited or missing (eg pregnant women, specific age groups, patients with renal or hepatic impairment)
- to provide evidence about the absence of a risk
- to assess patterns of drug utilisation that add knowledge on the safety of the medicinal product (eg indications, dosage, co-medication, medication errors)
- to measure the effectiveness of a risk minimisation activity.

- PASS initiated, managed or financed by a MAH
  - Pursuant to an obligation imposed by a competent authority
    - as a condition to the granting of the marketing authorisation, or after the granting of a marketing authorisation if there are concerns about the risks of the authorised medicinal product
    - as part of a marketing authorisation granted under exceptional circumstances.
  - Voluntarily
    - studies required in the risk management plan to investigate a safety concern or evaluate the effectiveness of risk minimisation activities
    - any other PASS

2. Obligations and requirements

▲ legal obligation ✓ recommended in the GVP ★ optional

Management of study

	PASS with MAH involvement	
	Imposed as an obligation	Conducted voluntarily
Standard format of protocol and study report	▲	✓
PRAC oversight	▲	(if in RMP)
Registration of study in EU PAS register	▲	✓
Study not to promote medicinal product	▲	▲
Restricted payment to HCP	▲	▲
Quality systems	▲	✓
ENCePP methodological standards	✓	✓
ENCePP checklist for study protocol	✓	✓
ENCePP CoC	✓	✓
ENCePP seal	★	★

2. Obligations and requirements

▲ legal obligation ✓ recommended in the GVP

Reporting of study information

	PASS with MAH involvement	
	Imposed as an obligation	Conducted voluntarily
Protocol and progress reports to be submitted upon request to NCA of MS where study is conducted	▲	▲
Final report to be sent to the NCA of the MS where the study is conducted within 12 months of the end of data collection	▲	▲
Data generated in the study to be monitored	▲	▲
Any information which may influence the B/R balance to be reported to NCAs of MS where the product is authorised	▲	▲
Reporting of suspected adverse reactions in studies with primary data collection	▲	▲
Final manuscript of article to be transmitted to NCAs within 15 days after acceptance by journal editor	✓	✓

Objectives

- transparency, exchange of information, peer review
- supports EMA to fulfil its obligation to make public protocols and results of PASS imposed as an obligation
- supports MS to ensure that the public is given important information on pharmacovigilance concerns
- repository of all non-interventional PAS conducted in the EU, irrespective of the source of funding and status of investigators (MAH, academia, regulatory or public health authorities,...)

- NOT to replace regulatory submission for imposed studies
- Accepted by MS as means for submitting information on studies conducted voluntarily (Annex 1 of GVP Module VIII)

3. EU PAS Register

EU PAS Register to be developed as upgrade of ENCePP E-Register of studies and will include already registered studies, including ENCePP seal

Transitional period:

- ENCePP E-Register of studies to be used
- Guide for study registration amended
- for MAH-sponsored non-interventional PASS required by a regulatory authority:
  - acknowledgment email sent by EMA to MAH
  - all Member States informed by EMA of the registration with: title, name of sponsor, countries, link to registry

Impact on ENCePP

"ENCePP study registry" will no longer exist

- confusion between "ENCePP study" and "study registered in ENCePP" will be avoided
- "ENCePP" trademark will refer to best methodological and ethical standards in pharmacoepidemiology
  - ENCePP Guide for methodological standards in pharmacoepidemiology
  - ENCePP Checklist for study protocols
  - ENCePP Code of conduct
  - ENCePP study seal

4. Guidance for PASS protocol submission

Objectives

- consistency in presentation and format of PASS protocols submitted by marketing authorisation holders
- provision of essential administrative information
- coverage of all important scientific aspects of a protocol

Legal obligation for imposed non-interventional PASS from 10 January 2013

Recommended for all other non-interventional PASS

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/10/WC500133174.pdf

EMA → Regulatory → Human Medicines → Pharmacovigilance → Guidance

Questions ?