EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Post-authorisation safety studies and the EU PAS Register

Sixth Stakeholders forum on the implementation of the new legislation

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PASS: Definition and objectives

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.

PASS: Definition and objectives

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: Definition and objectives

- 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

Non-interventional PASS: obligations and requirements

▲ legal obligation ✓ recommended in the GVP ★ optional

Management of study	PASS with MAH involvement	
	Imposed as an obligation	Conducted voluntarily
Standard formats of protocol and study report	▲	✓
PRAC oversight	▲	(if in RMP)
Registration of study in EU PAS register	▲	✓
Study shall not to promote medicinal product	▲	▲
Payment to HCP restricted to compensation of time and expenses incurred	▲	▲
Quality systems	▲	✓
ENCePP methodological standards	✓	✓
ENCePP checklist for study protocol	✓	✓
ENCePP Code of Conduct	✓	✓
ENCePP seal	★	★

Non-interventional PASS: 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 with consideration to benefit-risk of product concerned	▲	▲
Any new information which might influence the evaluation of 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 with 15 days (serious ADRs) or 90 days (non-serious ADRs) *	▲	▲
Final manuscript of article to be transmitted to NCAs of MS where product is authorised within 15 days after acceptance	✓	✓

* See interim and final arrangements in GVP Module VI, C.4

The EU PAS Register

- 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,…)

- For imposed studies: will not replace regulatory submission
- For studies conducted voluntarily: accepted by MS as means for submitting study information (Annex 1 of GVP Module VIII)

The EU PAS Register

EU PAS Register will be developed as upgrade of ENCePP study registry and will include already registered studies.

Transitional period:

- ENCePP study registry 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

Guidance for the format and content of the protocol of non-interventional PASS

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 before that date)

Recommended for all other non-interventional PASS

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

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