EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

ENCePP Plenary: New Pharmacovigilance legislation

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In this talk

1. New pharmacovigilance legislation: Why
2. New pharmacovigilance legislation: How
3. New pharmacovigilance legislation: What
4. New pharmacovigilance legislation: When

Why: To further strengthen pharmacovigilance

- 5% of all hospital admissions are for ADRs,
- 5% of all hospital patients suffer an ADR,
- ADRs are the 5th most common cause of hospital death
- Estimated 197,000 deaths per year in EU from ADRs
- EU Societal cost of ADRs Euro 79 Billion / year

Why: High level objectives

- Promote and protect public health by reducing burden of ADRs and optimising use of medicines:
  - Clear roles and responsibilities
  - Science based (move up hierarchy)
  - Risk based / proportionate
  - Increased proactivity / planning
  - Reduced duplication / redundancy
  - Integrate benefit and risk
  - Ensure robust and rapid EU decision-making
  - Strengthening EU Network Engage patients and professionals
  - Increase transparency and accountability
  - Better information on medicines

How: making new law...by European Commission

-2003: EC decision to undertake an assessment of the Community system of Pharmacovigilance

-2005: Independent study completed to map of strengths and weaknesses of EU system

-2006- 2008: Research, consultation, policy development

How: making new law

-December 2008: “Pharma package” (PhV, Information to Patients and Falsified medicines) adopted by the Commission and transmitted to Council and European Parliament for co decision procedure to start

-’Co-decision’ (European Council and European Parliament) work starts on revisions to Directive 2001/83/EC and revisions to Regulation (EC)2004/726

-23 June 2010: Agreement on final text (first reading agreement)

22 September 2010: Final favourable vote in the European Parliament

- Q1 2011: Directive 2001/83/EC and Regulation (EC) 726/2004 expected to published in the Official Journal (entry into force)

18 months to implement and transpose the provisions (most)

What: Scope of changes

-**Authorisation requirements** change (PSMF, key risk management measures in MA)

-**Risk Management Plan**, risk proportionate and for all new products (+justified old)

-**Legal basis for PASS** + legal basis for efficacy studies

-**Effectiveness of risk minimisation**

-**Product information** change – 'additional monitoring' + encourages ADR reporting

-**ADR reporting** simplified + patient reporting + medication errors + role of EV + literature monitoring + reporting to WHO

-**Signal detection** has clear roles and responsibilities

-**PSUR** submission simplified (electronic) and single assessment + benefit: risk

-**Committees** (PRAC/CMD/CHMP) and decision-making

-**Transparency and communication** (webportals, EV access, coordinate MSs, hearings)

-Enhanced coordination of **inspections**

-Regular EMA and MS + MAH **audit**

-**Fees** for pharmacovigilance

-Access in small markets – labelling exemption etc.

What: Key changes relevant to ENCePP

PRAC and Decision-making

-New **Pharmacovigilance Risk Assessment Committee** – mandate: all aspects of the risk management of the use of medicinal products including the detection, assessment, minimisation and communication relating to the risk of adverse reactions, having due regard to the therapeutic effect of the medicinal product, the design and evaluation of post-authorisation safety studies and pharmacovigilance audit

-Membership: MS appointees, patients and healthcare reps + **six members appointed by the Commission, with a view to ensuring that the relevant expertise is available within the Committee, including clinical pharmacology and pharmacoepidemiology, on the basis of a public call for expressions of interest**

N.B. ENCePP colleagues can apply!

What: Key changes relevant to ENCePP

Strengthened legal basis for Post-authorisation Safety Studies (PASS)

-Regulators can impose PASS on industry at first authorisation

-Regulators can impose PASS on industry post-authorisation

-PASS is a condition of the authorisation and is legally binding

-In the event that the same safety concern applies to **more than one medicinal product**, the EMA / national competent authority shall ..... encourage the marketing authorisation holders concerned to conduct a **joint post-authorisation safety study**;

NB: More PASS will be done!

What: Key changes relevant to ENCePP

Principles for and oversight of PASS

-Definition: 'Post-authorisation safety study: 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'

-Principles and oversight for non-interventional post-authorisation safety studies which are: initiated, managed or financed by the marketing authorisation holder voluntarily or pursuant to obligations imposed [*by regulators*] and which involve the collection of data on suspected adverse reactions from patients or healthcare professionals.

-Still may have additional MS requirements on well being and rights of participants in non-interventional post-authorisation safety studies

What: Key changes relevant to ENCePP

Principles for and oversight of all PASS

- The studies shall not be performed where the act of conducting the study promotes the use of a medicinal product
- Payments to healthcare professionals for participating in non-interventional post-authorisation safety studies shall be restricted to the compensation for time and expenses incurred.
- National competent authority may require the marketing authorisation holder to submit the protocol and the progress reports to the competent authorities of the Member States in which the study is conducted.
- Marketing authorisation holder shall send the final report to the competent authorities of the Member States in which the study was conducted within 12 months of the end of data collection
- Any new information which might influence the evaluation of the risk-benefit balance of the medicinal product shall be communicated *[by company]* to the competent authorities of the Member State in which the product has been authorised

What: Key changes relevant to ENCePP

Principles for and oversight of required PASS

- For studies required by regulators:

1. Protocols actively approved prior to study (single country = MS, multiple country = PRAC)
2. Protocol amendments actively approved
3. Company updates product information
4. Final report and abstract submitted
5. Automatic, formal assessment and decision-making based on results

NB: Impact on academics doing research for industry

What: Key changes relevant to ENCePP

Strengthened legal basis for Post-authorisation efficacy studies

-At authorisation: ‘where concerns relating to some aspects of the efficacy of the product are identified and can be resolved only after the product has been marketed’.

-Post authorisation: ‘when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be modified significantly’.

NB: More studies done –‘real world efficacy’

What: Key changes relevant to ENCePP

Risk Management Planning

-New definition: ‘a set of pharmacovigilance activities and interventions, such as studies and reports, designed to identify, characterise, prevent or minimise risks relating to a medicinal product, including the assessment of the effectiveness of those activities and interventions’

-Requirement for all new products but risk proportionate

-Legal basis to require a risk management system / plan for an authorised product. (‘if there are concerns about the risks affecting the risk-benefit balance’)

-Safety and Efficacy studies included (move towards integrated BR)

NB: Good basis for health outcome research

What: Key changes relevant to ENCePP

Effectiveness of Risk Minimisation

-New legal requirement:

EMA /MSs shall: ‘monitor the outcome of risk minimisation measures contained in risk management plans and of conditions’

NB: Further opportunities for health outcomes research.

What: Key changes relevant to ENCePP

Better ADR Reporting

-New ADR definition: 'A response to a medicinal product which is noxious and unintended'

-Medication errors that result in an ADR are reported

-Patient reporting – the debate on 'if' is over! Now debate 'how'!

-After transitional period:

-All ADRs from companies and from Member States are sent to Eudravigilance only

-Member States are 'auto-forwarded' their national data

-Companies access reports in Eudravigilance

NB: Greater access to Eudravigilance data for research

What: Key changes relevant to ENCePP

Signal detection

-For 1st time the concept is recognised

-Clear roles and responsibilities for EMA and Member States

-'monitor the data in the Eudravigilance database to determine whether there are new risks or whether risks have changed and whether those risks impact on the risk benefit balance'

-PRAC performs initial analysis and prioritisation of signals of new risks or risks that are changing or changes to the risk-benefit balance.

NB: Legal basis can empower and enrich research on signal detection and on strengthening

What: Key changes relevant to ENCePP

EU Medicinal Product Dictionary

-'the Agency shall establish a list of all medicinal products authorised in the Community. To this effect the following measures shall be taken:

-(a) the Agency shall…..make public a format for the electronic submission of medicinal product information;

-(b) MAHs shall, by (18 months after the entry into force of regulation), electronically submit to the Agency information for all medicinal products authorised or registered in the Community, using the format referred to in point (a);

-(c) from the date set out in point (b), MAHs shall inform the Agency of any new or varied authorisations (…).

NB: In time we will have a comprehensive EU product dictionary

What: Key changes relevant to ENCePP

Transparency and Communication

-EU and National Medicines web-portals

-Dramatic increase in transparency e.g. ‘protocols and public abstracts of results as regards post authorisation safety studies’

-EMA to coordinate MS safety announcements

-Public hearings

What: Key changes relevant to ENCePP

Clinical Trial Directive – not in scope of changes

-Not in scope

-Council Statement calling for revision of definition of ‘non-interventional’

-Commission will make legal proposals in 2012

-New / amended clinical trials legislation 2014 at the earliest.

When: making new law

18 months to implement and transpose most of the provisions

Transitional provisions on:

-Centralised reporting of Periodic Benefit Risk Reports to EMA

-Centralised reporting to Eudravigilance

Full implementation may take to 2013…..

regular dialogue with stakeholders along the way!

Thank you

Commission, Parliament and Council

Member State authorities and experts

EMA Colleagues / EMA Committees

ENCePP Partners

IMI Protect Partners

Stakeholders of EMA and EU Regulatory Network