3-year Report on European Union Pharmacovigilance Activities

Pharmaceutical Committee

18 October 2016

Helen Lee
European Commission
Directorate General for Health and Food Safety
Unit B5 - Medicines: policy, authorisation and monitoring
### EU pharmaceutical legislation

| Directive 2001/83/EC | Sets the procedures for the authorisation and supervision of medicinal products at EU level and establishes the European Medicines Agency:  
|                       | • Title II - Chapter 3 – Pharmacovigilance  
|                       | • Article 29  – report on performance of pharmacovigilance tasks by Member States |

| Regulation (EC) No 726/2004 | The core legislation governing the regulation of medicines in EU:  
|                             | • Title IX – Pharmacovigilance  
|                             | • Article 108b  – report on performance of pharmacovigilance tasks by Member States |
Commission report


• Includes pharmacovigilance activities of Member States and the European Medicines Agency

• Mainly covering July 2012 – December 2014
European Union Pharmacovigilance - a network approach

- Member States
- European Medicines Agency (including the Pharmacovigilance Risk Assessment Committee (PRAC))
- European Commission
Functioning of the system

**TRIGGERS OF THE DECISION MAKING PROCEDURE**

- Monitoring adverse drug reactions (ADRs)
- Signal of a new adverse event, ADR
- Periodic safety update reports (PSUR)
- Specific procedure: referrals
- Oversight of post-authorisation obligations

**ACTIONS BASED ON PHARMACOVIGILANCE CONCERNS**

- Change of marketing authorisation
- Suspension
- Withdrawal
- Revocation
- Non-renewal
Items on the PRAC agenda

Number of items on PRAC agenda

- Other safety issues - MS
- Other safety issues - CHMP (including CHMP requests to PRAC for Art.5.3 referrals)
- Pharmacovigilance Inspections
- Renewals, Conditional Renewals and Annual Reassessments
- PASS Results
- PASS Protocols
- PSLRs
- RNPs
- Signals
- Referrals
Monitoring adverse drug reactions

- Increasing number of reports
- Patient reporting increased by around 50%
Signal management

Aim

• Signal detection, validation, confirmation, analysis and prioritisation, assessment and recommendation for action

Process

• Through signal detection signals are identified. The data is evaluated during signal validation to verify the existence of a new potentially causal association or a new aspect of a known association. Confirmed signals are analysed and prioritisation by PRAC. Following the scientific evaluation of all the evidence available through the signal assessment by PRAC a recommendation is made.

Determined if there are new risks identified for a medicine and if changes to the marketing authorisation are required
Signals - collaborative validation

**Validated signals per year**

- **Jul-Dec 2012**: 43 validated signals, 19 CAPs or substances in both CAPs & NAPs, 24 NAPs
- **2013**: 63 validated signals, 29 CAPs or substances in both CAPs & NAPs, 34 NAPs
- **2014**: 55 validated signals, 16 CAPs or substances in both CAPs & NAPs, 39 NAPs

**Signals for NAPs**

- **Jul-Dec 2012**: 12 validated by NCAs as LMSs, 6 validated by NCAs, 1 validated by EMA
- **2013**: 11 validated by NCAs as LMSs, 17 validated by NCAs, 1 validated by EMA
- **2014**: 11 validated by NCAs as LMSs, 5 validated by NCAs, 0 validated by EMA
Signal detection recommendations

PRAC signals assessment Sep 2012 - Dec 2014, total=193

- Update of RMP, 2, 1%
- PASS, 1, 0%
- Referral, 11, 6%
- Routine pharmacovigilance, 46, 24%
- Assessment ongoing, 33, 17%
- Update of product information, 100, 52%
Risk management plans

Number of RMPs assessed by the PRAC per year

- Jul-Dec 2012: 48
- 2013: 637
- 2014: 597

RMPs submitted to NCAs

- 2012 Jul-Dec: 3000
- 2013: 7500
- 2014: 10000
Periodic Safety Update Reports

**Aim**
- Periodic safety update reports (PSURs) are reports providing an evaluation of the benefit-risk balance of a medicine
- Marketing authorisation holders must submit PSURs at defined time points following a medicine’s authorisation

**Scope**
- Cumulative data - focus on the new information
- Scientific assessment and integrated benefit-risk evaluation
- Single PSUR for all products containing the same active substance

Determined if there are new risks identified for a medicine or whether the balance of benefits and risks has changed
PSUR assessments

**PSUR assessments and PSUSA finalised per year**

- **2012 Jul-Dec:** 20
- **2013:** 430
- **2014:** 426

**PSURs submitted to NCAs**

- **2012 Jul-Dec:** 5000
- **2013:** 4000
- **2014:** 3000
PRAC PSUR assessments outcomes

Outcomes of PSUR assessments and PSUSAs

- Jul-Dec 2012: 17 Maintenance, 3 CHMP variation
- 2013: 360 Maintenance, 76 Suspension
- 2014: 383 Maintenance, 88 Revocation
Aim
- Resolves issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines
- EMA conducts a scientific assessment on behalf of the EU and makes a recommendation for a harmonised position across the EU

Safety-related referrals
- Based on evidence from pharmacovigilance – assessment and recommendation by PRAC, then:
  - Centrally authorised or centrally and nationally authorised medicines:
    - Assessed by the Committee for Medicinal Products for Human Use (CHMP)
  - Only nationally authorised medicines
    - Assessed by the Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh)

Procedure
- Can be started by the European Commission or any Member State
- For most referrals, the European Commission issues a decision to all Member States reflecting the measures to take to implement the Agency’s recommendation
Pharmacovigilance referrals

July 2012 – December 2014

- 6 Art. 107i - urgent safety referrals for nationally authorised medicines
- 7 Art. 20 - related to centrally authorised medicines only
- 18 Art. 31 - related to nationally or nationally and centrally authorised medicines
Referrals - collaborative effort
Referrals outcomes

• 24 variations of marketing authorisation (MA)
• 6 suspensions of indication or MA
• 4 revocations of indication or MA
Communications and information

- Information related to the PRAC – agendas, minutes
- Public safety communications – e.g. concerning referrals
- European database of suspected ADRs
- European Network of Centres in Pharmacoepidemiology and Pharmacovigilance e.g. outcomes of imposed PASS
- Risk management plan summaries
Systems and services

- Database of medicinal products authorised in the EU (Article 57 database)
- EudraVigilance enhancements
- Literature monitoring service
- PSUR repository
Future deliverables

• Continuing process improvements and complete implementation of systems and services (e.g. EudraVigilance, extension of literature monitoring, dedicated European medicines web portal)

• Continue training network

• Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action
Thank you for your attention

European Commission
Public Health information:
http://ec.europa.eu/health/index_en.htm