Outline of presentation

• Background - what new pharmacovigilance legislation sets out to achieve
• Establishment and functioning of Pharmacovigilance Risk Assessment Committee - PRAC
• Analysis of the initial experiences of PRAC
• Priorities and a look ahead
Pharmacovigilance legislative aims

- Strengthened Vigilance
- Transparency & communications
- Efficiency & simplification
Pharmacovigilance legislative aims

• Clarity on roles and responsibilities

• Proactive safety monitoring

• Robust and timely decision-making leading to consistent action on safety issues for nationally and centralised authorised products

• Greater inclusiveness for patients and healthcare professionals

• Best use of resources – avoiding duplication of effort

• High levels of transparency
European Commission estimate

5% of all hospital admissions due to ADRs

5% of all hospital patients experience an ADR

ADRs 5\textsuperscript{th} most common cause of hospital death

197,000 deaths per year in EU caused by ADRs

Total societal cost €79 billion

5910 lives per year and €237m could be saved
How will legislative aims be achieved?

The new Pharmacovigilance Risk Assessment Committee is playing a pivotal role.
Establishment of the PRAC

- Key reference - “Countdown to July 2012: the Establishment and Functioning of PRAC” 28 June 2012

- Summary of the outcome of the discussions within the EU Regulatory Network on topics including
  - PRAC mandate and tasks
  - PRAC outputs
  - PRAC Rapporteur appointment principles
  - Transparency and communication
  - PRAC-CHMP-CMD(h) interaction
Mandate of the Pharmacovigilance Risk Assessment Committee

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 of PRAC

Appointed by each Member State:

1 member + alternate
27 + EEA countries non voting members

Appointed by European Commission:

6 members - relevant expertise including clinical pharmacology and pharmacoepidemiology

1 member/alternate representing patient organisations

1 member/alternate representing healthcare professionals
EMA Committees - involvement in drug development

Pre-submission phase:
- Orphan Designation + Paed Req.: CHMP SAWP, PDCO, CAT
- Scientific Adv. Protocol assist.: COMP, SAWP
- Regulatory Filing Strategy: CHMP
- MAA Presub.: PDCO

Evaluation:
- MAA Evaluation: CHMP, COMP, CAT, PRAC, PDCO
- SAGs WPs

Post Authorisation:
- Changes MA + PhV: CHMP, PRAC, CAT
- Launch
It’s PRAC business...

- New safety signals
- **Urgent and non urgent union procedures** triggered due to safety concerns identified in medicinal product(s) authorised in more than one MS
- **Risk Management Plans**
- Non-interventional safety study protocols and study reports if the need for a **non-interventional post-authorisation safety study (PASS)** is identified
- **Periodic Safety Update Report (PSUR)**
- Recommendations on the need and scope of “for cause” pharmacovigilance inspections related to medicinal products of Community interest
- List of **medicines under additional monitoring**
PRAC Output with formal decision-making phase
- NAPs only

Referrals
Art.107 & Art.31

PRAC Recommendation & Assessment Report

Yes
In line with PRAC

| MAH | MS |

No

| Publication on EMA website (Art.26 Regulation) |

CMDh

Agreement by Consensus

Yes

CMDh, consensus and timetable
PRAC AR ± scientific grounds for disagreement

No

PRAC AR ± scientific grounds for disagreement

| MAH | MS |

| EC |

Publication on EMA website (Art.26 Regulation)
PRAC Output with formal decision-making phase
– includes one or more CAP

- Referrals: Art.107 & Art.31 & Art.20
- PSUR Single Assessment
- PASS Results

PRAC Recommendation & Assessment Report

In line with PRAC

European Commission Decision-making phase

CHMP

No

Public justification

Publication on EMA website (Art.26 Regulation)

Commission decision

MAH, MS
No formal decision-making phase: directly applicable - PASS protocol

MAH submits observational post-authorisation safety study protocol

EMA summarises the protocol to support PRAC assessment

PRAC assessment

Approve

MAH starts PASS

Minutes + advice

Publication of advice on EMA website + registration of protocol in PASS registry

Reject / amend

MAH revises protocol
PRAC Output without formal decision-making phase
Output = Advice

- RMP
- Renewal
- Type II Safety Variation
- Pharmacovigilance audit
- Pharmacovigilance Inspections

PRAC Advice + Minutes
(assessment report not systematically adopted by PRAC for all processes)

Publication on website (Art.26 Regulation)
Other PRAC advice
(no step through CHMP or CMDh)

Advice to EMA Management Board on EudraVigilance and PSUR databases

Advice on whether functional requirements met

Centralised ADR and PSUR reporting

Advice to EC on the additional monitoring back symbol

EC publishes symbol which is binding

Update relevant product information

Advice to EMA Director on literature ADR monitoring

Guidance plus lists of substances and journals

MAHs exempt monitoring substances and journals in the lists
PRAC advice on lists

1. URD Lists -> PRAC
2. PRAC -> Updated List
3. Updated List -> CMDh + CHMP
4. CMDh + CHMP -> Adopted List

List of products under additional monitoring

1. List of products under additional monitoring -> PRAC
2. PRAC -> Updated List
What has been PRAC experience to date?
PRAC activity – topics discussed by procedure

- September
- 1-3 October
- 29-31 October
- 26-29 November
- 7-10 January 2013
- 4-7 February 2013

Topics include:
- MSGs other
- CHMP - other inc. renewals MA
- PSURs
- PASSs
- RMPs
- Signals
- Referrals
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Number of discussions on referrals

- Art 107
- Art 31

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Referrals

• Codeine (analgesia) - toxicity in children
• Diclofenac - cardiovascular risk
• Short-Acting Beta-Agonists - in obstetric use
• Hydroxyethyl starch - morbidity/mortality
• Almitrine - neuropathy
• Diacerein - hepatotoxicity
• Combined hormonal contraceptives - venous thromboembolism

Under Article 31
Referrals

• Nicotinic acid / laropiprant*
  no reduction cardiovascular risk; higher frequency of serious adverse reactions - in obstetric use

• Tetrazepam
  serious cutaneous risks including Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiform, DRESS

• Cyproterone, ethinylestradiol (DIANE 35 & generics)
  venous and arterial thromboembolism

*Article 20 of Regulation (EC) No 726/2004, follows the procedural steps laid out in Article 107i of Directive 2001/83/EC.
PRAC advice on choice of Black Symbol

• For medicines subject to Additional Monitoring

• All new active substances and biologicals, including biosimilars; obligation to conduct a safety study, or to conditions or restrictions (optional)

• Explanation in product information and patient information leaflet

• Views of patient and consumer organisations taken into account
PRAC: Agendas, minutes and highlights

This page lists the agendas, minutes and meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) plenary meetings.

PRAC meeting highlights

- Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 1-3 October 2012
- Pharmacovigilance Risk Assessment Committee (PRAC) elects chair and vice-chair (07/09/2012)

Table of contents

- Agendas
- Minutes

Agendas

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Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 29-31 October 2012

PRAC begins second referral procedure

The European Medicines Agency’s Pharmacovigilance Risk Assessment Committee (PRAC) held its fourth meeting from 29 to 31 October 2012.

Since the first meeting of the PRAC in July 2011, the number of referrals to the PRAC has expanded substantially. At their most recent meeting, the PRAC was presented with a large volume of information on new safety issues for existing medicinal products as well as a growing number of up-and-coming medicines.
PRAC Publications timing schedule

- Agenda
- Highlights
- Safety referrals
- Minutes

- Day 1 of PRAC by mid-day
- Friday of PRAC week
- Following month after adoption
EMA Website Views and downloads

Number of accesses during the month of publication

- 3-6 September: 9,000
- 1-3 October: 5,000
- 29-31 October: 8,000
- 26-29 November: 7,000
- 7-10 January 2013: 9,000
Number of downloads during the month of publication

Position in the hit list of most downloaded EMA documents for the PRAC minutes

- 3-6 September: 2,000 downloads (23rd)
- 1-3 October: 3,000 downloads (26th)
- 29-31 October: 7,000 downloads (23rd)
- 26-29 November: 9,000 downloads (ongoing)
- 7-10 January 2013: 4,000 downloads (ongoing)
- 4-7 February 2013: 6,000 downloads (ongoing)
PRAC priorities

• Focus on application of best available science in risk assessment and risk management planning

• Efficiency and best use of resources – timeliness of outputs

• Transparency and openness – prompt availability of information

• Inclusiveness and stakeholder involvement
A look ahead

- Appointment of representatives from patient organisations
- Public hearings where appropriate
- Advice on request from EMA on safety communications
- Monitoring public health impact...
Public health outcomes

Demonstrably strengthening protection of public health—what this is all about
Conclusion

• Establishment of PRAC is key milestone in implementation of new Pharmacovigilance legislation

• Public health objectives and importance of robust scientific decision making are the main drivers

• Emphasis on proportionality and best use of resources and expertise will inform ways of working

• PRAC is committed to transparency and stakeholder engagement