The role of PRAC in Pharmacovigilance Decisions

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Pharmacovigilance Risk Assessment Committee is a public health focused committee of European Medicines Agency

Undertakes pharmacovigilance decisions using legislative public health protection tools
Role of PRAC in pharmacovigilance decisions

What is PRAC’s mandate and constitution?

What types of decision does PRAC undertake?

What are Member State pharmacovigilance requirements?
EU Pharmacovigilance Legislation – PRAC aims

- Public health protection
- Risk based / proportionate
- Based on science
- Simplification and efficiency
- Engagement of patients, Healthcare Professionals
- Greater openness and better information on medicines safety
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
28 + 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
What types of decisions does PRAC make?

- **Drug safety signals**
  - evaluating signals and advising on action

- **Regulatory action on benefit risk issues**
  - periodic safety update reports
  - referrals

- **Proactive pharmacovigilance**
  - advising on risk management plans
  - post-authorisation studies

- **Transparency & communication activities**
  - agenda, highlights, full committee minutes
% of PRAC plenary discussion time 2013, based on total hours

- Referrals: 33%
- PSURs: 16%
- RMPs: 19%
- PASSs: 4%
- Renewals: 4%
- Other: 14%
- Signals: 10%
Evaluation of signals by PRAC

Around 50% signals derive from Eudravigilance ICSRs

Other sources

- PSURs
- RMPs
- post-authorisation safety studies
- publications
PRAC signal in paediatric population

Images in neonatal medicine

Aqueous 2% chlorhexidine-induced chemical burns in an extremely premature infant

PRAC meeting June 2014
PRAC safety signal decisions

Number of signals
121

Data source
58 EudraVigilance
35 national review
11 literature
7 FDA/PMDA
5 historical (PhVWP)
6 studies

Outcome
57 labelling changes
17 no regulatory action
8 referral evaluation
2 update RMP
37 ongoing assessment

1 69 for CAPs, 43 for NAPs, 9 for both

Sept 2012 - Dec 2013
2. Benefit risk decisions by PRAC
Safety Referrals

Formal procedures with a legal framework to resolve concerns on safety or benefit-risk balance of medicine or class of medicines

EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of European union

Can be started by EU Commission, any Member State or by the company

PRAC aims for a scientific based consensus, if not formal vote taken & decision by majority

European Commission issues a binding decision to all Member States
Urgent Union Procedure

*Article 107i*

A Member State or EU Commission considers urgent action needed because of **safety issue** – they are considering - **suspension or revocation**, - **prohibition of supply** of a medicine, - **deletion of indications**, - **dose reduction** or - **new contraindications**

Fastest PRAC decision – 60 days
Example 107i procedure – Numeta 13%

Numeta 13% parenteral nutrition for preterm babies

Signal of 14 reports of hypermagnesaemia – July 2013

Voluntary recall of Numeta 13%

PRAC advised in September 2013 to suspend Numeta 13%, and introduce risk management for Numeta 16%
Stakeholder input to PRAC decisions

Stakeholders submissions for Article 107i referral procedures

- **Tetrazepam (Jan-13)**: 3 Patients, 1 Academia, 5 Healthcare Professionals, 1 Others
- **Diane (Feb-13)**: 5 Patients, 11 Academia, 1 Healthcare Professionals, 1 Others
- **Flupirtine (Mar-13)**: 1 Patients, 11 Academia, 7 Healthcare Professionals, 1 Others
- **Numeta (Jun-13)**: 1 Patients, 1 Academia, 1 Healthcare Professionals, 1 Others
- **HES (Jul-13)**: 1 Patients, 12 Academia, 93 Healthcare Professionals, 1 Others
Patient engagement in benefit risk

Maximum Acceptable PML Risk
Crohn’s Disease

Therapeutic Benefits

- Mild to Remission
- Moderate to Remission
- Severe to Remission

Physicians
Parents
Patients

0.00% 0.10% 0.16%

0.00% 0.16% 0.37%

0.45% 0.51% 0.98%

1st year risk 3rd year risk
Referral - interest of Community

Article 31

This type of referral is triggered following concerns relating to the **quality, safety or efficacy** of a medicine or a class of medicines.

Example – diclofenac and cardiovascular risk
Periodic Safety Update Reports
Example – *Strontium ranelate*

Periodic safety update report identified **increased risk of cardiac disorders** including myocardial infarction

PRAC advised **urgent variation** to restrict MA on safety grounds

Followed by Article 20 referral as Centrally Authorised Product

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London, UK - The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) has recommended restrictions in the use of *strontium ranelate* (Protelos/Osseor, Servier) to reduce the risk for adverse cardiovascular events in postmenopausal women [1].
Who receives PRAC decisions?

CMDh → PRAC → CHMP

Recommendations

EU Member States → European Commission
PRAC decisions - summary

Real-time signal detection monthly at PRAC is a major step forward for decisions.

Via referrals, PRAC takes decisions within prompt timescales proportionate to risk.

Via PSURs there is significant progress towards benefit risk evaluation throughout medicines' life cycle.

Improved stakeholder engagement means PRAC’s decisions include the perspective of medicines users.