3 September 2012
EMA/PRAC/432046/2012
Patient Health Protection

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda of meeting 3-5 September 2012

Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures
(Items 2 and 3 of the PRAC agenda)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

Signals assessment and prioritisation
(Item 4 of the PRAC agenda)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.
The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.
In most cases, the evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)
(Item 5 of the PRAC agenda)

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.
RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

Assessment of Periodic Safety Update Reports (PSURs)
(Item 6 of the PRAC agenda)

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A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.
PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

Post-authorisation Safety Studies (PASS)
(Item 7 of the PRAC agenda)

A PASS is a study of an authorised medicinal product carried out to obtain further information on its safety, or to measure the effectiveness of risk management measures. The results of a PASS help regulatory agencies to evaluate the safety and benefit-risk profile of a medicine.

Product related pharmacovigilance inspections
(Item 8 of the PRAC agenda)
Inspections carried out by regulatory agencies to ensure that marketing authorisation holders comply with their pharmacovigilance obligations.

More detailed information on the above terms can be found on the EMA website: www.europa.eu

Acting chair: Noel Wathion (EMA) – Election of Chair and Vice Chair

3 September 2012, 14:00 – 18:00, room 2/A (Training session for PRAC members and alternates)

4 September 2012, 09:00 – 18:00, room 2/A

5 September 2012, 09:00 – 16:00, room 2/A

1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

1.2. Agenda of the meeting of 3-5 September 2012

Status: *for adoption*

Document: PRAC Agenda Rev.2 published on 3 September 2012

1.3. Minutes of the previous meeting of the PRAC 19-20 July 2012

Status: *for adoption*

2. EU Referral Procedures for Safety Reasons: Urgent EU Procedures

2.1. Newly triggered procedures

None

2.2. Ongoing Procedures

None

2.3. Procedures for finalisation

None

2.4. Planned public hearings

None

3. EU Referral Procedures for Safety Reasons: Other EU Referral Procedures

3.1. Newly triggered procedures

None

3.2. Ongoing Procedures

None

3.3. Procedures for finalisation

None

3.4. Article 5(3) of Regulation (EC) No 726/2004 as amended: PRAC advice on CHMP request

None

4. Signals assessment and prioritisation

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. **Adalimumab – HUMIRA** (CAP)

- Signal of dermatomyositis

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Ulla Wändel-Liminga (SE)

4.1.2. Cinacalcet – MIMPARA (CAP)

- Signal of QT prolongation/ventricular arrhythmias

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

4.1.3. **Clopidogrel – PLAVIX** (CAP) **& generic products**

- Signal of eosinophilic pneumonia

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Maria Alexandra Pego (PT)

4.1.4. **Duloxetine – CYMBALTA, ARICLAIM, XERISTAR, YENTREVE** (CAP)

- Signal of increased serotonin syndrome due to a potential interaction with aripiprazole

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Dolores Montero (ES)

4.1.5. **Roxithromycin** (NAPs)

- Signal of hearing disorders

Status: *for initial discussion and Rapporteur appointment*

Regulatory details:

PRAC Rapporteur: to be appointed

4.1.6. **Roxithromycin** (NAPs)

- Signal of rhabdomyolysis secondary to interaction with statins

Status: *for initial discussion and Rapporteur appointment*

Regulatory details:

PRAC Rapporteur: to be appointed

4.1.7. **Sitagliptin - JANUVIA, RISTABEN, TESAVEL, XELEVIA** (CAP)

- Signal of rhabdomyolisis

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

4.1.8. **Somatropin –** NUTROPINAQ, OMNITROPE (CAPs, NAPs)

- Signal of convulsions (SMQs – Standardised MedDRA Queries)

Status: *for initial discussion and Rapporteur appointment*

Regulatory details:

PRAC Rapporteur: to be appointed

4.1.9. **Sunitinib** - **SUTENT** (CAP)

- Signal of cholecystitis

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Carmela Macchiarulo (IT)

4.1.10. Varenicline - CHAMPIX (CAP)

- Signal of seizures

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Doris Stenver (SE)

4.1.11. **Vemurafenib** - **ZELBORAF** (CAP)

- Signal of pancreatitis

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

4.2. New signals detected from other sources

4.2.1. **Codeine** (NAPs)

- Signal of fatal or life-threatening drug toxicity in CYP2D6 ultra-rapid metabolisers

Status: *for initial discussion and Rapporteur appointment*

Regulatory details:

PRAC Rapporteur: to be appointed

4.3. Signals follow-up and prioritisation

4.3.1. Pandemic influenza vaccine – PANDEMRIX (CAP)

- Signal of narcolepsy: further information following conclusion of the data review of Pandemrix and narcolepsy under Article 20 of Regulation (EC) No 726/2004

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: June Raine (UK)

5. Risk Management Plans

5.1. Medicines in the pre-authorisation phase

5.1.1. Phentermine/topiramate (initial CAP MAA)

- Evaluation of the RMP

Status: *for discussion and for PRAC advice*

5.2. Medicines already authorised

None

6. Assessment of Periodic Safety Update Reports (PSURs)

None

7. Post-authorisation Safety Studies (PASS)

7.1. P*ost-authorisation safety studies protocols*

None

7.2. Results of post-authorisation safety studies

None

8. Product related pharmacovigilance inspections

8.1. List of planned pharmacovigilance inspections

None

8.2. On-going or concluded pharmacovigilance inspections

Disclosure of information on results of pharmacovigilance inspections could undermine the protection of the purpose of these inspections, investigations and audits. Therefore such information is not reported in the agenda.

9. Other Safety issues for discussion requested by the CHMP

9.1. Safety related variations

None

9.2. Renewals

None

10. Other Safety issues for discussion requested by the Member States

10.1. Safety related variations

None

10.2. Renewals

None

10.3. Timing and message content in relation to MS safety announcements

None

10.4. Other

None

11. Organisational, regulatory and methodological matters

11.1. Mandate and organisation of the PRAC

11.1.1. Election of the Chair and Vice-Chair of the PRAC

Status: *for adoption*

11.1.2. Rules of Procedures of the PRAC

Status: *for information*

11.2. Pharmacovigilance audits and inspections

11.2.1. Pharmacovigilance Systems and their Quality Systems

None

11.2.2. Pharmacovigilance System Master File

None

11.2.3. Pharmacovigilance Inspections

None

11.2.4. Pharmacovigilance Audits

None

11.3. Periodic Safety Update Reports & Union Reference Date (EURD) List

11.3.1. Periodic Safety Update Reports

None

11.3.2. PSURs Repository

None

11.3.3. Union Reference Date List (EURD List)

11.3.3.1. Consultation on the draft List, version September 2012

Status: *For adoption*

11.4. Signal Management

11.4.1. Signal Management

11.4.1.1. List of substances subject to signal management worksharing

Status: *For adoption*

11.5. Adverse Drug Reactions reporting and additional reporting

11.5.1. Management and Reporting of Adverse Reactions to Medicinal Products

None

11.5.2. Additional Monitoring

None

11.5.3. List of Products under Additional Monitoring

11.5.3.1. Creation and maintenance of the List

Status: *For discussion*

11.5.3.2.

11.5.3.3. Selection of symbol for products subject to additional monitoring

Status: *for discussion*

11.6. EudraVigilance Database

None

11.7. Risk Management Plans and Effectiveness of risk Minimisations

11.7.1. Risk Management Systems

11.7.1.1. Draft PRAC Rapporteur RMP Assessment Report template

Status: *for initial discussion*

11.7.1.2. Draft PRAC Advice template

Status: *for initial discussion*

11.7.2. Tools, Educational Materials and Effectiveness Measurement for Risk Minimisation

None

11.8. Post-authorisation Safety Studies

11.8.1.1. Draft PRAC Rapporteur PASS protocol Assessment Report template

Status: *for initial discussion*

11.9. Community Procedures

None

11.10. Risk communication and Transparency

None

11.11. Continuous pharmacovigilance

11.11.1. Continuous Pharmacovigilance, Ongoing Benefit-Risk Evaluation, Regulatory Status and Planning of Public Communication

None

11.11.2. Incident Management

None

11.12. General regulatory matters

11.12.1.1. Good Vigilance Practice

Status: *For information*

11.13. Inter Status with EMA Committees and Working Parties

None

11.14. Inter Status within the EU regulatory network

None

11.15. Contacts of the PRAC with external parties and inter Status of the EMA with interested parties

11.15.1. Guidelines of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

None

12. Any other business

None