EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 October 2012
EMA/PRAC/519416/2012
Patient Health Protection

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda of meeting **1-3 October 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.
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

Chair: June Raine – Vice-Chair: Almath Spooner

1 October 2012, 13:00 – 19:00, room 2/A

2 October 2012, 09:00 – 19:00, room 2/A

3 October 2012, 09:00 – 17:00, room 2/A

1. Introduction

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

1.2. Agenda of the meeting of 1-3 October 2012

Status: for adoption

Document: PRAC Agenda Rev.3 published on 1 October 2012

1.3. Minutes of the previous meeting of the PRAC 3-5 September 2012

Status: for adoption

Document: PRAC 3-5 September Final Minutes to be published on 5 October 2012

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

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

3.1. Newly triggered Procedures

None

3.2. On-going 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. **Aripiprazole** – **ABILIFY** (CAP)

- Signal of hypothyroidism

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Maria Alexandra Pego (PT)

4.1.2. **Aripiprazole – ABILIFY** (CAP)

- Signal of serotonin syndrome due to a potential interaction with duloxetine

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Maria Alexandra Pego (PT)

4.1.3. **Erlotinib - TARCEVA** (CAP)

- Signal of pancreatitis

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Doris Stenver (DK)

4.1.4. **Erlotinib - TARCEVA** (CAP)

- Signal of palmar-plantar erythrodysaesthesia syndrome (PPES)

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Doris Stenver (DK)

4.1.5. **Erlotinib - TARCEVA** (CAP)

- Signal of vasculitis

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Doris Stenver (DK)

4.1.6. **Human papillomavirus vaccine [types 6,11, 16, 18] – GARDASIL** (CAP)

- Signal of bronchospasm in patients with or without asthma

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

4.1.7. **Influenza vaccines -** (NAPs)

- Signal of extensive limb swelling (ELS)

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: *to be appointed*

4.1.8. **Iplimumab - YERVOY** (CAP)

- Signal of anaphylactic reaction

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

4.1.9. **Mirtazapine** (NAPs)

- Signal of pancreatitis

Status: *for initial discussion and for Rapporteur appointment*

Regulatory details:

PRAC Rapporteur: to be appointed

4.1.10. **Sugammadex - BRIDION** (CAP)

- Signal of respiratory symptoms unrelated to hypersensitivity reaction

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Kirsti Villikka (FI)

4.1.11. **Temozolomide - TEMODAL** (CAP)

- Signal of hepatic failure

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: Martin Huber (DE)

4.1.12. **Trazodone** - (NAP)

- Signal of postural hypotension and somnolence at high starting dose

Status: *for initial discussion*

Regulatory details:

PRAC Rapporteur: *To be appointed*

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Anticholinergic drugs for inhaled use: ipratropium, ipratropium/salbutamol, tiotropium bromide (NAPs)

- Signal of increased incidence of myocardial infarction and stroke in patients with chronic obstructive pulmonary disease (COPD) – from literature

Status: *for initial discussion and for Rapporteur appointment*

Regulatory details:

PRAC Rapporteur: to be appointed

4.3.2. Codeine (NAPs)

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

Status: *for follow-up discussion*

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

4.3.3. Hormonal contraceptives: norelgestromin / ethinylestradiol - EVRA (CAP); etonogestrel; etonogestrel and ethinylestradiol; drospirenone and ethinylestradiol (NAPs)

- Signal of arterial thrombotic events

Action: *for follow-up discussion*

Regulatory details:

PRAC Rapporteur: *to be appointed*

5. Risk Management Plans

5.1. Medicines in the pre-authorisation phase

None

5.2. Medicines already authorised

5.2.1. Golimumab – SIMPONI (CAP)

- Evaluation of the updated RMP in the context of a Type II variation, extension of indication

Status: *for discussion and agreement of advice to CHMP*

Regulatory details:

PRAC Rapporteur: Ulla Wandel-Liminga (SE)
PRAC Co-Rapporteur: Isabelle Robine (FR)

5.2.2. Mannitol – **BRONCHITOL** (CAP)

- Evaluation of the updated RMP in the context of a RMP stand-alone procedure

Status: *for discussion and agreement of advice to CHMP*

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)
PRAC Co-Rapporteur: Isabelle Robine (FR)

5.2.3. **Saxagliptin – ONGLYZA** (CAP) , **Saxagliptin / metformin - KOMBOGLYZE** (CAP)

- Evaluation of the updated RMP in the context of a Type II variation, extension of indication

Status: *for discussion and agreement of advice to CHMP*

Regulatory details:

PRAC Rapporteur: Menno van der Elst (NL)
PRAC Co-Rapporteur: *to be appointed*

6. Assessment of Periodic Safety Update Reports (PSURs)

None

7. Post-authorisation Safety Studies (PASS)

7.1. Post-authorisation safety studies protocols

7.1.1. **Ivacaftor – KALYDECO** (CAP)

- Evaluation of PASS protocol: observational study to evaluate the long-term safety of ivacaftor in patients with cystic fibrosis (CF)

Status: *for discussion and agreement of PRAC letter of endorsement/objection/notification that study is a clinical trial*

Regulatory details:

PRAC Rapporteur: Miguel Angel Macia (ES)
PRAC Co-Rapporteur: Julia Pallos (HU)

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 inspection

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 considered confidential and it is not reported in the agenda.

9. Other Safety issues for discussion requested by the CHMP or the EMA

9.1. Safety related variations of the marketing authorisation (MA)

None

9.2. Renewals of the Marketing Authorisation

9.2.1. **Febuxostat** – **ADENURIC** (CAP)

- Renewal of the Marketing Authorisation after first 5 years

Status: *for discussion and agreement of advice to CHMP*

Regulatory details:

PRAC Rapporteur: Harald Herkner (AT)
PRAC Co-Rapporteur: Qun-Ying Yue (SE)

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

None

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

10.1. Renewals of the MAs

None

10.2. Safety related variations of the marketing authorisation

None

10.3. Timing and message content in relation to Member States' safety announcements

None

10.4. Other

11. Organisational, regulatory and methodological matters

None

11.1. Mandate and organisation of the PRAC

11.1.1. Establishment of PRAC review teams

Status: for discussion

11.2. Pharmacovigilance audits and inspections

11.2.1. Pharmacovigilance Systems and their Quality Systems

11.2.1.1. Use of the conditions of the Marketing Authorisation in relation to the existence of an adequate pharmacovigilance system

Status: for discussion

11.2.2. Pharmacovigilance System Master File

None

11.2.3. Pharmacovigilance Inspections

Pharmacovigilance Inspections

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 revised List, version October 2012

Status: *For adoption*

11.4. Signal Management

11.4.1. Signal Management worksharing

None

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 Product under Additional Monitoring

None

11.5.3.1. Selection of symbol for products subject to additional monitoring

Status: *for discussion and agreement of recommendations to the EC*

11.6. EudraVigilance Database

11.6.1. Activities related to the confirmation of full functionality

None

11.6.2. Changes to Eudravigilance Database and functional specifications

None

11.7. Risk Management Plans and Effectiveness of risk Minimisations

11.7.1. Risk Management Systems

None

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

None

11.8. Post-authorisation Safety Studies

11.8.1. Post-Authorisation Safety Studies

None

11.9. Community Procedures

11.9.1. Referral Procedures for Safety Reasons

None

11.10. Risk communication and Transparency

11.10.1. Public Participation in Pharmacovigilance

None

11.10.2. Safety Communication

11.10.2.1. Process for review of Direct Healthcare Professional Communications (DHPCs) by EMA

Status: *for discussion*

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. Inter Status with EMA Committees and Working Parties

11.12.1. Committees

None

11.12.2. Working Parties

None

11.13. Inter Status within the EU regulatory network

None

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

None

12. Any other business

None