8 April 2013
EMA/218110/2013
Pharmacovigilance Risk Assessment Committee (PRAC)

Pharmacovigilance Risk Assessment Committee (PRAC)

Agenda of meeting on 8-11 April 2013

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.ema.europa.eu/

Chair: June Raine – Vice-Chair: Almath Spooner

8 April 2013, 13:00 – 19:00, room 3/A

9 April 2013, 08:30 – 19:00, room 3/A

10 April 2013, 08:30– 19:00, room 3/A

11 April 2013, 08:30 – 13:30, room 3/A

Table of contents

1. Introduction

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

1.2. Adoption of agenda of the meeting of 8-11 April 2013

Status: for adoption

Document: PRAC Agenda Rev.3 due for publication on 8 April 2013

1.3. Minutes of the previous PRAC meeting on 4-7 March 2013

Status: for adoption

Document: PRAC Final Minutes to be published on 15 April 2013

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

2.1. Newly triggered procedures

None

2.2. Ongoing Procedures

2.2.1. **Cyproterone**, **ethinylestradiol – DIANE 35** & **other medicines containing cyproterone acetate 2 mg and ethinylestradiol 35 micrograms** (NAP)

- Review of the benefit-risk balance following the notification by France of a referral under Article 107i of Directive 2001/83/EC

Status*: for discussion*

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)
PRAC Co-Rapporteur: Evelyne Falip (FR)

2.3. Procedures for finalisation

2.3.1. **Tetrazepam** (NAP)

- Review of the benefit-risk balance of tetrazepam-containing medicines following the notification by France of a referral under Article 107i of Directive 2001/83/EC

Status*: for discussion and agreement of PRAC recommendation to CMDh*

Regulatory details:

PRAC Rapporteur: Jean-Michel Dogné (BE)
PRAC Co-Rapporteur: Evelyne Falip (FR)

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

3.2.1. **Almitrine** (NAP)

- Review of the benefit-risk balance of almitrine-containing medicines following the notification by France of a referral under Article 31 of Directive 2001/83/EC based on pharmacovigilance data

***Status**: for discussion and agreement of PRAC recommendation to CMDh (or list of outstanding issues and revised timetable)*

Regulatory details:

PRAC Rapporteur: Margarida Guimaraes (PT)
PRAC Co-Rapporteur: Evelyne Falip (FR)

3.2.2. **Codeine** (NAP)

- Review of the risk-benefit balance of codeine-containing medicines used following the notification by the United Kingdom of a referral under Article 31 of Directive 2001/83/EC based on pharmacovigilance data

***Status**: for discussion and agreement of PRAC recommendation to CMDh (or list of outstanding issues and revised timetable)*

Regulatory details:

PRAC Rapporteur: Dolores Montero (ES)
PRAC Co-Rapporteur: Julie Williams (UK)

3.2.3. **Diclofenac** (NAP)

- Review of the benefit-risk balance of diclofenac-containing medicines for systemic use following the notification by the United Kingdom of a referral under Article 31 of Directive 2001/83/EC based on pharmacovigilance data

***Status**: for discussion*

Regulatory details:

PRAC Rapporteur: Doris Stenver (DK)
PRAC Co-Rapporteur: Julie Williams (UK)

3.2.4. **Hydroxyethyl starch** (**HES**), **solutions for infusion** (NAP)

- Review of the benefit-risk balance of HES-containing products following the notification by Germany of a referral under Article 31 of Directive 2001/83/EC based on pharmacovigilance data

***Status**: for discussion*

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)
PRAC Co-Rapporteur: Martin Huber (DE)

3.3. Procedures for finalisation

None

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

3.4.1. **GLP-1 based therapy products** (**glucagon-like-peptide-1** (**GLP-1**) **agonists and dipeptidylpeptidase-4** (**DPP-4**) **inhibitors**) (CAP)

- Review of findings on pancreatic risks following notification by the European Medicines Agency (EMA) under Article 5(3) of Regulation (EC) 726/2004

***Status**: for discussion*

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)
PRAC Co-Rapporteur: Menno van der Elst (NL)

4. Signals assessment and prioritisation[1]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. **Adalimumab – HUMIRA** (CAP)

- Signal of skin ulcers

***Status:** for discussion*

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

4.1.2. **Adalimumab – HUMIRA** (CAP)

- Signal of glioblastoma and brain neoplasms

[1] Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products, including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP). PRAC recommendations will specify the products concerned in case of any regulatory action required.

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

4.1.3. Brentuximab vedotin – ADCETRIS (CAP)

- Signal of interstitial lung disease, pulmonary alveolar haemorrhage and pulmonary toxicity

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

4.1.4. Exenatide – BYDUREON (CAP)

- Signal of injection site abscess and cellulitis

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

4.2. New signals detected from other sources

4.2.1. Agents acting on the renin-angiotensin system (CAP, NAP)

- Signal from the literature of efficacy and safety of dual blockade of the renin-angiotensin system: meta-analysis of randomised trials

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: *to be appointed*

4.3. Signals follow-up

4.3.1. Azithromycin (NAP)

- Signal of potentially fatal heart events

Status: *for discussion*

Regulatory details:

PRAC Rapporteur*: to be appointed*

4.3.2. Docetaxel – TAXOTERE (CAP), DOCETAXEL WINTHROP (CAP)

- Signal of thrombotic microangiopathy

Status: *for discussion*

Regulatory details:

PRAC Rapporteur*:* Isabelle Robine (FR)

4.3.3. Docetaxel – TAXOTERE (CAP), **DOCETAXEL WINTHROP** (CAP)

- Signal of serious and fatal drug interactions involving CYP3A4 (grapefruit juice and dronedarone)

Status: *for discussion*

Regulatory details:

PRAC Rapporteur*:* Isabelle Robine (FR)

4.3.4. Fingolimod – GILENYA (CAP)

- Signal of haemophagocytic syndrome

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

4.3.5. Fluoroquinolones: **ciprofloxacin** (NAP), **enoxacin** (NAP), **flumequine** (NAP), **lomefloxacin** (NAP), **levofloxacin** (NAP), **moxifloxacin** (NAP), **ofloxacin** (NAP), **pefloxacin** (NAP), **prulifloxacin** (NAP), **rufloxacin** (NAP), **norfloxacin** (NAP)

- Signal of retinal detachment

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Martin Huber (DE)

4.3.6. Mirtazapine (NAP)

- Signal of pancreatitis

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

4.3.7. Pandemic influenza vaccine (**H1N1**)**v** (**split virion**, **inactivated**, **adjuvanted**) **A/California/7/2009** (**H1N1**)**v like strain** (**x-179a**) **– 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: Julie Williams (UK)

4.3.8. **Valproate** (NAP)

- Signal of neurodevelopmental effects following in utero exposure

Status: *for discussion and Rapporteur appointment*

Regulatory details:

PRAC Rapporteur: *to be appointed*

See also tolvaptan 10.1.

5. Risk Management Plans

5.1. Medicines in the pre-authorisation phase

5.1.1. Alogliptin

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.2. Alogliptin, metformin

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.3. Alogliptin, pioglitazone

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.4. Aripiprazole monohydrate

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.5. Avanafil

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.6. Canagliflozin

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.7. Dabrafenib

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.8. Dapagliflozin, metformin

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.9. Enzlutamide

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.10. Esomeprazole

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.11. Flutemetamol F-18

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.12. Fluticasone furoate, vilanterol

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.13. Levetiracetam

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.14. Lomitapide

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.15. Lorcaserin

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.16. Modified Vaccinia Ankara virus

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.17. Somatropin

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.1.18. Spheroids of human autologous matrix-associated chondrocytes

- Evaluation of an RMP in the context of an initial Marketing Authorisation Application procedure

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

5.2. Medicines already authorised

RMP in the context of a PSUR procedure

5.2.1. Aztreonam – CAYSTON (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

See also 6.1.4.

5.2.2. Bivalirudin – ANGIOX (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

See also 6.1.6.

5.2.3. Cetuximab – ERBITUX (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

See also 6.1.7.

5.2.4. Dabigatran – PRADAXA (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Doris Stenver (DK)

See also 6.1.8.

5.2.5. Daptomycin – CUBICIN (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

See also 6.1.9.

5.2.6. Deferiprone – FERRIPROX (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

See also 5.2.6.

5.2.7. Dexmedetomidine – DEXDOR (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

See 6.1.11.

5.2.8. Etravirine – INTELENCE (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

See also 6.1.14.

5.2.9. Exenatide – **BYDUREON** (CAP), **BYETTA** (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

See also 6.1.15.

5.2.10. Fingolimod – **GILENYA** (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

See also 6.1.16.

5.2.11. Memantine – **AXURA** (CAP), **EBIXA** (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Dolores Montero (ES)

See also 6.1.28.

5.2.12. Micafungin – **MYCAMINE** (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Martin Huber (DE)

See also 6.1.29.

5.2.13. Midazolam – **BUCCOLAM** (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

See also 6.1.30.

5.2.14. Orlistat – XENICAL (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

See also 6.1.31.

5.2.15. Oseltamivir – TAMIFLU (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Kirsti Villikka (FI)

See also 6.1.32.

5.2.16. Panitumumab – VECTIBIX (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julia Dunne (UK)

See also 6.1.35.

5.2.17. Retigabine – TROBALT (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Line Michan (DK)

See also 6.1.37.

5.2.18. Strontium ranelate – OSSEOR (CAP), **PROTELOS** (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

See also 6.1.40.

5.2.19. Tegafur, **gimeracil**, **oteracil – TEYSUNO** (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

See also 6.1.41.

5.2.20. Telaprevir – INCIVO (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

See also 6.1.42.

5.2.21. Vinflunine – JAVLOR (CAP)

- Evaluation of an RMP in the context of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julia Dunne (UK)

See also 6.1.50.

RMP in the context of a variation

5.2.22. Certolizumab pegol – CIMZIA (CAP)

- Evaluation of an RMP in the context of a variation, extension of indication

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

5.2.23. Human hepatitis B immunoglobulin – ZUTECTRA (CAP)

- Evaluation of an RMP in the context of a variation

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

Regulatory details:

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

5.2.24. Telaprevir – INCIVO (CAP)

- Evaluation of an RMP in the context of a variation

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

5.2.25. Ulipristal acetate - ELLAONE (CAP)

- Evaluation of an RMP in the context of a variation

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

Regulatory details:

PRAC Rapporteur: Menno van der Elst (NL)

5.2.26. Vardenafil – VIVANZA (CAP)

- Evaluation of an RMP in the context of a variation, line extension

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

Regulatory details:

PRAC Rapporteur: Miguel-Angel Macia (ES)

5.2.27. Voriconazole – VFEND (CAP)

- Evaluation of an RMP in the context of a variation

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

RMP in the context of a renewal of the marketing authorisation, conditional renewal or annual reassessment

5.2.28. Sugammadex – BRIDION (CAP)

- Evaluation of an RMP in the context of a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Kirsti Villikka (FI)

See also 8.1.5.

RMP in the context of a stand-alone RMP procedure

5.2.29. Cinacalcet – MIMPARA (CAP)

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

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

5.2.30. Dapagliflozin – FORXIGA (CAP)

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

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

6. Assessment of Periodic Safety Update Reports (PSURs)

6.1.1. Adefovir dipivoxil – HEPSERA (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

6.1.2. Aliskiren – RASILEZ (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Carmela Macchiarulo (IT)

6.1.3. Anagrelide – XAGRID (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

6.1.4. Aztreonam – CAYSTON (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

6.1.5. Belimumab – BENLYSTA (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

6.1.6. Bivalirudin – ANGIOX (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

6.1.7. Cetuximab – ERBITUX (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

6.1.8. Dabigatran – PRADAXA (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Doris Stenver (DK)

6.1.9. Daptomycin – CUBICIN (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

6.1.10. Deferiprone – **FERRIPROX** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

6.1.11. Dexmedetomidine – **DEXDOR** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

6.1.12. Eculizumab – **SOLIRIS** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Dolores Montero (ES)

6.1.13. Eltrombopag – **REVOLADE** (CAP)

- Evaluation a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Dolores Montero (ES)

6.1.14. Etravirine – **INTELENCE** (CAP)

- Evaluation a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

6.1.15. Exenatide – **BYDUREON** (CAP), **BYETTA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

6.1.16. Fingolimod – GILENYA (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

6.1.17. Hepatitis A and hepatitis B (rDNA) (HAB) vaccine – AMBIRIX (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julia Dunne (UK)

6.1.18. Hepatitis A and hepatitis B (rDNA) (HAB) vaccine – TWINRIX ADULT (CAP), TWINRIX PAEDIATRIC (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julia Dunne (UK)

6.1.19. Human fibrinogen thrombin – EVICEL (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

6.1.20. Iloprost – VENTAVIS (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

6.1.21. Indinavir – CRIXIVAN (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

6.1.22. Ipilimumab – YERVOY (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Dolores Montero (ES)

6.1.23. Lacosamide – VIMPAT (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

6.1.24. Leflunomide – ARAVA (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

6.1.25. Lopinavir, **ritonavir – ALUVIA** (Art 58), **KALETRA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

6.1.26. Measles, **mumps**, **rubella and varicella vaccine – PROQUAD** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

6.1.27. Memantine – AXURA (CAP), **EBIXA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Dolores Montero (ES)

6.1.28. Micafungin – MYCAMINE (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Martin Huber (DE)

6.1.29. Midazolam – BUCCOLAM (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

6.1.30. Orlistat – XENICAL (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

6.1.31. Oseltamivir – TAMIFLU (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Kirsti Villikka (FI)

6.1.32. **Pandemic influenza vaccine** (**whole virion**, **Vero cell derived**, **inactivated**) – **PANDEMIC INFLUENZA VACCINE H5N1 BAXTER** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

6.1.33. **Pandemic influenza vaccine** (**H1N1**)**v** (**split virion**, **inactivated**, **adjuvanted**) **A/California/7/2009** (**H1N1**)**v like strain** (**x-179a**) **– PANDEMRIX** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

6.1.34. **Panitumumab – VECTIBIX** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julia Dunne (UK)

6.1.35. **Pazopanib – VOTRIENT** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Doris Stenver (DK)

6.1.36. **Retigabine – TROBALT** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Line Michan (DK)

6.1.37. **Rivaroxaban – XARELTO** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

6.1.38. **Rosiglitazone**, **metformin – AVANDAMET** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Menno van der Elst (NL)

6.1.39. **Strontium ranelate – OSSEOR** (CAP), **PROTELOS** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

6.1.40. **Tegafur**, **gimeracil**, **oteracil – TEYSUNO** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

6.1.41. **Telaprevir – INCIVO** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

6.1.42. **Telavancin – VIBATIV** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

6.1.43. **Telbivudine – SEBIVO** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

6.1.44. Telmisartan, amlodipine – ONDUARP (CAP), TWYNSTA (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Martin Huber (DE)

6.1.45. Teriparatide – FORSTEO (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

6.1.46. Trabectedin – YONDELIS (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Line Michan (DK)

6.1.47. Trastuzumab – HERCEPTIN (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

6.1.48. Vandetanib – CAPRELSA (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

6.1.49. Vinflunine – JAVLOR (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:

PRAC Rapporteur: Julia Dunne (UK)

7. Post-authorisation Safety Studies (PASS)

7.1. Protocols of post-authorisation safety studies

7.1.1. Aclidinium Bromide – **BRETARIS GENUAIR** (CAP), **EKLIRA GENUAIR** (CAP)

- Evaluation of a PASS protocol pursuant to an obligation imposed in accordance with Article 21a and 22a of Directive 2001/83/EC

Status: *for discussion and agreement of PRAC letter of endorsement/objection/notification*

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

7.1.2. Aclidinium Bromide – **BRETARIS GENUAIR** (CAP), **EKLIRA GENUAIR** (CAP)

- PRAC consultation on a Drug Utilisation Study (DUS) included in a pharmacovigilance plan of the RMP in accordance with article 107m of Directive 2001/83/EC

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

7.1.3. Catridecacog – **NOVOTHIRTEEN** (CAP)

- PRAC consultation on a PASS protocol included in the pharmacovigilance plan of the RMP in accordance to Article 107m Directive 2001/83/EC

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

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

7.1.4. Glycopyrronium bromide – **ENUREV BREEZHALER** (CAP), **SEEBRI BREEZHALER** (CAP), **TOVANOR BREEZHALER** (CAP)

- Evaluation of a PASS protocol pursuant to an obligation imposed in accordance with Article 21a and 22a of Directive 2001/83/EC

Status: *for discussion and agreement of PRAC letter of endorsement/objection/notification*

Regulatory details:

PRAC Rapporteur: Line Michan (DK)

7.1.5. Glycopyrronium bromide – ENUREV BREEZHALER (CAP), SEEBRI BREEZHALER (CAP), TOVANOR BREEZHALER (CAP)

- PRAC consultation on a Drug Utilisation Study (DUS) included in the pharmacovigilance plan of the RMP in accordance with Article 107m of Directive 2001/83/EC

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

Regulatory details:

PRAC Rapporteur: Line Michan (DK)

7.1.6. Nomegestrol, estradiol – ZOELY (CAP)

- PRAC consultation on a PASS protocol included in the pharmacovigilance plan of the RMP in accordance to Article 107m Directive 2001/83/EC

Status: *for follow-up discussion*

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

7.1.7. Ulipristal acetate – ELLAONE (CAP)

- PRAC consultation on a PASS protocol included in the pharmacovigilance plan of the RMP in accordance to Article 107m Directive 2001/83/EC

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

Regulatory details:

PRAC Rapporteur: Menno van der Elst (NL)

7.2. Results of post-authorisation safety studies

None

8. Renewals of the Marketing Authorisation, Conditional Renewals and Annual Reassessments

8.1.1. Agalsidase alfa – REPLAGAL (CAP)

- PRAC consultation on an annual reassessment of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

8.1.2. Antithrombin alfa – ATRYN (CAP)

- PRAC consultation on an annual reassessment of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

8.1.3. Brinzolamide, **timolol – AZARGA** (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Line Michan (DK)

8.1.4. Histamine dihydrochloride – CEPLENE (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Almath Spooner (IE)

8.1.5. Sugammadex – BRIDION (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Kirsti Villikka (FI)

8.1.6. Tafamidis – VYNDAQEL (CAP)

- PRAC consultation on an annual reassessment of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Evelyne Falip (FR)

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. On-going or concluded pharmacovigilance inspection

None

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

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

10.1.1. Pazopanib – VOTRIENT (CAP)

- PRAC consultation on a safety-related type II variation upon CHMP request

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

Regulatory details:

PRAC Rapporteur: Doris Stenver (DK)

10.1.2. Tolvaptan – SAMSCA (CAP)

- PRAC consultation on a safety-related type II variation upon CHMP request

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

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

None

10.3. Other requests

10.3.1. Epoetins: **darbepoetin-alfa - ARANESP** (CAP), **epoetin-beta - NEORECORMON** (CAP); **epoetin-zeta - RETACRIT SILAPO** (CAP); **epoetin alfa – BINOCRIT** (CAP); **ABSEAMED** (CAP); **EPOETIN ALFA HEXAL** (CAP); **epoetin theta – EPORATIO** (CAP)

- PRAC consultation on risk of tumour growth progression and thromboembolic events in cancer patients, upon CHMP request

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

Regulatory details:

PRAC Rapporteur (overall): Isabelle Robine (FR)
PRAC Co-Rapporteur (overall): Martin Huber (DE)

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Ondansetron (NAP)

- Risk of QT prolongation and Torsade de Pointes

Status: *for discussion and agreement of advice to Member States*

Regulatory details:

Lead member: Julie Williams (UK)

11.2. Renewals of the Marketing Authorisation

None

11.3. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.2. Pharmacovigilance audits and inspections

12.2.1. Pharmacovigilance Systems and their Quality Systems

None

12.2.2. Pharmacovigilance Inspections

None

12.2.3. Pharmacovigilance Audits

None

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

12.3.1. Periodic Safety Update Reports

None

12.3.2. PSURs Repository

None

12.3.3. Union Reference Date List

- Consultation on the draft List, version April 2013

Status: *for discussion and agreement of the list*

12.4. Signal Management

12.4.1. Signal Management

- Feedback from Signal Management Review Technical (SMART) Working Group

Status: *for information*

12.4.2. PRAC recommendation leading to changes to the product Information

- Draft proposal on coordination of the implementation for nationally authorised products

Status: *for discussion*

12.5. Adverse Drug Reactions reporting and additional reporting

12.5.1. Management and Reporting of Adverse Reactions to Medicinal Products

None

12.5.2. Additional Monitoring

None

12.5.3. List of Product under Additional Monitoring

- Update on creation and maintenance of the List

Status: *For discussion*

12.6. EudraVigilance Database

12.6.1. Activities related to the confirmation of full functionality

None

12.6.2. Changes to EudraVigilance Database and functional specifications

None

12.7. Risk Management Plans and Effectiveness of risk Minimisations

12.7.1. Risk Management Systems

None

12.7.2. Champions in the review of the assessment process of RMPs

- Review of the assessment process of RMPs

Status: *for discussion*

12.7.3. Timetables for RMP assessment

- Proposed revised timetables for RMP assessment in pre-authorisation phase

Status: *for discussion*

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

None

12.8. Post-authorisation Safety Studies

12.8.1. Post-Authorisation Safety Studies

None

12.9. Community Procedures

12.9.1. Referral Procedures for Safety Reasons

None

12.10. Risk communication and Transparency

12.10.1. Public Participation in Pharmacovigilance

None

12.10.2. Safety Communication

None

12.11. Continuous pharmacovigilance

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

None

12.11.2. Incident Management

None

12.12. Interaction with EMA Committees and Working Parties

12.12.1. Committees

None

12.12.2. Pharmacogenomics Working Party

- Draft Guideline on conducting pharmacovigilance for medicines with pharmacogenomics associations

Status: *for information*

12.13. Interaction within the EU regulatory network

None

12.14. Contacts of the PRAC with external parties and interaction status of the EMA with interested parties

12.14.1. European Network Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP)

- Proposal for an EMA funded study on the use of metformin in renal impaired patients and the risk of lactic acidosis

Status: *for discussion*

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

None

12.14.3. Others

None

13. Any other business

None