2 December 2013
EMA/PRAC/748572/2013
Pharmacovigilance Risk Assessment Committee (PRAC)

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 2-5 December 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

2 December 2013, 13:00 – 19:00, room 3/A

3 December 2013, 08:30 – 19:00, room 3/A

4 December 2013, 08:30– 19:00, room 3/A

5 December 2013, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

19 December 2013, 10:30 – 12:30, room 2/B, via teleconference

Table of contents

1. Introduction

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

1.2. Adoption of agenda for the meeting of 2-5 December 2013

Status: for adoption

Document: PRAC Agenda Rev.3 due for publication on 2 December 2013

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

Status: for adoption

Document: PRAC Final Minutes due for publication by 13 December 2013

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

3.1.1. **Ponatinib – ICLUSIG** (CAP)

- Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20(8) of Regulation (EC) No 726/2004, following procedural steps of Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Status: *for discussion and adoption of a list of questions and procedure timetable*

Regulatory details:
PRAC Rapporteur: Julia Dunne (UK)
PRAC Co-Rapporteur: Ulla Wändel Liminga (SE)

3.2. Ongoing Procedures

3.2.1. **Domperidone** (NAP)

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

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)
PRAC Co-Rapporteur: Jean-Michel Dogné (BE)

3.2.2. **Zolpidem** (NAP)

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

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Menno van der Elst (NL)
PRAC Co-Rapporteur: Carmela Macchiarulo (IT)

3.3. Procedures for finalisation

3.3.1. **Octocog alfa – HELIXATE NEXGEN** (CAP), **KOGENATE BAYER** (CAP)

- Review of the benefit-risk balance following a notification by the European Commission of a referral under Article 20(8) of Regulation (EC) No 726/2004, following procedural steps of Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

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

Regulatory details:

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)
PRAC Co-Rapporteur: Ulla Wändel Liminga (SE)

3.4. Re-examination procedures

3.4.1. **Diacerein** (NAP)

- Re-examination procedure of the PRAC recommendation following the review of the benefit-risk balance following notification by France of a referral under Article 31 of Directive 2001/83/EC based on pharmacovigilance data

Status*: for discussion*

Regulatory details:

PRAC Rapporteur: *to be appointed*
PRAC Co-Rapporteur: *to be appointed*

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

None

3.6. Others

3.6.1. **Dihydrocodeine** (NAP)

- Follow-up to PRAC September 2013 discussion

***Status**: for discussion*

Regulatory details:
PRAC Rapporteur: *Not applicable*

4. Signals assessment and prioritisation

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. **Clindamycin** (NAP)

- Signal of drug interaction with warfarin leading to international normalised ratio (INR) increased

***Status:** for discussion*

Regulatory details:
PRAC Rapporteur: *to be appointed*

4.1.2. **Lamotrigine** (NAP)

- Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

***Status:** for discussion*

Regulatory details:
PRAC Rapporteur: *to be appointed*

4.1.3. **Strontium ranelate - OSSEOR** (CAP), **PROTELOS** (CAP)

- Signal of eye disorders

***Status:** for discussion*

Regulatory details:
PRAC Rapporteur: Ulla Wändel Liminga (SE)

4.2. New signals detected from other sources

4.2.1. **Fentanyl**, transdermal patch (NAP)

- Signal of accidental exposure

***Status:** for discussion*

Regulatory details:
PRAC Rapporteur: *to be appointed*

4.3. Signals follow-up and prioritisation

4.3.1. **Cabazitaxel - JEVTANA** (CAP)

- Signal of medication error potentially leading to inappropriate dose

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Isabelle Robine (FR)

4.3.2. **Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) – CERVARIX** (CAP)
Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) – GARDASIL (CAP), **SILGARD** (CAP)

- Signal of complex regional pain syndrome (CRPS) linked to the process of vaccination

Status: *for discussion*

Regulatory details:

PRAC Rapporteurs: Jean-Michel Dogné (BE), Qun-Ying Yue (SE)

4.3.3. **Sitagliptin – JANUVIA** (CAP), **RISTABEN** (CAP), **TESAVEL** (CAP), **XELEVIA** (CAP)
Sitagliptin, **metformin – EFFICIB** (CAP), **JANUMET** (CAP), **RISTFOR** (CAP), **VELMETIA** (CAP), **Angiotensin-converting enzyme (ACE) inhibitors** (NAP)

- Signal of angioedema due to interaction between sitagliptin and ACE inhibitors

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Menno van der Elst (NL)

4.3.4. **Thiopental** (NAP)

- Signal of hypokalaemia and rebound hyperkalamaemia

Status: *for discussion*

Regulatory details:

PRAC Rapporteur: Ruchika Sharma (IE)

4.3.5. **Tiotropium bromide** (NAP)

- Signal of increased mortality from cardiovascular disease and all-cause mortality – results of TIOSPIR[1] trial

Status*: for discussion*

Regulatory details:

PRAC Rapporteur: Sabine Straus (NL)

[1] Tiotropium Safety and Performance in Respimat

5. Risk Management Plans

5.1. Medicines in the pre-authorisation phase

5.1.1. Acetylsalicylic acid, clopidogrel

- 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. Ataluren

- 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. Bedaquiline

- 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. Budesonide, formoterol

- 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. Busulfan

- 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. Cabozantinib

- 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. Canagliflozin, metformin

- Evaluation of an RMP in the context of an initial marketing authorisation application procedure

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

5.1.8. Diphteria, tetanus, pertussis and hepatitis B vaccine

- 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. Elosulfase alfa

- 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. Empagliflozin

- 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. Florbetaben (^{18}F)

- 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. 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*

5.1.13. Laquinimod

- 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. Lurasidone

- 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. Masitinib

- 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. Misoprostol

- 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. Oseltamivir

- 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. Propranolol

- Evaluation of an RMP in the context of an initial marketing authorisation application procedure

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

5.1.19. Serelaxin

- Evaluation of an RMP in the context of an initial marketing authorisation application procedure

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

5.1.20. Travoprost

- Evaluation of an RMP in the context of an initial marketing authorisation application procedure

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

5.1.21. Vedolizumab

- 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. Azacitidine – VIDAZA (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 6.1.3.

5.2.2. Boceprevir – VICTRELIS (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 6.1.4.

5.2.3. Cetrorelix – CETROTIDE (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 6.1.8.

5.2.4. Denosumab – **PROLIA** (CAP), **XGEVA** (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 6.1.10.

5.2.5. Linaclotide – **CONSTELLA** (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 6.1.16.

5.2.6. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) – **ADJUPANRIX** (CAP), **PUMARIX** (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 6.1.19.

5.2.7. Pixantrone dimaleate – **PIXUVRI** (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 6.1.22.

5.2.8. Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) – **PREPANDRIX** (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 6.1.24.

5.2.9. Tafamidis – VYNDAQEL (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 6.1.30.

5.2.10. Tolvaptan – SAMSCA (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 6.1.31.

5.2.11. Varenicline – CHAMPIX (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 6.1.33.

RMP in the context of a variation

5.2.12. Bazedoxifene – CONBRIZA (CAP)

- Evaluation of an RMP in the context of a variation

Status: *for discussion and agreement of PRAC Assessment Report to CHMP*

Regulatory details:
PRAC Rapporteur: Martin Huber (DE)

5.2.13. Bevacizumab – AVASTIN (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: Doris Stenver (DK)

5.2.14. Catridecacog – NOVOTHIRTEEN (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: Isabelle Robine (FR)

5.2.15. Denosumab – PROLIA (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)

5.2.16. Human normal immunoglobulin – HIZENTRA (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)

5.2.17. Linagliptin, metformin – JENTADUETO (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: Menno van der Elst (NL)

5.2.18. Nitisinone – ORFADIN (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: Carmela Macchiarulo (IT)

5.2.19. Posaconazole – NOXAFIL (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: Julia Dunne (UK)

5.2.20. Raltegravir – ISENTRESS (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: Julie Williams (UK)

5.2.21. Regorafenib – STIVARGA (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: Sabine Straus (NL)

5.2.22. Saquinavir – INVIRASE (CAP)

- Evaluation of an RMP in the context of a variation

Status: *for discussion and agreement of PRAC Assessment Report to CHMP*

Regulatory details:
PRAC Rapporteur: Harald Herkner (AT)

5.2.23. Tocilizumab – ROACTEMRA (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: Brigitte Keller-Stanislawski (DE)

5.2.24. Trabectedin – YONDELIS (CAP)

- Evaluation of an RMP in the context of a variation

Status: *for discussion and agreement of PRAC Assessment Report to CHMP*

Regulatory details:
PRAC Rapporteur: Line Michan (DK)

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

See Bazedoxifene (CONBRIZA) under 8.1.3. ; Efavirenz (STOCRIN, SUSTIVA) under 8.1.5. ; Liraglutide (VICTOZA) under 8.1.9. ; Pneumococcal conjugate vaccine (adsorbed) (SYNFLORIX) under 8.1.12. ; Sevelamer (RENVELA) under 8.1.13. ; Tacrolimus (MODIGRAF) under 8.1.14.

RMP in the context of a stand-alone RMP procedure

5.2.25. Capsaicin – QUTENZA (CAP)

- Evaluation of a stand-alone RMP procedure

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

Regulatory details:
PRAC Rapporteur: Maria Alexandra Pêgo (PT)

5.2.26. Fentanyl – EFFENTORA (CAP)

- Evaluation of a stand-alone RMP procedure

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

Regulatory details:
PRAC Rapporteur: Martin Huber (DE)

5.2.27. Fentanyl – INSTANYL (CAP)

- Evaluation of a stand-alone RMP procedure

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

Regulatory details:
PRAC Rapporteur: Evelyne Falip (FR)

5.2.28. Fentanyl – PECFENT (CAP)

- Evaluation of a stand-alone RMP procedure

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

Regulatory details:
PRAC Rapporteur: Martin Huber (DE)

5.2.29. Interferon alfa-2b – INTRONA (CAP)

- Evaluation of a stand-alone RMP procedure

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

Regulatory details:
PRAC Rapporteur: Jean-Michel Dogné (BE)

5.2.30. Pramipexole – MIRAPEXIN (CAP), SIFROL (CAP)

- Evaluation of a stand-alone RMP procedure

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

Regulatory details:
PRAC Rapporteur: Doris Stenver (DK)

6. Periodic Safety Update Reports (PSURs)

6.1. Evaluation of PSUR procedures[2]

6.1.1. Anakinra – KINERET (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Doris Stenver (DK)

[2] Where a regulatory action is recommended (variation, suspension or revocation of the terms of Marketing Authorisation(s)), the assessment report and PRAC recommendation are transmitted to the CHMP for adoption of an opinion. Where PRAC recommends the maintenance of the terms of the marketing authorisation(s), the procedure finishes at the PRAC level.

6.1.2. Apixaban – **ELIQUIS** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Sabine Straus (NL)

6.1.3. Azacitidine – **VIDAZA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Sabine Straus (NL)

See also 5.2.1.

6.1.4. Boceprevir – **VICTRELIS** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

See also 5.2.2.

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

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Line Michan (DK)

6.1.6. Bromfenac – **YELLOX** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Line Michan (DK)

6.1.7. Capsaicin – **QUTENZA** (CAP), NAP

- Evaluation of a PSUSA[3] procedure

[3] PSUR single assessment, referring to CAP, NAP

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

Regulatory details:
PRAC Rapporteur: Maria Alexandra Pêgo (PT)

6.1.8. Cetrorelix – **CETROTIDE** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Martin Huber (DE)

See also 5.2.3.

6.1.9. Conestat alfa – **RUCONEST** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Julia Dunne (UK)

6.1.10. Denosumab – **PROLIA** (CAP), **XGEVA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Ulla Wändel Liminga (SE)

See also 5.2.4.

6.1.11. Eribulin – **HALAVEN** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Ulla Wändel Liminga (SE)

6.1.12. Fentanyl – **EFFENTORA** (CAP), **INSTANYL** (CAP), **PECFENT** (CAP), NAP

- Evaluation of a PSUSA procedure

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

Regulatory details:
PRAC Rapporteur: Evelyne Falip (FR)

6.1.13. Hydrocortisone – **PLENADREN** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Qun-Ying Yue (SE)

6.1.14. Influenza vaccine (split virion, inactivated) – **IDFLU** (CAP), **INTANZA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Miguel-Angel Macia (ES)

6.1.15. Laronidase – **ALDURAZYME** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Julia Dunne (UK)

6.1.16. Linaclotide – **CONSTELLA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Martin Huber (DE)

See also 5.2.5.

6.1.17. Linagliptin – **TRAJENTA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Menno van der Elst (NL)

6.1.18. Methylthioninium – **METHYLTHIONINIUM CHLORIDE PROVEBLUE** (CAP)

- Evaluation of a PSUSA procedure

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

Regulatory details:
PRAC Rapporteur: Qun-Ying Yue (SE)

6.1.19. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) – **ADJUPANRIX** (CAP), **PUMARIX** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

See also 5.2.6.

6.1.20. Parathyroid hormone (rDNA) – PREOTACT (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Line Michan (DK)

6.1.21. Piperaquine tetraphosphate, dihydroartemisinin – EURARTESIM (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

6.1.22. Pixantrone dimaleate – PIXUVRI (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Julia Dunne (UK)

See also 5.2.7.

6.1.23. Pramipexole – MIRAPEXIN (CAP), SIFROL (CAP), NAP

- Evaluation of a PSUSA procedure

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

Regulatory details:
PRAC Rapporteur: Doris Stenver (DK)

6.1.24. Prepandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) – PREPANDRIX (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

See also 5.2.8.

6.1.25. Rilpivirine – **EDURANT** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Sabine Straus (NL)

6.1.26. Saxagliptin, metformin – **KOMBOGLYZE** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Menno van der Elst (NL)

6.1.27. Sevelamer – **RENAGEL** (CAP), **RENVELA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Jean-Michel Dogné (BE)

6.1.28. Shingles (herpes zoster) vaccine (live) – **ZOSTAVAX** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

6.1.29. Stiripentol – **DIACOMIT** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

6.1.30. Tafamidis – **VYNDAQEL** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Evelyne Falip (FR)

See also 5.2.9.

6.1.31. Tolvaptan – SAMSCA (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

See also 5.2.10.

6.1.32. Ulipristal – ELLAONE (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Menno van der Elst (NL)

6.1.33. Varenicline – CHAMPIX (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Doris Stenver (DK)

See also 5.2.11.

6.2. Follow-up to PSUR procedures[4]

6.2.1. Capecitabine – XELODA (CAP)

- Evaluation of a follow-up to a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Martin Huber (DE)

6.2.2. Clofarabine – EVOLTRA (CAP)

- Evaluation of a follow-up to a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

6.2.3. Denosumab – PROLIA (CAP), XGEVA (CAP)

- Evaluation of a follow-up to a PSUR procedure

[4] Follow up as per the conclusions of the previous PSUR procedure, assessed outside next PSUR procedure.

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

Regulatory details:
PRAC Rapporteur: Ulla Wändel Liminga (SE)

7. Post-authorisation Safety Studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[5]

7.1.1. Pomalidomide – IMNOVID (CAP)

- Evaluation of an imposed PASS protocol

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

Regulatory details:
PRAC Rapporteur: Julia Dunne (UK)

7.1.2. Rivaroxaban – XARELTO (CAP)

- Evaluation of an imposed PASS protocol

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

Regulatory details:
PRAC Rapporteur: Qun-Ying Yue (SE)

7.1.3. Trimetazidine (NAP)

- Evaluation of an imposed PASS protocol

Status: *for discussion and appointment of PRAC Rapporteur*

Regulatory details:
PRAC Rapporteur: *to be appointed*

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[6]

7.2.1. Aflibercept – ZALTRAP (CAP)

- Evaluation of a PASS protocol

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

Regulatory details:
PRAC Rapporteur: Ulla Wändel Liminga (SE)

7.2.2. Aripiprazole – ABILIFY (CAP)

- Evaluation of a PASS protocol

[5] In accordance with Article 107n of Directive 2001/83/EC
[6] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

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

Regulatory details:
PRAC Rapporteur: Margarida Guimarães (PT)

7.2.3. Ceftaroline fosamil – ZINFORO (CAP)

- Evaluation of a PASS protocol

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

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

7.2.4. Dextromethorphan, quinidine – NUEDEXTA (CAP)

- Evaluation of a PASS protocol

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

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

7.2.5. Florbetapir (^{18}F) – AMYVID (CAP)

- Evaluation of a PASS protocol

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

Regulatory details:
PRAC Rapporteur: Valerie Strassmann (DE)

7.2.6. Human coagulation factor VIII, human von Willebrand factor – VONCENTO (CAP)

- Evaluation of a PASS protocol

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

Regulatory details:
PRAC Rapporteur: Sabine Straus (NL)

7.2.7. Pertuzumab – PERJETA (CAP)

- Evaluation of a PASS protocol

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

Regulatory details:
PRAC Rapporteur: Doris Stenver (DK)

7.2.8. Ulipristal – ESMYA (CAP)

- Evaluation of a PASS protocol

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

Regulatory details:
PRAC Rapporteur: Ulla Wändel Liminga (SE)

7.3. Results of PASS imposed in the marketing authorisation(s)[7]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[8]

7.4.1. **Retigabine – TROBALT** (CAP)

- Evaluation of PASS results

Status: *for discussion and adoption of PRAC Assessment Report*

Regulatory details:
PRAC Rapporteur: Line Michan (DK)

7.5. Interim results of imposed and non-imposed PASS and results of non-imposed PASS submitted before the entry into force of the revised variations regulation[9]

7.5.1. **Etanercept – ENBREL** (CAP)

- Evaluation of interim PASS results

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

Regulatory details:
PRAC Rapporteur: Julia Dunne (UK)

7.5.2. **Fentanyl – EFFENTORA** (CAP)

- Evaluation of interim PASS results

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

Regulatory details:
PRAC Rapporteur: Martin Huber (DE)

7.5.3. **Rotigotine – LEGANTO** (CAP), **NEUPRO** (CAP)

- Evaluation of interim PASS results

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

Regulatory details:
PRAC Rapporteur: Maria Alexandra Pêgo (PT)

7.5.4. **Rotigotine – LEGANTO** (CAP), **NEUPRO** (CAP)

- Evaluation of interim PASS results

[7] In accordance with Article 107p-q of Directive 2001/83/EC
[8] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013
[9] In line with the revised variations regulation for any submission before 4 August 2013

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

Regulatory details:
PRAC Rapporteur: Maria Alexandra Pêgo (PT)

7.5.5. Somatropin – OMNITROPE (CAP)

- Evaluation of interim PASS results

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

Regulatory details:
PRAC Rapporteur: Sabine Straus (NL)

7.5.6. Tigecycline – TYGACIL (CAP)

- Evaluation of interim PASS results

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

Regulatory details:
PRAC Rapporteur: Miguel-Angel Macia (ES)

7.5.7. Ulipristal – ESMYA (CAP)

- Evaluation of interim PASS results

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

Regulatory details:
PRAC Rapporteur: Ulla Wändel Liminga (SE)

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. Alipogene tiparvovec – GLYBERA (CAP)

- PRAC consultation on an annual reassessment of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

8.1.3. Bazedoxifene – CONBRIZA (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Martin Huber (DE)

8.1.4. Caffeine – PEYONA (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Harald Herkner (AT)

8.1.5. Efavirenz – STOCRIN (CAP), SUSTIVA (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Margarida Guimarães (PT)

8.1.6. Follitropin beta – FERTAVID (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

8.1.7. Gefitinib – IRESSA (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

8.1.8. Japanese encephalitis vaccine (inactivated, adsorbed) – IXIARO (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

8.1.9. Liraglutide – VICTOZA (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Menno van der Elst (NL)

8.1.10. Panitumumab – VECTIBIX (CAP)

- PRAC consultation on a conditional renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Julia Dunne (UK)

8.1.11. Pantoprazole – CONTROLOC CONTROL (CAP), PANTECTA CONTROL (CAP), PANTOLOC CONTROL (CAP), PANTOZOL CONTROL (CAP), SOMAC CONTROL (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Julia Dunne (UK)

8.1.12. Pneumococcal polysaccharide conjugate vaccine (adsorbed) – SYNFLORIX (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Qun-Ying Yue (SE)

8.1.13. Sevelamer – RENVELA (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Jean-Michel Dogné (BE)

8.1.14. Tacrolimus – MODIGRAF (CAP)

- PRAC consultation on a renewal of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

8.1.15. Tocofersolan – VEDROP (CAP)

- PRAC consultation on an annual reassessment of the marketing authorisation

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

Regulatory details:

PRAC Rapporteur: Julie Williams (UK)

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

9.1.1. Risk-based programme for routine pharmacovigilance inspections of Marketing Authorisation Holders of Centrally Authorised Products for human use

***Status**: for discussion and agreement of the programme*

9.2. 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 not reported in the agenda.

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. Cetuximab – ERBITUX (CAP)

- PRAC consultation on a safety-related variation, upon CHMP request

Regulatory details:

PRAC Rapporteur: Ulla Wändel Liminga (SE)

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

None

10.3. Other requests

10.3.1. Epoetins:

Darbepoetin alfa – ARANESP (CAP);**Epoetin alfa – ABSEAMED** (CAP), **BINOCRIT** (CAP), **EPOETIN ALFA HEXAL** (CAP); **Epoetin beta – NEORECORMON** (CAP); **Epoetin theta – BIOPOIN** (CAP), **EPORATIO** (CAP); **Epoetin zeta – RETACRIT** (CAP), **SILAPO** (CAP)

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

10.3.2. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) – CERVARIX (CAP)

Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) – GARDASIL (CAP), **SILGARD** (CAP)

- PRAC consultation on the need for further investigation and/or communication further to media attention in France, on EMA's request

Status: *for discussion*

Regulatory details:
PRAC Rapporteurs: Jean-Michel Dogné (BE), Qun-Ying Yue (SE)

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

11.1. Safety related variations of the marketing authorisation

None

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

None

12.2. Pharmacovigilance audits and inspections

12.2.1. Pharmacovigilance Systems and their Quality Systems

None

12.2.2. Pharmacovigilance Inspections

12.2.2.1. Union Procedure on Follow-up to Pharmacovigilance Inspections

- Union procedure on the management of pharmacovigilance inspection findings with potential significant impact on the benefit-risk profile of the concerned medicinal products

***Status**: for discussion*

12.2.3. Pharmacovigilance Audits

12.2.3.1. One-year report to the European Commission on EMA Human Medicines Pharmacovigilance tasks

***Status**: for information*

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

12.3.1. Periodic Safety Update Reports

None

12.3.2. PSURs Repository functionalities

12.3.2.1. Repository specifications and confirmation of full functionality

***Status**: for discussion and endorsement*

12.3.3. Union Reference Date List

12.3.3.1. Consultation on the draft List, version December 2013

***Status**: for discussion and agreement of the list*

12.4. Signal Management

12.4.1. Signal Management Review Technical (SMART) Working Group

- Feedback from the SMART Working Group

***Status:** for information*

12.5. Adverse Drug Reactions reporting and Additional Reporting

12.5.1. Management and Reporting of Adverse Reactions to Medicinal Products

12.5.1.1. Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products: Reports from patient support programmes and market research programmes

***Status**: for discussion*

12.5.2. Additional Monitoring

None

12.5.3. List of Product under Additional Monitoring

12.5.3.1. Consultation on the draft List, version December 2013

Status: *for discussion*

12.6. EudraVigilance Database

12.6.1. EudraVigilance functionalities

12.6.1.1. Activities related to the confirmation of full functionality

Status*: for discussion and endorsement*

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. 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. Blood Products Working Party

12.12.2.1. Intravenous immunoglobulins and haemolysis – Draft strategy

Status: *for discussion*

12.13. Interaction within the EU regulatory network

None

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

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

None

12.14.2. Data Collection on Adverse events of Anti-HIV Drugs (D:A:D) study

- Follow up on MAH's responses to the PRAC letter adopted in March 2013

Status: *for discussion*

12.14.3. Others

None

13. Any other business

None