EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

4 March 2013
EMA/PRAC/141813/2013
Pharmacovigilance Risk Assessment Committee (PRAC)

# Pharmacovigilance Risk Assessment Committee (PRAC)

## Agenda of the meeting on 4-7 March 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

4 March 2013, 13:00 – 19:00, room 3/A

5 March 2013, 08:30 – 19:00, room 3/A

6 March 2013, 08:30– 19:00, room 3/A

7 March 2013, 08:30 – 13:30, room 3/A

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# 1. Introduction

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

## *1.2. Adoption of agenda of the meeting on 4-7 March 2013*

**Status:** for adoption

**Document:** PRAC Agenda Rev.3 due for publication on 4 March 2013

## *1.3. Adoption of Minutes of the previous PRAC meeting on 4-7 February 2013*

**Status:** for adoption

**Document:** PRAC Final Minutes to be published on 11 March 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 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)

**2.2.2. Tetrazepam** (NAP)

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

***Status:*** *for discussion*

***Regulatory details:***

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

## *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. Nicotinic acid and related substances: acipimox, xantinol nicotinate (NAP)

- Review of the benefit-risk balance of medicinal products containing nicotinic acid and related substances indicated for treatment of lipid disorders based on pharmacovigilance data following notification by Denmark of a referral under Article 31 of Directive 2001/83/EC

***Status:*** *for initial discussion and Rapporteur appointment*

***Regulatory details:***

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

## *3.2. Ongoing Procedures*

### 3.2.1. Combined hormonal contraceptives: desogestrel, gestodene, norgestimate, etonogestrel, drospirenone, dienogest, chlormadinone, norgestimate (NAP), nomegestrol acetate / estradiol – IOA (CAP), ZOELY (CAP), norelgestromin / ethinylestradiol - EVRA (CAP)

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

***Status:*** *for discussion*

***Regulatory details:***

PRAC Rapporteur: Julie Williams (UK)
PRAC Co-Rapporteur: Evelyne Falip (FR)

### 3.2.2. Diacerein (NAP)

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

***Status:*** *for information on the revised timetable and discussion*

***Regulatory details:***

PRAC Rapporteur: Miguel-Angel Macia (ES)
PRAC Co-Rapporteur: Evelyne Falip (FR)

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

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

***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*

None

## 4. Signals assessment and prioritisation

### *4.1. New signals detected from EU spontaneous reporting systems*

#### 4.1.1. **Clopidogrel – ISCOVER** (CAP), **PLAVIX** (CAP) & generics (CAP and NAP)

- Signal of acquired haemophilia A

***Status:*** *for discussion*

***Regulatory details:***

PRAC Rapporteur: Margarida Guimarães (PT)

#### 4.1.2. **Clopidogrel – ISCOVER** (CAP), **PLAVIX** (CAP) & generics (CAP and NAP)

- Signal of cross-reactivity between clopidogrel and ticlopidine among patients with previous allergic and/or haematologic reactions to one of these products

***Status:*** *for discussion*

***Regulatory details:***

PRAC Rapporteur: Margarida Guimarães (PT)

#### 4.1.3. **Levetiracetam – KEPPRA** (CAP)

- Signal of Syndrome of Inappropriate Antidiuretic Hormones Secretion (SIADH)

***Status:*** *for discussion*

***Regulatory details:***

PRAC Rapporteur: Jean-Michel Dogne (BE)

## *4.2. New signals detected from other sources*

### 4.2.1. **Cinacalcet – MIMPARA** (CAP)

- Signal of a fatal case with severe hypocalcemia in a pediatric clinical study

***Status:*** *for discussion*

***Regulatory details:***

PRAC Rapporteur: Ulla Wändel Liminga (SE)

## *4.3. Signals follow-up*

### 4.3.1. **Filgrastim** - **BIOGRASTIM** (CAP), **FILGRASTIM HEXAL** (CAP), **NIVESTIM** (CAP), **RATIOGRASTIM** (CAP), **TEVAGRASTIM** (CAP), **ZARZIO** (CAP) and NAP **Pegfilgrastim** - **NEULASTA** (CAP)

- Signal of systemic capillary leak syndrome (SCLS) and cytokine release syndrome (CRS)

***Status:*** *for discussion*

***Regulatory details:***

PRAC Rapporteur (overall): Julie Williams (UK)

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

- Signal of retinal detachment

***Status:*** *for discussion*

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

### 4.3.3. **Temozolomide - TEMODAL** (CAP)

- Signal of hepatic failure

***Status:*** *for discussion*

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

# 5. Risk Management Plans

## *5.1. Medicines in the pre-authorisation phase*

### 5.1.1. **Afamelanotide**

- 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. Autologous peripheral blood mononuclear cells activated with Pap-Gm-Csf

- 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. Bosentan 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. Cabozantinib

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

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

#### 5.1.6. Cd52 antigen

- 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. Delamanid

- 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. Enzalutamide

- 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. Etarfolatide

- 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. Folic acid

- 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. Follitropin alfa

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

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

#### 5.1.12. Macicentan

- 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. Mercaptine bitartrate

- 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. Para-aminosalicylic acid

- 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. Pomalidomide

- 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. Ponatinib

- 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. Recombinant human follicle-stimulating hormone, follitropin alfa

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

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

#### 5.1.18. Regorafenib

- 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. Turoctocog alfa

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

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

#### 5.1.20. Vintafolide

- 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. Voriconazole

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

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

#### 5.1.22. Zoledronic acid

- 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. Emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA (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 6.1.9.

#### 5.2.2. Epoetin alfa – ABSEAMED (CAP), BINOCRIT (CAP), EPOETIN ALFA HEXAL (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 6.1.10.

#### 5.2.3. Fentanyl – PECFENT (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 6.1.12.

### 5.2.4. Influenza vaccine – IDFLU (CAP), INTANZA (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: Miguel-Angel Macia (ES)

See also 6.1.14.

### 5.2.5. Maraviroc – CELSENTRI (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 6.1.17.

### 5.2.6. Moroctocog alfa – REFACTO AF (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 5.2.6.

### 5.2.7. Nonacog alfa – BENEFIX (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: Brigitte Keller-Stanislawski (DE)

See also 6.1.20.

### 5.2.8. Pandemic influenza vaccine – 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 6.1.22.

### 5.2.9. Prifenidone – **ESBRIET** (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 6.1.25.

### 5.2.10. Silodosin – **SILODYX** (CAP), **UROREC** (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 6.1.27.

### 5.2.11. Ulipristal – **ESMYA** (CAP)

- Evaluation of an RMP in the context a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Ulla Wändel Liminga (SE)

See also 6.1.29.

### 5.2.12. Vernakalant – **BRINAVESS** (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: Menno van der Elst (NL)

See also 6.1.32.

### 5.2.13. Zoledronic acid – **ZOMETA** (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 of the marketing authorisation***

**5.2.14. Aflibercept – EYLEA** (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: Evelyne Falip (FR)

**5.2.15. Anakinra – KINERET** (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: Doris Stenver (DK)

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

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***

PRAC Rapporteur: Isabelle Robine (FR)

**5.2.17. 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)

**5.2.18. Certolizumab pegol – CIMZIA** (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***

PRAC Rapporteur: Ulla Wändel Liminga (SE)

### 5.2.19. Denosumab – XGEVA (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)

### 5.2.20. Eculizumab – SOLIRIS (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: Dolores Montero (ES)

### 5.2.21. Eptacog alfa – NOVOSEVEN (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)

### 5.2.22. Icatibant – FIRAZYR (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: Qun-Ying Yue (SE)

### 5.2.23. Omalizumab – XOLAIR (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)

### 5.2.24. Ranibizumab – LUCENTIS (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)

### 5.2.25. Rituximab – MABTHERA (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***

PRAC Rapporteur: Doris Stenver (DK)

### 5.2.26. Rivastigmine – EXELON (CAP), PROMETAX (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: Evelyne Falip (FR)

### 5.2.27. Ustekinumab – STELARA (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: Julie Williams (UK)

### 5.2.28. Vildagliptin –GALVUS (CAP), JALRA (CAP), XILIARX (CAP); vildagliptin, metformin – EUCREAS (CAP), ICANDRA (CAP), ZOMARIST (CAP)

- Evaluation of an RMP in the context of a worksharing variation

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

***Regulatory details:***

PRAC Rapporteur: Qun-Ying Yue (SE)

### 5.2.29. 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)

### 5.2.30. 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***

**5.2.31. Iloprost – VENTAVIS** (CAP)

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

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

***Regulatory details:***

PRAC Rapporteur: Evelyne Falip (FR)

See also 8.1.6.

**5.2.32. Lacosamide – VIMPAT** (CAP)

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

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

***Regulatory details:***

PRAC Rapporteur: Qun-Ying Yue (SE)

See also 8.1.7.

**5.2.33. Methylnaltrexone bromide – RELISTOR** (CAP)

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

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

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

See also 8.1.8.

***RMP in the context of a stand-alone RMP procedure***

**5.2.34. Azacitidine – VIDAZA** (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: Sabine Straus (NL)

### 5.2.35. Catridecacog – NOVOTHIRTEEN (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: Evelyne Falip (FR)

### 5.2.36. Doripenem – DORIBAX (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)

### 5.2.37. Ferumoxitol – RIENSO (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: Martin Huber (DE)

### 5.2.38. Mecasermin – INCRELEX (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: Kirsti Villikka (FI)

### 5.2.39. Tenofovir disoproxil fumarate – VIREAD (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: Isabelle Robine (FR)

### 5.2.40. Vemurafenib – ZELBORAF (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)

# 6. Assessment of Periodic Safety Update Reports (PSURs)

### 6.1.1. A/H5N1 pre-pandemic influenza vaccine – VEPACEL (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Jean-Michel Dogne (BE)

### 6.1.2. Aliskiren, amlodipine – RASILAMLO (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. Aliskiren, amlodipine, hydrochlorothiazide – RASITRIO (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Carmela Macchiarulo (IT)

### 6.1.4. Asenapine – SYCREST (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Julie Williams (UK)

### 6.1.5. Azilsartan medoxomil – EDARBI (CAP), IPREZIV (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Menno van der Elst (NL)

### 6.1.6. Colistimethate – COLOBREATHE (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Julia Dunne (UK)

### 6.1.7. Collagenase clostridium histolyticum – XIAPEX (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

### 6.1.8. Eflornithine – VANIQA (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Almath Spooner (IE)

### 6.1.9. Emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Sabine Straus (NL)

### 6.1.10. Epoetin alfa – ABSEAMED (CAP), BINOCRIT (CAP), EPOETIN ALFA HEXAL (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. Eptotermin alfa – OPGENRA (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Kirsti Villikka (FI)

### 6.1.12. Fentanyl – PECFENT (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

**6.1.13. Human protein C – CEPROTIN** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

**6.1.14. Influenza vaccine – 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. Influenza vaccine – OPTAFLU** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Sabine Straus (NL)

**6.1.16. Lapatinib – TYVERB** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Ulla Wändel Liminga (SE)

**6.1.17. Maraviroc – CELSENTRI** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Qun-Ying Yue (SE)

**6.1.18. Mecasermin – INCRELEX** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Kirsti Villika (FI)

**6.1.19. Moroctocog alfa – REFACTO AF** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Doris Stenver (DK)

**6.1.20. Nonacog alfa – BENEFIX** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

**6.1.21. Octocog alfa – ADVATE** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Brigitte Keller-Stanislawski (DE)

**6.1.22. Pandemic influenza vaccine – PUMARIX** (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Julie Williams (UK)

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

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Julia Dunne (UK)

### 6.1.24. Prasugrel – EFIENT (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Doris Stenver (DK)

### 6.1.25. Prifenidone – ESBRIET (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Julie Williams (UK)

### 6.1.26. Rotigotine – LEGANTO (CAP), NEUPRO (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Maria-Alexandra Pego (PT)

### 6.1.27. Silodosin – SILODYX (CAP), UROREC (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Julie Williams (UK)

### 6.1.28. Strontium ranelate – PROTELOS (CAP), OSSEOR (CAP)

- Evaluation of a PSUR procedure

***Status:*** *for preliminary discussion*

***Regulatory details:***

PRAC Rapporteur: Ulla Wändel Liminga (SE)

### 6.1.29. Ulipristal – ESMYA (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Ulla Wändel-Liminga (SE)

#### 6.1.30. Velaglucerase alfa – VPRIV (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

#### 6.1.31. Vemurafenib – ZELBORAF (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Ulla Wändel Liminga (SE)

#### 6.1.32. Vernakalant – BRINAVESS (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. Zoledronic acid – ZOMETA (CAP)

- Evaluation of a PSUR procedure

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

***Regulatory details:***

PRAC Rapporteur: Doris Stenver (DK)

# 7. Post-authorisation Safety Studies (PASS)

## *7.1. Protocols of post-authorisation safety studies*

#### 7.1.1. Dapagliflozin – FORXIGA (CAP)

- PRAC consultation on PASS protocol 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: Qun-Ying Yue (SE)

#### 7.1.2. Ivacaftor – KALYDECO (CAP)

- PRAC consultation on PASS protocol conducted pursuant 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: Miguel-Angel Macia (ES)
PRAC Co-Rapporteur: Melinda Palfi (HU)

#### 7.1.3. Mifamurtide – MEPACT (CAP)

- PRAC consultation on a PASS protocol 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: Sabine Straus (NL)

#### 7.1.4. Tenofovir disoproxil fumarate – VIREAD (CAP)

- PRAC consultation on a PASS protocol 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: Isabelle Robine (FR)

### *7.2. Results of post-authorisation safety studies*

#### 7.2.1. Finasteride (NAP)

- PRAC consultation on PASS results, upon Member State's request

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

***Regulatory details:***

PRAC Rapporteur: *to be appointed*

#### 7.2.2. Stavudine – ZERIT (CAP)

- PRAC consultation on results of 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: Qun-Ying Yue (SE)

# 8. Renewals of the Marketing Authorisation, Conditional Renewals and Annual Reassessments[1]

### 8.1.1. Anagrelide – XAGRID (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)

### 8.1.2. Etravirine – INTELENCE (CAP)

- PRAC consultation on a renewal procedure of the marketing authorisation

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

***Regulatory details:***

PRAC Rapporteur: Isabelle Robine (FR)

### 8.1.3. Everolimus – VOTUBIA (CAP)

- PRAC consultation on a renewal procedure of the marketing authorisation

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

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

### 8.1.4. Fampridine – FAMPYRA (CAP)

- PRAC consultation on a renewal procedure of the conditional marketing authorisation

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

***Regulatory details:***

PRAC Rapporteur: Sabine Straus (NL)

### 8.1.5. Filgrastim – BIOGRASTIM (CAP), RATIOGRASTIM (CAP), TEVAGRASTIM (CAP)

- PRAC consultation on a renewal procedure of the marketing authorisation

[1] Given that the PRAC is systematically involved in renewals of the marketing authorisation (MA), annual re-assessment of MA under exceptional circumstances and renewals of conditional MA as anticipated in the document 'Countdown to July 2012: the establishment and functioning of the PRAC' EMA/315258/2012 and 'Guideline on the processing of renewals in the centralised procedure' EMEA/CHMP/2990/00 Rev.4 such topics are now listed in a new section of the PRAC agenda under point 8

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

***Regulatory details:***

PRAC Rapporteur: Kirsti Villikka (FI)

**8.1.6. Iloprost – VENTAVIS** (CAP)

- PRAC consultation on a renewal procedure of the marketing authorisation
- 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)

**8.1.7. Lacosamide – VIMPAT** (CAP)

- PRAC consultation on a renewal procedure of the marketing authorisation

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

***Regulatory details:***

PRAC Rapporteur: Qun-Ying Yue (SE)

**8.1.8. Methylnaltrexone Bromide – RELISTOR** (CAP)

- PRAC consultation on a renewal procedure of the marketing authorisation

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

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

**8.1.9. Olanzapine – OLANZAPINE MYLAN** (CAP)

- PRAC consultation on a renewal procedure of the marketing authorisation

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

***Regulatory details:***

PRAC Rapporteur: Terhi Lehtinen (FI)

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

- PRAC consultation on a renewal procedure of the marketing authorisation

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

***Regulatory details:***

PRAC Rapporteur: Qun-Ying Yue (SE)

#### 8.1.11. Tadalafil – ADCIRCA (CAP)

- PRAC consultation on a renewal procedure of the marketing authorisation

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

***Regulatory details:***

PRAC Rapporteur: Miguel-Angel Macia (ES)

# 9. Product related pharmacovigilance inspections

## *9.1. List of planned pharmacovigilance inspections*

None

## *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. Telaprevir – INCIVO (CAP)

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

***Status:*** *for follow-up discussion*

***Regulatory details:***

PRAC Rapporteur: Qun-Ying Yue (SE)

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

None

## *10.3. Other requests*

#### 10.3.1. Mipomersen

- PRAC consultation on a re-examination procedure of an initial Marketing Authorisation

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

See also: dapaglifloxin 7.1.1. ; mifamurtide 7.1.3.

# 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*

See Finasteride 7.2.1.

# 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

None

### 12.2.3. Pharmacovigilance Audits

None

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

### *12.3.1. Good Pharmacovigilance Practices (GVP) Module VII Periodic Safety Update Reports*

- Revision 1 of GVP Module VII for consultation

***Status:*** *for information*

### 12.3.2. Union Reference Date List

- Consultation on the draft List, version March 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*

## *12.5. Adverse Drug Reactions reporting and additional reporting*

### 12.5.1. Management and Reporting of Adverse Drug Reactions (ADR) to Medicinal Products

- New Legislation: Impact on ADR Reporting

***Status:*** *for information*

### 12.5.2. Additional Monitoring

None

### 12.5.3. List of Products under Additional Monitoring

- Update on creation and maintenance of the List

***Status:*** *For discussion*

## *12.6. EudraVigilance Database*

### 12.6.1. Other

- 2012 EudraVigilance (human) Annual report

***Status:*** *for information*

## *12.7. Risk Management Plans and Effectiveness of risk Minimisations*

### 12.7.1. Summaries of RMPs

- Publication process

**Status:** for information

### 12.7.2. Timetables for RMP assessment

- New timetables for RMP assessment in pre-authorisation phase

***Status:*** *for information*

## *12.8. Post-authorisation Safety Studies*

None

### *12.9. Community Procedures*

None

### *12.10. Risk communication and Transparency*

None

### *12.11. Continuous pharmacovigilance*

None

### *12.12. Interaction with EMA Committees and Working Parties*

#### 12.12.1. Blood Products Working Party

- Draft Letter to the Editor of Haemophilia: Comment on: P.M. Mannucci. Evaluation of the European Guidelines for the Clinical Development of Factor VIII products: little progress towards improved patient management. Haemophilia 2012: 18:1-5

### *12.13. Status: for information**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. Highly Active Antiretroviral Therapy (HAART)

- Data Collection on Adverse events of Anti-HIV Drugs (D:A:D); regulatory representation in the HAART Oversight Committee

**Status:** for discussion and appointment of EMA representatives

## 13. Any other business

None