09 March 2015
EMA/PRAC/165779/2015
Pharmacovigilance Risk Assessment Committee (PRAC)

# Pharmacovigilance Risk Assessment Committee (PRAC)

## Draft agenda for the meeting on 9-12 March 2015

Chair: June Raine – Vice-Chair: Almath Spooner

09 March 2015, 13:00 – 19:00, room 2/A

10 March 2015, 08:30 – 19:00, room 2/A

11 March 2015, 08:30 – 19:00, room 2/A

12 March 2015, 08:30 – 16:00, room 2/A

Organisational, regulatory and methodological matters (ORGAM)

26 March 2015, 10:00-12:00, room 6/B, via teleconference

### Health and Safety Information

In accordance with the Agency's Health and Safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

### Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also change during the course of the review. Additional details on some of these procedures will be published in the PRAC meeting highlights once the procedures are finalised. The start of referrals will also be announced in the meeting highlights. For orphan medicinal products, the applicant name is published as this information is already publicly available.

### Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents under Regulation (EC) No 1049/2001 as they relate to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006).

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## 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)

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 9 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/

## 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 09-12 March 2015*

***Status:*** *for adoption*

**Document:** PRAC Agenda Rev.3 due for publication on 09 March 2015

## *1.3. Minutes of the previous PRAC meeting on 09-12 February 2015*

***Status:*** *for adoption*

**Document:** PRAC final Minutes due for publication by 20 March 2015

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

## *2.1. Newly triggered procedures*

None

## *2.2. Ongoing Procedures*

None

## *2.3. Procedures for finalisation*

None

## *2.4. Planned public hearings*

None

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

## *3.1. Newly triggered Procedures*

None

## *3.2. Ongoing Procedures*

### 3.2.1. **Dexibuprofen** (NAP); **ibuprofen** (NAP)

- Review of the benefit-risk balance 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 a list of outstanding issues*

***Regulatory details:***

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

***Administrative details:***
Procedure number(s): EMEA/H/A-31/1401
MAH(s): various
***Documents:***
For adoption: List of outstanding issues (LoOI), revised timetable (or PRAC AR, PRAC recommendation)

## *3.3. Procedures for finalisation*

### 3.3.1. **Codeine** (NAP)

- Review of the benefit-risk balance of codeine indicated for the treatment of cough in paediatric patients following the notification by Germany of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

***Status:*** *for discussion and agreement of a recommendation to CMD(h)*

***Regulatory details:***

PRAC Rapporteur: Julie Williams (UK)
PRAC Co-Rapporteur: Martin Huber (DE)

***Administrative details:***
Procedure number: EMEA/H/A-31/1394
MAH(s): various
***Documents:***
For adoption: PRAC AR, PRAC recommendation (or list of outstanding issues (LoOI), revised procedure timetable)

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

None

## *3.5. Others*

None

# 4. Signals assessment and prioritisation[1]

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

### 4.1.1. Bisphosphonates: **alendronic acid** (NAP); **alendronic acid, colecalciferol - ADROVANCE** (CAP), **FOSAVANCE** (CAP), **VANTAVO** (CAP); **etidronic acid** (NAP); **ibandronic acid – BONDRONAT** (CAP), **BONVIVA** (CAP), **neridronic acid** (NAP); **pamidronic acid** (NAP); **risedronic acid** (NAP); **tiludronic acid** (NAP); **zoledronic acid – ACLASTA** (CAP), **ZOMETA** (CAP) **Denosumab – PROLIA** (CAP), **XGEVA** (CAP)

- Signal of osteonecrosis of the external auditory canal

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

***Regulatory details:***

PRAC Rapporteur: *to be appointed*

***Administrative details:***
EPITT 18256 – New signal
MAH(s): various
Lead MS: UK
***Documents:***
For adoption: PRAC recommendation

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

### 4.2.1. **Adalimumab - HUMIRA** (CAP)

- Signal of convulsion

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

***Regulatory details:***

PRAC Rapporteur: Ulla Wändel Liminga (SE)

***Administrative details:***
EPITT 18211 – New signal
MAH(s): AbbVie Ltd.
Lead MS: SE
***Documents:***
For adoption: PRAC recommendation

### 4.2.2. **Amiodarone** (NAP)

- Signal of pancreatitis

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

***Regulatory details:***

PRAC Rapporteur: *to be appointed*

[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) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

***Administrative details:***
EPITT 18216 – New signal
MAH(s): Sanofi
Lead MS: NL
***Documents:***
For adoption: PRAC recommendation

### 4.2.3. **Donepezil** (NAP)

- Signal of rhabdomyolysis

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

***Regulatory details:***
PRAC Rapporteur: *to be appointed*

***Administrative details:***
EPITT 18261 – New signal
MAH(s): Eisai Ltd.
Lead MS: UK
***Documents:***
For adoption: PRAC recommendation

### 4.2.4. **Fingolimod - GILENYA** (CAP)

- Signal of occurrence of one case of progressive multifocal leukoencephalopathy (PML)

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

***Regulatory details:***
PRAC Rapporteur: *to be appointed*

***Administrative details:***
EPITT 18241– New signal
MAH(s): Novartis Europharm Ltd
Lead MS: FR
***Documents:***
For adoption: PRAC recommendation

### 4.2.5. **Palifermin - KEPIVANCE** (CAP)

- Signal of increased mortality for unlicensed use in acute lung injury

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
EPITT 18160 – New signal
MAH(s): Swedish Orphan Biovitrum AB (publ)
Lead MS: UK
***Documents:***
For adoption: PRAC recommendation

### 4.2.6. **Warfarin** (NAP)

- Signal of bone density decrease

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

***Regulatory details:***
PRAC Rapporteur: *To be appointed*

***Administrative details:***
EPITT 18173 – New signal
MAH(s): various
Lead MS: DK
***Documents:***
For adoption: PRAC recommendation

## *4.3. Signals follow-up and prioritisation*

### 4.3.1. Aflibercept – **EYLEA** (CAP)

- Signal of higher systemic exposure compared to ranibizumab after intravitreal injection

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

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

***Administrative details:***
EPITT 18112 – Follow-up October 2014
Procedure number(s): EMEA/H/C/002392/SDA/012
MAH(s): Bayer Pharma AG
***Documents:***
For adoption: PRAC recommendation

### 4.3.2. Aripiprazole – **ABILIFY** (CAP), **ABILIFY MAINTENA** (CAP)

- Signal of aggression and related events

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

***Regulatory details:***
PRAC Rapporteur: Margarida Guimarães (PT)

***Administrative details:***
EPITT 18127 – Follow-up November 2014
Procedure number(s): EMEA/H/C/000471/SDA/072
MAH(s): Otsuka Pharmaceutical Europe Ltd
***Documents:***
For adoption: PRAC recommendation

### 4.3.3. Infliximab – **INFLECTRA** (CAP), **REMICADE** (CAP), **REMSIMA** (CAP)

- Signal of rhabdomyolysis

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

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

***Administrative details:***
EPITT 18129 – Follow-up November 2014

Procedure number(s): EMEA/H/C/002778/SDA/020, EMEA/H/C/000240/SDA/152, EMEA/H/C/002576/SDA/019
MAH(s): Hospira UK Limited (Inflectra), Janssen Biologics B.V. (Remicade), Celltrion Healthcare Hungary Kft. (Remsima)
***Documents:***
For adoption: PRAC recommendation

#### 4.3.4. Recombinant Factor VIII:
**Antihemophilic factor (recombinant)** (NAP)
**Moroctocog alfa – REFACTO AF** (CAP)
**Octocog alfa – ADVATE** (CAP), **HELIXATE NEXGEN** (CAP), **KOGENATE** (CAP)

- Signal of inhibitor development in previously untreated patients

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

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

***Administrative details:***
EPITT 18134 – Follow-up January 2015
MAH(s): Baxter AG (Advate, Recombinate), Bayer Pharma AG (Kogenate, Helixate NexGen), Pfizer Limited (ReFacto AF), various
***Documents:***
For discussion: draft study protocol

#### 4.3.5. Sodium containing formulations of effervescent, dispersible and soluble medicines (NAP)

- Signal of cardiovascular events

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
EPITT 17931 – Follow-up February 2015
MAH: various
***Documents:***
For adoption: PRAC recommendation

#### 4.3.6. Sorafenib – NEXAVAR (CAP)

- Signal of acute generalised exemanthous pustulosis (AGEP)

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

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

***Administrative details:***
EPITT 18109 – Follow-up November 2014
Procedure number(s): EMEA/H/C/000690/SDA/033
MAH(s): Bayer Pharma AG
***Documents:***
For adoption: PRAC recommendation

# 5. Risk Management Plans

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

### 5.1.1. Allogeneic cells genetically modified to express suicide gene

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

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

***Administrative details:***
Product number(s): EMEA/H/C/002801, *Orphan, ATMP*
Intended indication(s): Treatment in haploidentical haematopoietic stem cell transplantation
Applicant: MolMed SpA
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.2. Allogenic human heterologous liver cells

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003750, *Orphan*
Intended indication(s): Treatment of urea cycle disorders (UCD)
Applicant: Cytonet GmbH&Co KG
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.3. Aripiprazole

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

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

***Administrative details:***
Product number(s): EMEA/H/C/004008, *Generic, Hybrid*
Intended indication(s): Treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.4. Asfotase alfa

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003794, *Orphan*
Intended indication(s): Treatment of paediatric-onset hypophosphatasia
Applicant: Alexion Europe SAS
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.5. Atazanavir, cobicistat

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003904
Intended indication(s): Treatment of HIV-1 infected patients
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.6. Bortezomib

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003984, *Generic*
Intended indication(s): Treatment of multiple myeloma
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.7. Dasiprotimut-T

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

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

***Administrative details:***
Product number(s): EMEA/H/C/002772, *Orphan*
Intended indication(s): Treatment of non-Hodgkin's lymphoma (FL)
Applicant: Biovest Europe Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.8. Dexamethasone

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

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

***Administrative details:***
Product number(s): EMEA/H/C/004071, *Orphan, Hybrid*
Intended indication(s): Treatment of symptomatic multiple myeloma in combination with other medicinal products
Applicant: Laboratoires CTRS
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.9. Docetaxel

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003925, *Generic*
Intended indication(s): Treatment of breast cancer, non-small cell lung cancer, prostate cancer, metastatic gastric adenocarcinoma and head and neck cancer
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.10. Duloxetine

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003981, *Generic*
Intended indication(s): Treatment of major depressive disorder, diabetic peripheral neuropathic pain and generalised anxiety disorder
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.11. Empagliflozin, metformin

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003770
Intended indication(s): Treatment of type II diabetes
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.12. Ferric citrate coordination complex

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003776
Intended indication(s): Treatment of hyperphosphataemia
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.13. Guanfacine

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003759
Intended indication(s): Treatment of attention deficit hyperactivity disorder (ADHD)
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.14. Human alfa1-proteinase inhibitor

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

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

***Administrative details:***
Product number(s): EMEA/H/C/002739
Intended indication(s): Maintenance treatment to slow the underlying destruction of lung tissue leading to emphysema in adults with alpha1-proteinase inhibitor deficiency with clinically evident lung disease
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.15. Human papillomavirus [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed)

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003852
Intended indication(s): Treatment of human papillomavirus (HPV) diseases
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.16. Lenvatinib

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003727, *Orphan*
Intended indication(s): Treatment of papillary thyroid cancer, treatment of follicular thyroid cancer
Applicant: Eisai Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.17. Levodopa, carbidopa

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

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

***Administrative details:***
Product number(s): EMEA/H/C/002611
Intended indication(s): Treatment of Parkinson's disease
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.18. Lumacaftor, ivacaftor

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003954, *Orphan*
Intended indication(s): Treatment of cystic fibrosis (CF)
Applicant: Vertex Pharmaceuticals (U.K.) Ltd.
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.19. Mepolizumab

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003860
Intended indication(s): Treatment of asthma
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.20. Mercaptamine

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

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

***Administrative details:***
Product number(s): EMEA/H/C/004038, *Orphan*
Intended indication(s): Treatment of corneal cystine deposits
Applicant: Lucane Pharma
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.21. Netupitant, palonosetron

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003728
Intended indication(s): Prevention of chemotherapy-induced nausea and vomiting (CINV)
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.22. Nivolumab

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003985
Intended indication(s): Treatment of advanced (unresectable or metastatic) melanoma in adults
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.23. Panobinostat

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003725, *Orphan*
Intended indication(s): Treatment of multiple myeloma
Applicant: Novartis Pharmaceuticals UK Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.24. Parathyroid hormone

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003861, *Orphan*
Intended indication(s): Treatment of hypoparathyroidism
Applicant: NPS Pharma Holdings Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.25. Pemetrexed

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

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

***Administrative details:***
Product number(s): EMEA/H/C/004072, *Generic*
Intended indication(s): Treatment of unresectable malignant pleural mesothelioma metastatic non-small cell lung cancer
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.26. Pregabalin

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

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

***Administrative details:***
Product number(s): EMEA/H/C/004010, EMEA/H/C/004070, *Generics*
Intended indication(s): Treatment of epilepsy and generalised anxiety disorder (GAD)
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.1.27. Pregabalin

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003900, *Generic*
Intended indication(s): Treatment of epilepsy and generalised anxiety disorder (GAD)
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

#### 5.1.28. Voriconazole

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

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

***Administrative details:***
Product number(s): EMEA/H/C/003737, *Generic*
Intended indication(s): Treatment of fungal infections
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

## *5.2. Medicines already authorised*

***RMP in the context of a variation[2] – PRAC-led procedure***

#### 5.2.1. Desloratadine – **AERIUS** (CAP), **AZOMYR** (CAP), **NEOCLARITYN** (CAP)

- Evaluation of an RMP in the context of a variation

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000313/WS0641/0077, EMEA/H/C/000310/WS0641/0080, EMEA/H/C/000314/WS0641/0075
Procedure scope: Updated RMP (version 1.0) in line with the request of the EMA as a result of the assessment of the follow-up measure FUM PSU 048 of the ninth PSUR for Aerius, Azomyr and Neoclarityn
MAH(s): Merck Sharp & Dohme Limited
***Documents:***
For adoption: PRAC AR

#### 5.2.2. Ibritumomab tiuxetan – **ZEVALIN** (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Torbjorn Callreus (DK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000547/II/0043

[2] In line with the revised variation regulation for submissions as of 4 August 2013

Procedure scope: Updated RMP (version 4.0) to reflect the completion and analysis of study SAG 307722. A type II variation (EMEA/H/C/000547/II/0039) to update the product information following analysis of the data from study SAG 307722 was approved in April 2014
MAH(s): Spectrum Pharmaceuticals B.V.
***Documents:***
For adoption: PRAC AR

### 5.2.3. Oseltamivir – TAMIFLU (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Kirsti Villikka (FI)

***Administrative details:***
Procedure number(s): EMEA/H/C/000402/II/0114
Procedure scope: Proposal for a new and alternative study BV29684 'assessing the safety of prenatal exposure to oseltamivir' as category 3 study (MEA 099) to replace the agreed 2-year extension of the Danish-Swedish registry (NV25577)
MAH(s): Roche Registration Ltd
***Documents:***
For adoption: PRAC AR

### 5.2.4. Pioglitazone – ACTOS (CAP), GLUSTIN (CAP) pioglitazone, metformin – COMPETACT (CAP), GLUBRAVA (CAP) pioglitazone, glimepiride – TANDEMACT (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Almath Spooner (IE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000285/WS0705/0067, EMEA/H/C/000286/WS0705/0065, EMEA/H/C/000655/WS0705/0052, EMEA/H/C/000893/WS0705/0038, EMEA/H/C/000680/WS0705/0042
Procedure scope: Change of the due date for reporting of the pan-European multiple database bladder cancer risk characterisation study ER12-9433 from 30 December 2014 to 31 July 2015. In addition, an administrative change has been introduced to include mention of a drug utilisation study using the medical registries in Denmark (Pioglitazone 5019) and associated timelines
MAH(s): Takeda Pharma A/S
***Documents:***
For adoption: PRAC AR

### 5.2.5. Pregabalin – LYRICA (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Sabine Straus (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/000546/II/0073/G
Procedure scope: Revised RMP (version 11.2) to update targeted report form/follow-up questionnaire for abuse, misuse, dependence and change risk of misuse, abuse and dependence from potential to identified as requested by the PRAC during the EMEA/H/C/000546/PSUV/0069 procedure - change the due date of PASS A0081096
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC AR

### 5.2.6. Teduglutide – REVESTIVE (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Torbjorn Callreus (DK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002345/II/0009
Procedure scope: Updated RMP (version 6.0) proposing the use of nursing services as a risk minimisation measure to decrease the adverse events of fluid overload
MAH(s): NPS Pharma Holdings Limited
***Documents:***
For adoption: PRAC AR

***RMP in the context of a variation – CHMP-led procedure***

### 5.2.7. Abatacept – ORENCIA (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Kirsti Villikka (FI)

***Administrative details:***
Procedure number(s): EMEA/H/C/000701/II/0087/G
Procedure scope: Introduction of a prefilled pen presentation for Orencia 125 mg solution for injection (pack size of 4 pre-filled pens) and addition of a pack size of 12 pre-filled pens for Orencia 125 mg solution for injection
MAH(s): Bristol-Myers Squibb Pharma EEIG
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.8. Aflibercept – EYLEA (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/C/002392/II/0018

Procedure scope: Update of SmPC sections 4.8, 5.1 and 5.2 to reflect full 2 year efficacy and safety data from the ongoing studies VIVID-DME and VISTA-DME, post-authorisation measures (RECs) agreed as part of variation II/09. The package leaflet has been revised accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in SmPC section 5.1
MAH(s): Bayer Pharma AG
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.9. Ambrisentan – VOLIBRIS (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Dolores Montero Corominas (ES)

***Administrative details:***
Procedure number(s): EMEA/H/C/000839/II/0041
Procedure scope: Update of SmPC sections 4.1, 4.2, 4.4, 4.8 and 5.1 to include an expanded therapeutic indication for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1). In addition, the MAH took the opportunity to update Annex II to reflect a change in the PSUR frequency. The package leaflet is updated accordingly
MAH(s): Glaxo Group Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.10. Capsaicin – QUTENZA (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: Magda Pedro (PT)

***Administrative details:***
Procedure number(s): EMEA/H/C/000909/II/0039
Procedure scope: Extension of indication to include treatment of diabetic patients with peripheral neuropathic pain based on the results of studies E05-CL-3004 (STEP) and E05-CL-3002 (PACE). As a consequence, SmPC sections 4.1, 4.4 and 4.8 have been updated, and Annex II (additional risk minimisation measures) and the package leaflet have been updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC, Annex II, labelling and package leaflet
MAH(s): Astellas Pharma Europe B.V.
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.11. Crizotinib – XALKORI (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: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/C/002489/II/0024
Procedure scope: Extension of indication to the first-line treatment anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) and to update SmPC sections 4.2, 4.4, 4.8, 5.1 and 5.2 to include results of the pivotal Study A8081014, a multinational, multicentre, randomized, open-label, phase 3 study comparing the efficacy and safety of crizotinib to first-line chemotherapy (pemetrexed/cisplatin or pemetrexed/carboplatin) in patients with previously untreated ALK-positive advanced non-squamous NSCLC and updated safety results from studies A8081001, A8081005 and A8081007. In addition, SmPC section 5.1 was revised to include updated overall survival data from studies A8081001 and A8081005
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.12. Dolutegravir, abacavir, lamivudine – TRIUMEQ (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002754/II/0005 (with RMP)
Procedure scope: In compliance with the agreed RMP (MEA 02, category 3 study), submission of in vitro study report to assess the affinity of dolutegravir for melanocortin receptors
MAH(s): ViiV Healthcare UK Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.13. Dolutegravir, abacavir, lamivudine – TRIUMEQ (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002754/II/0006 (with RMP)
Procedure scope: In compliance with the agreed RMP (MEA 03, category 3 study), submission of in vitro study report to assess the affinity of dolutegravir
MAH(s): ViiV Healthcare UK Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.14. Dolutegravir, abacavir, lamivudine – TRIUMEQ (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002754/II/0004/G

Procedure scope: Grouped variations to update: 1) SmPC section 5.2 following the results of an in vitro study to investigate whether dolutegravir might be a substrate for the hepatic uptake transporters OATP1B1 and OATP1B3; 2) SmPC section 4.5 on the basis of pharmacokinetic analyses from the dolutegravir-boceprevir interaction study ING115697; 3) SmPC section 4.5 and 5.2 on the potential for interaction with midazolam/CYP3A4
MAH(s): ViiV Healthcare UK Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.15. Eltrombopag – REVOLADE (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***

PRAC Rapporteur: Dolores Montero Corominas (ES)

***Administrative details:***
Procedure number(s): EMEA/H/C/001110/II/0019
Procedure scope: Update of SmPC section 4.8 to include 'thrombotic microangiopathy (TMA) with acute renal failure'. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to make a minor change to SmPC section 4.8 clarifying that the safety data included are derived both from studies and from post-marketing reports
MAH(s): GlaxoSmithKline Trading Services
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.16. Epoetin beta – NEORECORMON (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***

PRAC Rapporteur: Valerie Strassmann (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000116/II/0083
Procedure scope: Update of the product information to implement the outcome of the PSUR (covering the period 2007-2010) concerning the increased risk of retinopathy of prematurity (RoP)
MAH(s): Roche Registration Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.17. Golimumab – SIMPONI (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/000992/II/0063
Procedure scope: Update of SmPC sections 4.2 and 5.1 to reflect the data from a multicentre, placebo-controlled, double-blind, randomised-withdrawal, parallel group study (GO KIDS) in children (2 to 17

years of age) with active polyarticular juvenile idiopathic arthritis (pJIA). The package leaflet is updated accordingly
MAH(s): Janssen Biologics B.V.
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.18. Insulin degludec, liraglutide – XULTOPHY (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/002647/II/0001/G
MAH(s): Novo Nordisk A/S
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.19. Insulin degludec, liraglutide – XULTOPHY (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/002647/II/0002
Procedure scope: Extension of indication to include the transfer of patients from glucagon-like peptide-1 (GLP1) receptor agonist (RA) treatment to Xultophy. Consequently, SmPC sections 4.1, 4.2, 4.4, and 5.1 as well as the package leaflet are updated accordingly
MAH(s): Novo Nordisk A/S
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.20. Lenalidomide – REVLIMID (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: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/C/000717/II/0079
Procedure scope: Extension of indication to add treatment of adult patients with relapsed and/or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 as well as the package leaflet are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and package leaflet
MAH(s): Celgene Europe Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.21. Maraviroc – CELSENTRI (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/000811/II/0041
Procedure scope: Update of SmPC sections 4.4 and 5.1 further to the 48-week time-point results of study A4001098 conducted to evaluate the safety of Maraviroc in combination with other antiretroviral agents in HIV-1-infected subjects co-infected with hepatitis C and/or hepatitis B virus (MEA 010.3)
MAH(s): ViiV Healthcare UK Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.22. Methylnaltrexone bromide – RELISTOR (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: Valerie Strassmann (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000870/II/0030
Procedure scope: Extension of indication for the treatment of opioid induced constipation in adult non cancer pain patients. Consequently, the MAH proposed the update of SmPC sections 4.1, 4.2, 4.4 and 5.1. The package leaflet is updated accordingly
MAH(s): TMC Pharma Services Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.23. Perampanel – FYCOMPA (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/002434/II/0016
Procedure scope: Extension of indication as adjunctive treatment of primary generalised tonic-clonic seizures in patients with epilepsy aged 12 years and older. SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 and the package leaflet are updated accordingly
MAH(s): Eisai Europe Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.24. Ponatinib – ICLUSIG (CAP)

- Evaluation of an RMP in the context of a variation

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

***Regulatory details:***

PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002695/II/0017
Procedure scope: Update of SmPC sections 4.8 and 5.1 to update the safety information and to update pharmacology information after the availability of the updated Clinical Study report for Study AP24534-10-201 (PACE). The RMP is updated accordingly. The MAH take this opportunity to update the RMP as for the requests received during the referral procedure (EMEA/H/C/002695/A-20/0003)
MAH(s): Ariad Pharma Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.25. Regorafenib – STIVARGA (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/002573/II/0008
Procedure scope: Update of SmPC section 5.1 to reflect final results from study 15808 (randomized, double blind, placebo controlled phase III study of regorafenib plus best supportive care (BSC) versus placebo plus BSC in Asian subjects with metastatic colorectal cancer (CRC) who have progressed after standard therapy). The MAH took also the opportunity to introduce minor corrections and editorial changes throughout the product information
MAH(s): Bayer Pharma AG
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.26. Ritonavir – NORVIR (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: Sabine Straus (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/000127/X/0127
Procedure scope: Line extension for a new oral powder formulation of Norvir (ritonavir) as a replacement for the currently marketed Norvir oral solution for a more suitable ritonavir formulation for the paediatric population
MAH(s): AbbVie Ltd.
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.27. Rituximab – MABTHERA (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/000165/X/0101/G
Procedure scope: Grouped variation: 1) line extension to add a new strength 1,600 mg solution for subcutaneous injection as well as a new indication for this strength; 2) update the product information of the existing strengths as a consequence of the line extension application; 3) update of the RMP (version 13.0)
MAH(s): Roche Registration Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.28. Tigecycline – TYGACIL (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: Miguel-Angel Macia (ES)

***Administrative details:***
Procedure number(s): EMEA/H/C/000644/II/0092
Procedure scope: Addition of a new restricted indication in children aged eight year-old and older. SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 have been updated accordingly. The package leaflet is also updated
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.29. Vemurafenib – ZELBORAF (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/002409/II/0018
Procedure scope: Update of SmPC section 4.8 to add pancreatitis with an uncommon frequency further to a cumulative review conducted by the MAH. The package leaflet is updated accordingly
MAH(s): Roche Registration Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

### 5.2.30. Vismodegib – ERIVEDGE (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)

***Administrative details:***
Procedure number(s): EMEA/H/C/002602/II/0015/G
Procedure scope: Grouped variation to update: 1) SmPC section 4.3 following the review of the GP28465 study report to delete the contraindication with St John's wort, section 4.4 to delete the warning regarding concomitant treatment with strong CYP inducers and section 4.5 to update the effects of concomitant medicinal products on vismodegib. The package leaflet is updated accordingly, the RMP has been updated to reflect the newly generated clinical pharmacology data; 2) SmPC section 4.2 following the review of the GP27839 study report as well as new clinical pharmacokinetic (PK) and PK modelling data generated since the initial marketing authorisation to change the posology information for patients with hepatic and renal impairment and section 5.2 to reflect the new PK data generated in patients with hepatic and renal impairment. In addition the RMP has been updated to reflect the newly generated data in patients with hepatic and renal impairment; 3) Submission of a summary document outlining new non-clinical, clinical PK data generated since the initial marketing authorisation to complement the existing oral contraceptive drug-drug interaction data
MAH(s): Roche Registration Ltd
***Documents:***
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

***RMP evaluated in the context of a PSUR procedure***

None

***RMP evaluated in the context of PASS results***

See also Dabigatran – PRADAXA 7.4.2. ; Dolutegravir – TIVICAY 7.4.3. , 7.4.4. ; 7.4.7. Human papillomavirus vaccine – GARDASIL, SILGARD 7.4.7. ; Human rotavirus, live attenuated – ROTARIX 7.4.8.

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

**5.2.31. Filgrastim – NIVESTIM** (CAP)

- Evaluation of an RMP on the context of a five year-renewal of the marketing authorisation

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

***Regulatory details:***
PRAC Rapporteur: Kirsti Villikka (FI)

***Administrative details:***
Procedure number(s): EMEA/H/C/001142/R/0025
MAH(s): Hospira UK Limited
***Documents:***
For adoption: PRAC advice

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

# 6. Periodic Safety Update Reports (PSURs)

## *6.1. Evaluation of PSUR procedures*[3]

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

- Evaluation of a PSUSA[4] procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/002293/PSUSA/00280/201408, EMEA/H/C/002517/PSUSA/00280/201408
MAH(s): Takeda Pharma A/S
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.2. Bexarotene – TARGRETIN (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/C/000326/PSUSA/00404/201409
MAH(s): Eisai Ltd
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.3. Bosutinib – BOSULIF (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Martin Huber (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/002373/PSUSA/10073/201409
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

[3] 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
[4] PSUR single assessment

### 6.1.4. Brentuximab vedotin – ADCETRIS (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Sabine Straus (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/002455/PSUSA/10039/201408
MAH(s): Takeda Pharma A/S
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.5. Brimonidine – MIRVASO (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002642/PSUSA/10093/201408
MAH(s): Galderma International
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.6. Cobicistat – TYBOST (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002572/PSUSA/10081/201408
MAH(s): Gilead Sciences International Ltd
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.7. Cobicistat, elvitegravir, emtricitabine, tenofovir disoproxil – STRIBILD (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002574/PSUSA/10082/201408
MAH(s): Gilead Sciences International Ltd

***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.8. Crizotinib – XALKORI (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/C/002489/PSUSA/10042/201408
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.9. Dabrafenib – TAFINLAR (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/002604/PSUSA/10084/201408
MAH(s): GlaxoSmithKline Trading Services
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.10. Deferiprone – FERRIPROX (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/C/000236/PSUSA/00940/201408
MAH(s): Apotex Europe BV
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.11. Dexmedetomidine – DEXDOR (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002268/PSUSA/00998/201409
MAH(s): Orion Corporation
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

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

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Dolores Montero Corominas (ES)

***Administrative details:***
Procedure number(s): EMEA/H/C/000552/PSUSA/01187/201408, EMEA/H/C/000573/PSUSA/01187/201408, EMEA/H/C/000572/PSUSA/01187/201408, EMEA/H/C/000545/PSUSA/01187/201408
MAH(s): Eli Lilly Nederland B.V.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.13. Elosulfase alfa – **VIMIZIM** (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002779/PSUSA/10218/201408
MAH(s): BioMarin Europe Ltd
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.14. Elvitegravir – **VITEKTA** (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002577/PSUSA/02577/201408
MAH(s): Gilead Sciences International Ltd
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.15. Enzalutamide – **XTANDI** (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***

PRAC Rapporteur: Dolores Montero Corominas (ES)

***Administrative details:***
Procedure number(s): EMEA/H/C/002639/PSUSA/10095/201408
MAH(s): Astellas Pharma Europe B.V.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.16. Fenofibrate, simvastatin – CHOLIB (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***

PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002559/PSUSA/10096/201408
MAH(s): Abbott Healthcare Products Ltd.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.17. Florbetaben ($^{18}$F) – NEURACEQ (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***

PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002553/PSUSA/10094/201408
MAH(s): Piramal Imaging Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.18. Pioglitazone - ACTOS (CAP), GLUSTIN (CAP), NAP pioglitazone, glimepiride - TANDEMACT (CAP) pioglitazone, metformin – COMPETACT (CAP), GLUBRAVA (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***

PRAC Rapporteur: Almath Spooner (IE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000285/PSUSA/02417/201407, EMEA/H/C/000655/PSUSA/02417/201407, EMEA/H/C/000893/PSUSA/02417/201407, EMEA/H/C/000286/PSUSA/02417/201407, EMEA/H/C/000680/PSUSA/02417/201407
MAH(s): Takeda Pharma A/S
***Documents:***

For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.19. Human coagulation factor VIII, human von willebrand factor – VONCENTO (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Sabine Straus (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/002493/PSUSA/10102/201408
MAH(s): CSL Behring GmbH
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.20. Ibuprofen – PEDEA (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Almath Spooner (IE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000549/PSUSA/01712/201407
MAH(s): Orphan Europe S.A.R.L.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.21. Influenza vaccine (split virion, inactivated) – IDFLU (CAP), INTANZA (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000966/PSUSA/01743/201408,
EMEA/H/C/000957/PSUSA/01743/201408
MAH(s): Sanofi Pasteur
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.22. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) – OPTAFLU (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000758/PSUSA/01745/201408
MAH(s): Novartis Vaccines and Diagnostics GmbH
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.23. Linaclotide – CONSTELLA (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Valerie Strassmann (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/002490/PSUSA/10025/201408
MAH(s): Almirall S.A
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.24. Loxapine – ADASUVE (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Sabine Straus (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/002400/PSUSA/10113/201408
MAH(s): Alexza UK Ltd.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.25. Mecasermin – INCRELEX (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Kirsti Villikka (FI)

***Administrative details:***
Procedure number(s): EMEA/H/C/000704/PSUSA/01942/201408
MAH(s): Ipsen Pharma
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.26. Midazolam – BUCCOLAM (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Sabine Straus (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/002267/PSUSA/10118/201409
MAH(s): ViroPharma SPRL
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.27. Moroctocog alfa – REFACTO AF (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Doris Stenver (DK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000232/PSUSA/02089/201408
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.28. Nalmefene – SELINCRO (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Martin Huber (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/002583/PSUSA/10120/201408
MAH(s): H. Lundbeck A/S
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.29. Natalizumab – TYSABRI (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000603/PSUSA/02127/201408
MAH(s): Biogen Idec Ltd
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.30. Nonacog alfa – BENEFIX (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000139/PSUSA/02183/201408
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.31. Pirfenidone – ESBRIET (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002154/PSUSA/02435/201408
MAH(s): InterMune UK Ltd.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.32. Pomalidomide – IMNOVID (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002682/PSUSA/10127/201408
MAH(s): Celgene Europe Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.33. Pandemic influenza vaccine (H5N1, whole virion, vero cell derived, inactivated) – PANDEMIC INFLUENZA VACCINE H5N1 BAXTER (CAP), prepandemic influenza vaccine (H5N1) (whole virion, inactivated, prepared in cell culture) - VEPACEL (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/001200/PSUSA/02282/201408, EMEA/H/C/002089/PSUSA/02282/201408
MAH(s): Baxter AG
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.34. Protein C – CEPROTIN (CAP), NAP

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000334/PSUSA/02563/201407
MAH(s): Baxter AG
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.35. Pyronaridine, artesunate – PYRAMAX (Art 58)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/W/002319/PSUV/0009
Scientific Opinion Holder(s) (SOH): Shin Poong Pharmaceutical Co., Ltd.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.36. Ruxolitinib – JAKAVI (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/002464/PSUSA/10015/201408
MAH(s): Novartis Europharm Ltd
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.37. Sitagliptin – JANUVIA (CAP), RISTABEN (CAP), TESAVEL (CAP), XELEVIA (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***

PRAC Rapporteur: Menno van der Elst (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/000722/PSUSA/02711/201408, EMEA/H/C/001234/PSUSA/02711/201408, EMEA/H/C/000910/PSUSA/02711/201408, EMEA/H/C/000762/PSUSA/02711/201408
MAH(s): Merck Sharp & Dohme Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.38. Tasonermin – BEROMUN (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***

PRAC Rapporteur: Doris Stenver (DK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000206/PSUSA/02850/201408
MAH(s): Boehringer Ingelheim International GmbH
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.39. Teduglutide – REVESTIVE (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***

PRAC Rapporteur: Torbjorn Callreus (DK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002345//PSUSA/09305/201408
MAH(s): NPS Pharma Holdings Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.40. Temozolomide – TEMODAL (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***

PRAC Rapporteur: Martin Huber (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000229/PSUSA/02886/201407
MAH(s): Merck Sharp & Dohme Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.41. Teriparatide – FORSTEO (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000425/PSUSA/02903/201409
MAH(s): Eli Lilly Nederland B.V.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.42. Trastuzumab emtansine – KADCYLA (CAP)

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Doris Stenver (DK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002389/PSUSA/10136/201408
MAH(s): Roche Registration Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.43. Ulipristal – ESMYA (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/002041/PSUSA/09325/201408
MAH(s): Gedeon Richter Plc.
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### 6.1.44. Vemurafenib – ZELBORAF (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/002409/PSUSA/09329/201408
MAH(s): Roche Registration Ltd

***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

#### 6.1.45. Vernakalant – BRINAVESS (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/001215/PSUSA/03109/201408
MAH(s): Cardiome UK Limited
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

#### 6.1.46. Zaleplon – SONATA (CAP), NAP

- Evaluation of a PSUSA procedure

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

***Regulatory details:***
PRAC Rapporteur: Almath Spooner (IE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000227/PSUSA/03140/201407
MAH(s): Meda AB
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

#### 6.1.47. Zoledronic acid – ACLASTA (CAP)

- Evaluation of a PSUSA procedure

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000595/PSUSA/09334/201408
MAH(s): Novartis Europharm Ltd
***Documents:***
For adoption: PRAC PSUR AR, PRAC recommendation

### *6.2. Follow-up to PSUR procedures*[5]

#### 6.2.1. Tacrolimus – PROTOPIC (CAP)

- Evaluation of a follow-up to a PSUR procedure

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

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

***Regulatory details:***
PRAC Rapporteur: Almath Spooner (IE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000374/LEG 056
Procedure scope: MAH's responses to the outcome of the evaluation of PSU 055 as adopted in October 2014
MAH(s): Astellas Pharma Europe B.V.
***Documents:***
For adoption: Updated PRAC Rapp AR

#### 6.2.2. Telmisartan, amlodopine – TWYNSTA (CAP)

- Evaluation of a follow-up to a PSUR procedure

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

***Regulatory details:***
PRAC Rapporteur: Valerie Strassmann (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/001224/LEG 012
Procedure scope: MAH's responses to the outcome of the evaluation of PSUR#6 as adopted in November 2014
MAH(s): Boehringer Ingelheim International GmbH
***Documents:***
For adoption: Updated PRAC Rapp AR

# 7. Post-authorisation Safety Studies (PASS)

## *7.1. Protocols of PASS imposed in the marketing authorisation(s)*[6]

#### 7.1.1. Aprotinin (NAP)

- Evaluation of an imposed PASS protocol

***Status:*** *decision*

***Regulatory details:***
PRAC Rapporteur: Veerle Verlinden (BE)

***Administrative details:***
Procedure number(s): EMEA/H/N/PSP/0004.1
Procedure scope: Evaluation of a revised protocol for a non-interventional post-authorisation safety study of pattern of use of Nordic aprotinin
MAH(s): Disphar International B.V (Nordic Group) (Trasylol, Aprotinin 10,000 KIU/ml injection BP)
***Documents:***
For adoption: PRAC AR, letter of endorsement/objection/notification that study is a clinical trial

#### 7.1.2. Dexamfetamine (NAP)

- Evaluation of imposed PASS protocols

[6] In accordance with Article 107n of Directive 2001/83/EC

***Status:*** *for appointment of Rapporteur and agreement of timetable*

***Regulatory details:***
PRAC Rapporteur: *to be appointed*

***Administrative details:***
Procedure number(s): EMEA/H/N/PSP/0018, EMEA/H/N/PSP/0021
Procedure scope: EMEA/H/N/PSP/0018: Protocol for a post-authorisation safety study to evaluate the long-term safety profile of dexamfetamine in children with attention deficit hyperactivity disorder (ADHD), specifically targeting key issues such as cardiovascular events, growth and psychiatric related adverse events
EMEA/H/N/PSP/0021: Protocol for a drug utilisation study of dexamfetamine to follow the use of prescribed dexamfetamine in the European Union using multiple data sources
MAH(s): Kohne Pharma GmbH
***Documents:***
For adoption: Procedure timetables

### 7.1.3. **Flupirtine** (NAP)

- Evaluation of an imposed PASS protocol

***Status:*** *for decision*

***Regulatory details:***
PRAC Rapporteur: Valerie Strassmann (DE)

***Administrative details:***
Procedure number: EMEA/H/N/PSP/0005.3
Procedure scope: Evaluation of a revised protocol for a non-interventional post-authorisation safety study to evaluate the effectiveness of the risk minimisation measures for the use of flupirtine 100 mg immediate-release capsules in daily practice
MAH(s): Meda Pharma (Flupigil, Metanor)
***Documents:***
For adoption: PRAC AR, letter of endorsement/objection/notification that study is a clinical trial

### 7.1.4. **Sodium, magnesium, potassium sulphates** for bowel preparation (NAP)

- Evaluation of an imposed PASS protocol

***Status:*** *for decision*

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

***Administrative details:***
Procedure number: EMEA/H/N/PSP/0007.2
Procedure scope: Evaluation of a revised protocol for a multi-centre European observational drug utilisation study (DUS) of post-commitment BLI800 to assess drug utilisation in the real life setting in a representative sample of the European target population
MAH(s): Ipsen Pharma (Eziclen, Izinova)
***Documents:***
For adoption: PRAC AR, letter of endorsement/objection/notification that study is a clinical trial

### 7.1.5. **Umeclidinium bromide – INCRUSE** (CAP)
### **Umeclidinium bromide, vilanterol – ANORO** (CAP), **LAVENTAIR** (CAP)

- Evaluation of an imposed PASS protocol

***Status:*** *for decision*

***Regulatory details:***
PRAC Rapporteur: Carmela Macchiarulo (IT)

***Administrative details:***
Procedure number: EMEA/H/C/PSP/J/003.1
Procedure scope: Revised PASS protocol for a non-interventional observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with UMEC/VI compared with tiotropium (study 201038) as a condition of the licence
MAH(s): Glaxo Group Ltd
***Documents:***
For adoption: PRAC AR, Letter of endorsement/objection/notification that study is a clinical trial

## *7.2. Protocols of PASS non-imposed in the marketing authorisation(s)*[7]

### 7.2.1. Dulaglutide – TRULICITY (CAP)

- Evaluation of a PASS protocol

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

***Regulatory details:***
PRAC Rapporteur: Carmela Macchiarulo (IT)

***Administrative details:***
Procedure number(s): EMEA/H/C/002825/MEA 001
Procedure scope: PASS protocol for a drug utilisation study to provide information on the use of dulaglutide after approval in the EU
MAH(s): Eli Lilly Nederland B.V.
***Documents:***
For adoption: PRAC advice

### 7.2.2. Dulaglutide – TRULICITY (CAP)

- Evaluation of a PASS protocol

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

***Regulatory details:***
PRAC Rapporteur: Carmela Macchiarulo (IT)

***Administrative details:***
Procedure number(s): EMEA/H/C/002825/MEA/002
Procedure scope: PASS protocol for a prospective study to monitor the occurrence of events of interest and ensure that the profile and rate remains consistent with what has been seen in clinical trials
MAH(s): Eli Lilly Nederland B.V.
***Documents:***
For adoption: PRAC advice

### 7.2.3. Flutemetamol ($^{18}$F) – VIZAMYL (CAP)

- Evaluation of a PASS protocol

[7] 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: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002557/MEA 003
Procedure scope: PASS protocol for a drug utilisation study as an additional pharmacovigilance activity to further characterise the safety concern (GE067-028)
MAH(s): GE Healthcare Ltd
***Documents:***
For adoption: PRAC advice

### 7.2.4. Linaclotide – CONSTELLA (CAP)

- Evaluation of a PASS protocol

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

***Regulatory details:***
PRAC Rapporteur: Valerie Strassmann (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/002490/MEA 009
Procedure scope: Revised PASS protocol for the linaclotide safety study for the assessment of diarrhoea—complications and associated risk factors in selected European populations with irritable bowel syndrome with constipation (IBS-C)
MAH(s): Almirall S.A
***Documents:***
For adoption: PRAC advice

### 7.2.5. Linaclotide – CONSTELLA (CAP)

- Evaluation of a PASS protocol

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

***Regulatory details:***
PRAC Rapporteur: Valerie Strassmann (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/002490/MEA 010
Procedure scope: Revised PASS protocol for the linaclotide utilisation study in selected European populations
MAH(s): Almirall S.A
***Documents:***
For adoption: PRAC advice

### 7.2.6. Ramucirumab – CYRAMZA (CAP)

- Evaluation of a PASS protocol

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/002829/MEA 001
Procedure scope: PASS protocol for a prospective observational registry of safety and effectiveness of ramucirumab in patients with advanced gastric cancer in the European Union and North America (I4T-MC-JVDD)
MAH(s): Eli Lilly Nederland B.V.
***Documents:***
For adoption: PRAC advice

## *7.3. Results of PASS imposed in the marketing authorisation(s)*[8]

None

## *7.4. Results of PASS non-imposed in the marketing authorisation(s)*[9]

### 7.4.1. **Boceprevir – VICTRELIS** (CAP)

- Evaluation of PASS results

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

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/C/002332/II/0033 (without RMP)
Procedure scope: Final report of healthcare professionals (HCP) educational material impact study for Victrelis compiling the results of all the EU countries where the product is marketed (France, Germany, Spain, United Kingdom and Italy)
MAH(s): Merck Sharp & Dohme Limited
***Documents:***
For adoption: PRAC AR

### 7.4.2. **Dabigatran – PRADAXA** (CAP)

- Evaluation of PASS results

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

***Regulatory details:***
PRAC Rapporteur: Torbjorn Callreus (DK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000829/II/0066 (with RMP)
Procedure scope: Final clinical study report (CSR) for study 1160.86 (open label, non-comparative pharmacokinetic and pharmacodynamic study to evaluate the effect of Pradaxa on coagulation parameters including a calibrated thrombin time test in patients with moderate renal impairment undergoing primary unilateral elective total knee or hip replacement surgery). The RMP has been updated accordingly
MAH(s): Boehringer Ingelheim International GmbH
***Documents:***
For adoption: PRAC AR

[8] In accordance with Article 107p-q of Directive 2001/83/EC
[9] 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

### 7.4.3. Dolutegravir – TIVICAY (CAP)

- Evaluation of PASS results

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002753/II/0010 (with RMP)
Procedure scope: Results of a study investigating the in vitro potential for dolutegravir to inhibit a series of melanocortin receptors
MAH(s): ViiV Healthcare
***Documents:***
For adoption: PRAC AR

### 7.4.4. Dolutegravir – TIVICAY (CAP)

- Evaluation of PASS results

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002753/II/0011 (with RMP)
Procedure scope: Results of a phototoxicity study (category 3) to assess phototoxicity in dolutegravir
MAH(s): ViiV Healthcare
***Documents:***
For adoption: PRAC AR

### 7.4.5. Etanercept – ENBREL (CAP)

- Evaluation of PASS results

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000262/II/0179 (without RMP)
Procedure scope: Final report from the organisation of teratology information specialists (OTIS) registry
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC AR

### 7.4.6. Etanercept – ENBREL (CAP)

- Evaluation of PASS results

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000262/II/0180 (without RMP)
Procedure scope: Clinical study report for study British Society for Rheumatology Biologics register (BSRBR)
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC AR

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

- Evaluation of PASS results

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000703/WS0698/0056/G, EMEA/H/C/000732/WS0698/0052/G (with RMP)
Procedure scope: Final report for vaccine impact population study in 4 Nordic countries for P033 and the extension of the due date to December 2015 (instead of June 2015) for submission of final study report MEA 20.6 for Protocol 018 (long-term follow up study in adolescents)
MAH(s): Sanofi Pasteur MSD SNC
***Documents:***
For adoption: PRAC AR

### 7.4.8. Human rotavirus, live attenuated – **ROTARIX** (CAP)

- Evaluation of PASS results

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000639/II/0062 (with RMP)
Procedure scope: Final report of genetic stability study EPI-ROTA-014 VS BE – 112560 that addresses post-approval measure ME2 005.2 in which the MAH commits to monitor for the potential occurrence of genetic drifts and shifts in the vaccine strain in post-marketing settings
MAH(s): GlaxoSmithKline Biologicals S.A.
***Documents:***
For adoption: PRAC AR

### 7.4.9. Pandemic influenza vaccine H1N1 (split virion, inactivated, adjuvanted) – **PANDEMRIX** (CAP)

- Evaluation of PASS results

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

***Regulatory details:***
PRAC Rapporteur: Rafe Suvarna (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000832/II/0077 (without RMP)

Procedure scope: Report on a retrospective pharmacoepidemiological study in Canada (Quebec) and follow-up cases. This submission fulfils condition ANX-115 of the marketing authorisation. Annex II is updated accordingly
MAH(s): GlaxoSmithKline Biologicals
***Documents:***
For adoption: PRAC AR

## *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[10]*

### 7.5.1. Azilsartan medoxomil – EDARBI (CAP)

- Evaluation of interim PASS results

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/002293/MEA 001.2
Procedure scope: First annual study report on a drug utilisation study one and five years post-launch in the European Union
MAH(s): Takeda Pharma A/S
***Documents:***
For adoption: PRAC advice

### 7.5.2. Bazedoxifene – CONBRIZA (CAP)

- Evaluation of interim PASS results

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

***Regulatory details:***
PRAC Rapporteur: Martin Huber (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000913/MEA 012.6
Procedure scope: Third progress report on PASS study B1781044: cohort study of venous thromboembolism and other clinical endpoints among osteoporotic women prescribed bazedoxifene, bisphosphonates or raloxifene in Europe
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC advice

### 7.5.3. Boceprevir – VICTRELIS (CAP)

- Evaluation of interim PASS results

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

***Regulatory details:***
PRAC Rapporteur: Arnaud Batz (FR)

[10] In line with the revised variations regulation for any submission before 4 August 2013

***Administrative details:***
Procedure number(s): EMEA/H/C/002332/MEA 017.6
Procedure scope: Third interim status report on observational PASS of Victrelis (boceprevir) amongst chronic hepatitis C patients (P08518)
MAH(s): Merck Sharp & Dohme Limited
***Documents:***
For adoption: PRAC advice

**7.5.4. Imatinib – GLIVEC** (CAP)

- Evaluation of interim PASS results

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

***Regulatory details:***
PRAC Rapporteur: Dolores Montero Corominas (ES)

***Administrative details:***
Procedure number(s): EMEA/H/C/000406/ANX 191.1
Procedure scope: First progress report on the European observational registry collecting efficacy and safety data in newly diagnosed paediatric Philadelphia positive (Ph+) acute lymphoblastic leukemia (ALL) patients treated with chemotherapy + imatinib ± hematopoietic stem cell treatment (±HSCT) (study STI571I2201)
MAH(s): Novartis Europharm Ltd
***Documents:***
For adoption: PRAC advice

**7.5.5. Indacaterol – HIROBRIZ BREEZHALER** (CAP), **ONBREZ BREEZHALER** (CAP), **OSLIF BREEZHALER** (CAP)

- Evaluation of interim PASS results

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

***Regulatory details:***
PRAC Rapporteur: Torbjorn Callreus (DK)

***Administrative details:***
Procedure number(s): EMEA/H/C/001211/MEA 015, EMEA/H/C/001114/MEA 017, EMEA/H/C/001210/MEA 015
Procedure scope: Fourth interim report for a PASS study QAB149B2432 of indacaterol prescribing and safety (using HealthCore database in the US)
MAH(s): Novartis Europharm Ltd
***Documents:***
For adoption: PRAC advice

**7.5.6. Infliximab – REMICADE** (CAP)

- Evaluation of interim PASS results

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/000240/MEA 133.9
Procedure scope: Seventh annual paediatric inflammatory bowel disease (IBD) registry (DEVELOP) report

MAH(s): Janssen Biologics B.V.
***Documents:***
For adoption: PRAC advice

### 7.5.7. Oseltamivir – TAMIFLU (CAP)

- Evaluation of interim PASS results

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

***Regulatory details:***
PRAC Rapporteur: Kirsti Villikka (FI)

***Administrative details:***
Procedure number(s): EMEA/H/C/000402/MEA 102
Procedure scope: Annual review of the safety and efficacy of oseltamivir in immunocompromised patients up to final submission of the clinical trial NV20234 study report (treatment) as flu and season permits
MAH(s): Roche Registration Ltd
***Documents:***
For adoption: PRAC advice

### 7.5.8. Perampanel – FYCOMPA (CAP)

- Evaluation of interim PASS results

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

***Regulatory details:***
PRAC Rapporteur: Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/002434/MEA 004.2
Procedure scope: Annual progress report for a post-marketing observational safety study to evaluate the long-term safety and tolerability of Fycompa as add-on therapy in epilepsy patients (PASS Study E2007-G000-402)
MAH(s): Eisai Europe Ltd.
***Documents:***
For adoption: PRAC advice

### 7.5.9. Voriconazole – VFEND (CAP)

- Evaluation of interim PASS protocol

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

***Regulatory details:***
PRAC Rapporteur: Sabine Straus (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/000387/MEA 090
Procedure scope: Final feasibility assessment for a potential non-interventional study to evaluate the association between voriconazole use and squamous cell carcinoma (SCC) of the skin in children aged less than 18 years
MAH(s): Pfizer Limited
***Documents:***
For adoption: PRAC advice

## *7.6. Others*

### 7.6.1. **Ferumoxytol – RIENSO** (CAP)

- Evaluation of a PASS feasibility study

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

***Regulatory details:***
PRAC Rapporteur: Martin Huber (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/002215/MEA 017
Procedure scope: Evaluation of European databases for studies evaluating the risk of hypersensitivity reactions in users of intravenous iron compounds (database feasibility evaluation report)
MAH(s): Takeda Pharma A/S
***Documents:***
For adoption: PRAC advice

See also under 11.3.

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

### 8.1.1. **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: Arnaud Batz (FR)

***Administrative details:***
Procedure number(s): EMEA/H/C/000587/S/0021 (without RMP)
MAH(s): GTC Biotherapeutics UK Limited
***Documents:***
For adoption: PRAC advice

### 8.1.2. **Fampridine – FAMPYRA** (CAP)

- PRAC consultation on a conditional renewal of the marketing authorisation

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

***Regulatory details:***
PRAC Rapporteur: Sabine Straus (NL)

***Administrative details:***
Procedure number(s): EMEA/H/C/002097/R/0021 (without RMP)
MAH(s): Biogen Idec Ltd.
***Documents:***
For adoption: PRAC advice

#### 8.1.3. Vismodegib – ERIVEDGE (CAP)

- PRAC consultation on a conditional renewal of the marketing authorisation

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

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

***Administrative details:***
Procedure number(s): EMEA/H/C/002602/R/0016 (without RMP)
MAH(s): Roche Registration Ltd
***Documents:***
For adoption: PRAC advice

See under 5.2

# 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. Epoetin beta – NEORECORMON (CAP)

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

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

***Regulatory details:***
PRAC Rapporteur: Valerie Strassmann (DE)

***Administrative details:***
Procedure number(s): EMEA/H/C/000116/II/083
Procedure scope: Submission of measures to minimise the potential risk of retinopathy of prematurity (RoP) as requested in the PSUR procedure covering the period 2007-2010
MAH(s): Roche Registration Ltd
***Documents:***
For adoption: PRAC advice

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

None

## *10.3. Other requests*

**10.3.1. Antiretroviral medicinal products:**
**Abacavir – ZIAGEN** (CAP); **abacavir, lamivudine – KIVEXA** (CAP); **abacavir, lamivudine, zidovudine – TRIZIVIR** (CAP); **atazanavir– REYATAZ** (CAP); **darunavir – PREZISTA** (CAP); **efavirenz – STOCRIN** (CAP), **SUSTIVA** (CAP); **efavirenz, emtricitabine, tenofovir disoproxil – ATRIPLA** (CAP); **elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil – STRIBILD** (CAP); **emtricitabine – EMTRIVA** (CAP); **emtricitabine, tenofovir disoproxil – TRUVADA** (CAP); **emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA** (CAP); **etravirine – INTELENCE** (CAP); **fosamprenavir – TELZIR** (CAP); **indinavir – CRIXIVAN** (CAP); **lamivudine – EPIVIR** (CAP), **LAMIVUDINE VIIV** (CAP); **lamivudine, zidovudine – COMBIVIR** (CAP); **lopinavir, ritonavir –ALUVIA** (CAP), **KALETRA** (CAP); **nevirapine – VIRAMUNE** (CAP); **rilpivirine – EDURANT** (CAP); **ritonavir – NORVIR** (CAP); **saquinavir – INVIRASE** (CAP); **stavudine – ZERIT** (CAP); **tenofovir disoproxil – VIREAD** (CAP); **tipranavir - APTIVUS** (CAP)

- PRAC consultation on post-authorisation measures, upon CHMP request

***Regulatory details:***
PRAC Rapporteur (lead): Qun-Ying Yue (SE)
PRAC Co-Rapporteur: Arnaud Batz (FR), Julie Williams (UK)

***Administrative details:***
Procedure number(s): EMEA/H/C/000252/LEG 089; EMEA/H/C/000581/LEG 045; EMEA/H/C/000338/LEG 090; EMEA/H/C/000494/LEG 080; EMEA/H/C/000707/LEG 070; EMEA/H/C/000250/LEG 071; EMEA/H/C/000249/LEG 080; EMEA/H/C/000797/LEG 040; EMEA/H/C/002574/LEG 014; EMEA/H/C/000533/LEG 049; EMEA/H/C/000594/LEG 043; EMEA/H/C/002312/LEG 031; EMEA/H/C/000900/LEG 048; EMEA/H/C/000534/LEG 076; EMEA/H/C/000128/LEG 039; EMEA/H/C/000107/LEG 052; EMEA/H/C/000673/LEG 007; EMEA/H/C/000190/LEG 038; EMEA/H/C/000764/LEG 031; EMEA/H/C/000368/LEG 118; EMEA/H/C/000183/LEG 061; EMEA/H/C/002264/LEG 026; EMEA/H/C/000127/LEG 039; EMEA/H/C/000113/LEG 065; EMEA/H/C/000110/LEG 060; EMEA/H/C/000419/LEG 270; EMEA/H/C/000631/LEG 068
Procedure scope: Review of class labelling on mitochondrial dysfunction, lactic acidosis and lipodystrophy
MAH(s): AbbVie Ltd (Kaletra, Norvir), Boehringer Ingelheim International GmbH (Aptivus, Viramune), Bristol-Myers Squibb Pharma EEIG (Reyataz, Sustiva, Zerit), Bristol-Myers Squibb and Gilead Sciences Ltd.(Atripla), Gilead Sciences International Ltd.(Emtriva, Eviplera, Stribild, Truvada, Tybost, Viread), Janssen-Cilag International N.V.(Edurant, Intelence, Prezista), Merck Sharp & Dohme Ltd (Crixivan, Isentress, Stocrin), Roche Registration Ltd. (Invirase), ViiV Healthcare UK Limited (Celsentri, Combivir, Epivir, Lamivudine Viiv, Kivexa, Telzir, Trizivir, Ziagen)

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

- PRAC consultation on post-authorisation measures, upon CHMP request

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

***Regulatory details:***
PRAC Rapporteur (overall): Valerie Strassmann (DE)
PRAC Co-Rapporteurs: Arnaud Batz (FR), Dolores Montero Corominas (ES)

***Administrative details:***
Procedure number(s): EMEA/H/C/000332/LEG 083.4 (Aranesp), EMEA/H/C/000727/LEG 023.4 (Abseamed), EMEA/H/C/000725/LEG 022.4 (Binocrit), EMEA/H/C/000726/LEG 023.4 (epoetin Alfa Hexal), EMEA/H/C/000739 LEG 032.4 (Mircera), EMEA/H/C/000116/LEG 049.4 (NeoRecormon),

EMEA/H/C/001036/LEG 019.4 (Biopoin), EMEA/H/C/001033/LEG 019.4 (Eporatio), EMEA/H/C/000872/LEG 036.4 (Retacrit), EMEA/H/C/000760/LEG 035.4 (Silapo)
Scope: Erythropoiesis-stimulating agents (ESA): Evaluation of the outcome of statistical analysis of clinical trial data in chronic kidney disease (CKD) patients on dialysis/not on dialysis (treatment of anaemia)
MAH(s): Amgen Europe B.V. (Aranesp), Medice Arzneimittel Pütter GmbH & Co. KG (Abseamed), Sandoz GmbH (Binocrit), Hexal AG (Epoetin Alfa Hexal), Roche Registration Ltd (Mircera, NeoRecormon), CT Arzneimittel GmbH (Biopoin), Ratiopharm GmbH (Eporatio)
***Documents:***
For adoption: PRAC advice

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

## *11.1. Safety related variations of the marketing authorisation*

**11.1.1. Azithromycin** for oral and intravenous use (NAP)

- PRAC consultation on a safety-related variations upon Finland's request

***Status:*** *for discussion and agreement of PRAC advice*

***Regulatory details:***
Lead member: Terhi Lehtinen (FI)

***Administrative details:***
Procedure number: FI/H/XXXX/WS/23
Procedure scope: PRAC consultation on a variation procedure evaluating the draft PASS protocol (A0661209) for a non-imposed non-interventional study in the Kaiser Permanente databases to examine the effects of azithromycin use on cardiovascular outcome
MAH(s): Pfizer (Zithromax)
***Documents:***
For adoption: PRAC advice

## *11.2. Renewals of the Marketing Authorisation*

None

## *11.3. Other requests*

**11.3.1. Iron** for intravenous (IV) use (NAP)

- PRAC consultation on the evaluation of a PASS feasibility study upon Member State's request

***Status:*** *for discussion and agreement of PRAC advice*

***Regulatory details:***
Lead member: Arnaud Batz (FR)

***Administrative details:***
Procedure number: *Not applicable*
Procedure scope: Evaluation of European databases for studies evaluating the risk of hypersensitivity reactions in users of intravenous iron compounds (database feasibility evaluation report), literature review of ferumoxytol and other IV iron containing medicinal products and hypersensitivity reactions, annual cumulative reviews of hypersensitivity reactions for IV iron-containing medicinal products
MAH(s): various

***Documents:***
For adoption: PRAC advice

# 12. Organisational, regulatory and methodological matters

## *12.1. Mandate and organisation of the PRAC*

- Implementation of new Committee's agenda template

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

***Documents:***
For information: agenda template

## *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

#### *12.3.2.1. Audit report and PRAC recommendation: timelines*

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

#### *12.3.2.2. Pilot and phased implementation: Update*

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

#### *12.3.2.3. Post-audit functionalities: action plan*

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

### 12.3.3. Periodic Safety Update Single Assessment (PSUSA)

- PRAC assessment report publication

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

#### 12.3.4. Union Reference Date List

- Consultation on the draft list, version March 2015
- Feedback from the Granularity and Periodicity Advisory Group (GPAG)

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

***Documents:***
For adoption: Revised EURD list

### *12.4. Signal Management*

#### 12.4.1. Signal Management

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

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

- Statistical guideline update

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

### *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 Products under Additional Monitoring

- Consultation on the draft list, version March 2015

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

***Documents:***
For discussion: Revised additional monitoring list

## *12.6. EudraVigilance Database*

### 12.6.1. Activities related to the confirmation of full functionality

#### *12.6.1.1. EudraVigilance: revised business requirements*

***Status:*** *for adoption*

#### *12.6.1.2. Individual Case Safety Report (ICSR): revised form*

***Status****: for adoption*

### 12.6.2. EudraVigilance annual report

- 2014 EudraVigilance (human) annual report

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

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

### 12.7.1. Risk Management Systems

### 12.7.2. RMP assessment process

- Implementation of the revised process

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

### 12.7.3. 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. Renewals, conditional renewals, annual reassessments*

None

## *12.11. Risk communication and Transparency*

### 12.11.1. Public Participation in Pharmacovigilance

None

#### 12.11.2. Safety Communication

None

## *12.12. Continuous pharmacovigilance*

None

#### 12.12.1. Incident Management

None

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

#### 12.13.1. Committees

None

#### 12.13.2. Working Parties

None

#### 12.13.3. Others

##### *12.13.3.1. Geriatric Expert Group (GEG)*

- Points to Consider on frailty evaluation instruments for baseline characterisation of clinical trial populations

***Status**: for discussion*

***Documents:***
For discussion: Points to consider documents

##### *12.13.3.2. Scientific Advisory Group (SAG) Oncology*

- Bisphosphonates, denosumab: effectiveness of risk minimisation measures: consultation of the SAG oncology on the risk of osteonecrosis of the jaw (ONJ) and action plan for implementation

***Status:** for discussion*

## *12.14. Interaction within the EU regulatory network*

None

## *12.15. Contacts of the PRAC with external parties and interaction of the EMA with interested parties*

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

None

### 12.15.2. Others

#### *12.15.2.1. International Society for Pharmaceutical Engineering (ISPE)*

- Analysis of patient and healthcare professional input in EMA oral contraceptive communication, following the symposium, October 2014

## *12.16. Others*

- Interaction with patients, consumers and organisations: revised framework

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

# 13. Any other business

## *13.1. Medication errors*

- Risk minimisation strategy for medication errors with high strength/fixed combination insulins

***Status****: for agreement*

***Documents:***
For adoption: Revised guidance, EMA safety communication

## *13.2. Pharmacovigilance programme and revised implementation governance*

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

## *13.3. Product Information: revision of the review process for initial marketing authorisation*

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

## *13.4. Type II variations: revised procedural timetables*

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