7 July 2014
EMA/PRAC/412722/2014
Pharmacovigilance Risk Assessment Committee (PRAC)

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 7-10 July 2014

Chair: June Raine – Vice-Chair: Almath Spooner

7 July 2014, 13:00 – 19:00, room 3/A

8 July 2014, 08:30 – 19:00, room 3/A

9 July 2014, 08:30– 19:00, room 3/A

10 July 2014, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

24 July 2014, 10:00-12:00, room 6/A, 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 vary 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 and start of referrals will also be available. 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 are subject 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/

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1. Introduction

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

1.2. Adoption of agenda of the meeting of 7-10 July 2014

Status: *for adoption*

Document: PRAC Agenda Rev.3 due for publication on 7 July 2014

1.3. Minutes of the previous PRAC meeting on 10-13 June 2014

Status: *for adoption*

Document: PRAC final Minutes due for publication by 18 July 2014

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

2.3.1. **Methadone medicinal products for oral use containing povidone** (NAP)

- Review of the benefit-risk balance following the notification by Norway of a referral under Article 107i of Directive 2001/83/EC, based on pharmacovigilance data

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

Regulatory details:
PRAC Rapporteur: Qun-Ying Yue (SE)
PRAC Co-Rapporteur: Karen Pernille Harg (NO)

Administrative details:
Procedure number(s): EMEA/H/A-107i/1395
MAH(s): Martindale Pharma, various
Documents:
For adoption: PRAC AR, PRAC recommendation

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. Ivabradine – **CORLENTOR** (CAP), **PROCORALAN** (CAP)

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

Status: *for discussion and agreement of a list of outstanding issues*

Regulatory details:
PRAC Rapporteur: Menno van der Elst (NL)
PRAC Co-Rapporteur: Kirsti Villikka (FI)

Administrative details:
Procedure number(s): EMEA/H/C/000598/A20/0031, EMEA/H/C/000597/A20/0032
MAH(s): Les Laboratoires Servier
Documents:
For adoption: List of outstanding issues (LoOI), revised timetable (or PRAC AR, PRAC recommendation)

3.2.2. **Testosterone** (NAP)

- Review of the benefit-risk balance following the notification by Estonia 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: Torbjörn Callréus (DK)
PRAC Co-Rapporteur: Maia Uusküla (EE)

Administrative details:
Procedure number(s): EMEA/H/A-31/1396
MAH(s): various
Documents:
For adoption: List of outstanding issues (LoOI), revised timetable (or PRAC AR, PRAC recommendation)

3.2.3. Valproate and related substances: sodium valproate, valproic acid, valproate semisodium, valpromide (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: Sabine Straus (NL)
PRAC Co-Rapporteur: Julie Williams (UK)

Administrative details:
Procedure number(s): EMEA/H/A-31/1387
MAH(s): Sanofi-aventis GmbH, various

Documents:
For adoption: List of outstanding issues (LoOI), revised timetable (or PRAC AR, PRAC recommendation)

3.3. Procedures for finalisation

3.3.1. **Bromocriptine** (NAP)

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

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

Regulatory details:
PRAC Rapporteur: Sabine Straus (NL)
PRAC Co-Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/A-31/1379
MAH(s): Sanofi-aventis, Meda Pharma, various
Documents:
For adoption: PRAC AR, PRAC recommendation

3.3.2. **Ponatinib - ICLUSIG** (CAP)

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

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

Regulatory details:
PRAC Rapporteur: Rafe Suvarna (UK)
PRAC Co-Rapporteur: Ulla Wändel Liminga (SE)

Administrative details:
Procedure number(s): EMEA/H/C/002695/A-20/0003
MAH(s): Ariad Pharma Ltd
Documents:
For adoption: PRAC AR, PRAC recommendation

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

None

3.5. Others

3.5.1. **Diacerein** (NAP)

- Review of recommendations of a referral procedure under Article 31 of Directive 2001/83/EC adopted in March 2014, at the request of the European Commission

Status: *for discussion*

Regulatory details:
PRAC Rapporteur (re-examination): Margarida Guimarães (PT)
PRAC Co-Rapporteur (re-examination): Harald Herkner (AT)

Administrative details:
Procedure number(s): EMEA/H/A-31/1349
MAH(s): Negma-Wockhardt, TRB Chemedica, various

4. Signals assessment and prioritisation[1]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. **Buprenorphine**, transdermal patches (NAP)

- Signal of skin depigmentation

Status: *for discussion*

Regulatory details:
PRAC Rapporteur: *to be appointed*

Administrative details:
EPITT 18040 – New signal
MAH(s): various
Lead MS: FR
Documents:
For adoption: PRAC recommendation

4.1.2. **Sildenafil – VIAGRA** (CAP)

- Signal of increased risk of incident melanoma

Status: *for discussion*

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

Administrative details:
EPITT 17997 – New signal
MAH(s): Pfizer Limited
Documents:
For adoption: PRAC recommendation

4.2. New signals detected from other sources

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

- Signal of spontaneous splenic rupture/haemorrhage

Status: *for discussion*

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

Administrative details:
EPITT 18020 – New signal
MAH(s): Bayer Pharma AG

[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

Documents:
For adoption: PRAC recommendation

4.3. Signals follow-up and prioritisation

4.3.1. **Azithromycin** (NAP)

- Signal of potentially fatal heart events

Status: *for discussion*

Regulatory details:
PRAC Rapporteur: Terhi Lehtinen (FI)

Administrative details:
EPITT 16156 – Follow-up May 2014
MAH(s): Pfizer, various
Documents:
For adoption: PRAC recommendation

4.3.2. **Bisphosphonates** (CAP, NAP):
alendronate (NAP); **risedronate** (NAP); **alendronate, colcalciferol – ADROVANCE** (CAP), **FOSAVANCE** (CAP)**, VANTAVO** (CAP)
Strontium ranelate – OSSEOR (CAP), **PROTELOS** (CAP)

- Signal of heart valves disorders

Status*: for discussion*

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

Administrative details:
EPITT 13832 – Follow-up May 2014
MAH(s): Merck Sharp & Dohme Limited (Adrovance, Fosavance, Vantavo), Les Laboratoires Servier (Osseor, Protelos), various
Documents:
For adoption: PRAC recommendation

4.3.3. **Bupropion** (NAP)

- Signal of pancytopenia

Status: *for discussion*

Regulatory details:
PRAC Rapporteur: Sabine Straus (NL)

Administrative details:
EPITT 17727 - Follow-up March 2014
MAH(s): GlaxoSmithKline, various
Documents:
For adoption: PRAC recommendation

4.3.4. **Calcium channel blockers** (CAP, NAP):
Aliskiren, amlodipine - RASILAMLO (CAP)
Amlodipine, telmisartan - ONDUARP (CAP), **TWYNSTA** (CAP)
Amlodipine, valsartan – **COPALIA** (CAP), **DAFIRO** (CAP), **EXFORGE** (CAP), **IMPRIDA** (CAP)

Amlodipine, valsartan, hydrochlorothiazide - **COPALIA HCT** (CAP), **DAFIRO HCT** (CAP), **EXFORGE HCT** (CAP)

- Signal of breast cancer risk

Status: *for discussion*

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

Administrative details:
EPITT 17750 – Follow-up November 2013
MAH(s): Novartis Europharm Ltd (Copalia, Copalia HCT, Dafiro, Dafiro HCT, Exforge, Exforge HCT, Imprida, Rasilamlo), Boehringer Ingelheim (Onduarp, Twynsta), various
Documents:
For adoption: PRAC recommendation

4.3.5. Tacrolimus for systemic use - **ADVAGRAF** (CAP), **MODIGRAF** (CAP), NAP
Febuxostat – **ADENURIC** (CAP)

- Signal of potential drug-drug interaction between systemic tacrolimus and febuxostat

Status: *for discussion*

Regulatory details:
PRAC Rapporteur: Almath Spooner (IE)

Administrative details:
EPITT 17809 – Follow-up March 2014
MAH(s): Astellas Pharma Europe B.V. (Advagraf, Modigraf), Menarini International Operations Luxembourg S.A. (Adenuric), various

5. Risk Management Plans

5.1. Medicines in the pre-authorisation phase

5.1.1. Aclidinium, formoterol

- 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/003969, EMEA/H/C/003745
Intended indication: Maintenance bronchodilator treatment for airflow obstruction and relief of symptoms in adult patients with chronic obstructive pulmonary disease (COPD)
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.2. Allogeneic T 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, *ATMP, Orphan*
Intended indication: Treatment in haploidentical haematopoietic stem cell transplantation

Applicant: MolMed SpA
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.3. Budesonide, formoterol

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

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

Administrative details:
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.4. Busulfan

- 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/002806, *Generic*
Intended indication: Conditioning treatment prior to conventional haematopoietic progenitor cell transplantation (HPCT)
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.5. Ceritinib

- 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/003819
Intended indication: Treatment of adult patients with previously treated anaplastic lymphoma; treatment of anaplastic lymphomakinase (ALK)-positive locally advanced or metastatic non-small cell lung cancer (NSCLC)
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.6. 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/004000, *Informed consent*
Intended indication: Treatment of major depressive disorder; diabetic peripheral neuropathic pain; generalised anxiety disorder
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.7. Eliglustat

- 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/003724, *Orphan*
Intended indication: Treatment of Gaucher disease type 1
Applicant: Genzyme Europe BV
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.8. 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: Treatment of hyperphosphataemia
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.9. Filgrastim

- 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/003956, *Biosimilar*
Intended indication: Reduction in the duration of neutropenia and the incidence of febrile
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.10. 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: Treatment of attention deficit hyperactivity disorder (ADHD)
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.11. Human papillomavirus (rDNA)

- 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: Treatment of human papillomavirus (HPV) diseases
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.12. Ibrutinib

- 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/003791, *Orphan*
Intended indication: Treatment of mantle cell lymphoma, chronic lymphocytic leukaemia (CLL), small lymphocytic lymphoma
Applicant: Janssen-Cilag International N.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.13. Idelalisib

- 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/003843
Intended indication: Treatment of patients with relapsed chronic lymphocytic leukaemia (CLL) and for the treatment of patients with refractory indolent non-Hodgkin lymphoma (iNHL)
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.14. Lamivudine, raltegravir

- 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/003823
Intended indication: Treatment of human immunodeficiency virus (HIV-1)
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.15. Naltrexone, bupropion

- 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/003687
Intended indication: Management of obesity
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.16. Nintedanib

- 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:
Procedure number(s): EMEA/H/C/002569
Intended indication: Treatment of non-small cell lung cancer (NSCLC)
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.1.17. Nonacog gamma

- 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/003771
Intended indication: Treatment of haemophilia B
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.18. Ospemifene

- 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/002780
Intended indication: Treatment of vulvar and vaginal atrophy (VVA)
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.19. Sofosbuvir, ledipasvir

- 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/003850
Intended indication: Treatment of chronic hepatitis C
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.1.20. 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: 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. Boceprevir – VICTRELIS (CAP)

- Evaluation of an RMP in the context of a variation

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

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/C/002332/II/0029
Procedure scope: Submission of an updated RMP (version 8.0) to address the CHMP requests following the evaluation of the RMP version 7 (EMEA/H/C/2332/RMP/029, dated 19 December 2013). This update includes addition of the new important identified risk of pancytopenia, modifications of the timelines for P05063 and P07755 and inclusion of the completed study report for the mechanistic study of anaemia and proposes the update of the educational material. Furthermore, the MAH proposes the early termination of study P05063
MAH(s): Merck Sharp & Dohme Limited
Documents:
For adoption: PRAC AR

5.2.2. Dabigatran – PRADAXA (CAP)

- Evaluation of an RMP in the context of a variation

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

Regulatory details:
PRAC Rapporteur: Torbjörn Callréus (DK)

Administrative details:
Procedure number(s): EMEA/H/C/000829/II/0062
Procedure scope: Update of the RMP (version 28.4) following the modification to the study 1160 - 144 (post-authorisation non-interventional study aiming to evaluate the potential off-label use of dabigatran in Europe)
MAH(s): Boehringer Ingelheim International GmbH
Documents:
For adoption: PRAC AR

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

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

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

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

Administrative details:
Procedure number(s): EMEA/H/C/000276/WS0557/0160, EMEA/H/C/000275/WS0557/0165
Procedure scope: Submission of an update to the RMP (version 6.0)
MAH(s): Bayer Pharma AG
Documents:
For adoption: PRAC AR

5.2.4. Pertuzumab – PERJETA (CAP)

- Evaluation of an RMP in the context of a variation

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

Regulatory details:
PRAC Rapporteur: Doris Stenver (DK)

Administrative details:
Procedure number(s): EMEA/H/C/002547/II/0009
Procedure scope: Update of the RMP to amend the protocol of the Annex II obligation PERUSE study and its due date. Annex II is updated accordingly. In addition, the MAH proposed a change to the Annex of the EU RMP description of the global enhanced pharmacovigilance pregnancy programme regarding the duration of contraception in relation to concomitant treatment
MAH(s): Roche Registration Ltd
Documents:
For adoption: PRAC AR

5.2.5. Vemurafenib – ZELBORAF (CAP)

- Evaluation of an RMP in the context of a variation

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

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

Administrative details:
Procedure number(s): EMEA/H/C/002409/II/0017
Procedure scope: Submission of an update to the RMP (version 8.0)
MAH(s): Roche Registration Ltd
Documents:
For adoption: PRAC AR

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

5.2.6. Alogliptin – VIPIDIA (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/002182/II/0001
Procedure scope: Update of SmPC sections 4.2, 4.4, 4.8, and 5.1 in order to reflect the results of study 402 (phase IIIb, randomised, double-blind, placebo-controlled, event-driven study, designed to demonstrate that no excess risk of a major adverse cardiovascular event (MACE) exists following treatment with alogliptin compared with placebo when added to standard of care in adults with T2DM and acute coronary syndrome (ACS)
MAH(s): Takeda Pharma A/S
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.7. Alogliptin – VIPIDIA (CAP)
alogliptin, metformin – VIPDOMET (CAP)

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

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/002182/WS0520/0002, EMEA/H/C/002654/WS0520/0001

Procedure scope: Update of SmPC sections 4.4, 4.8, and 5.1 in order to reflect the results of study 305 (phase III, randomised, double-blind, active-controlled, 2-year study, designed to assess the efficacy and safety of alogliptin in combination with metformin compared with glipizide in combination with metformin in adults with type 2 diabetes mellitus (T2DM). The MAH took this opportunity to propose amendments to the RMP in order to reflect study 305 results. The requested worksharing procedure proposed amendments to the SmPC and RMP
MAH(s): Takeda Pharma A/S
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.8. Alogliptin, pioglitazone – INCRESYNC (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/002178/II/0002
Procedure scope: Update of SmPC sections 4.4 and 4.8 in order to reflect the results of study 305 (phase III, randomised, double-blind, active-controlled, 2-year study, designed to assess the efficacy and safety of alogliptin in combination with metformin compared with glipizide in combination with metformin in adults with type 2 diabetes mellitus (T2DM). The package leaflet was proposed to be updated accordingly. The MAH took this opportunity to propose amendments to the RMP in order to reflect study 305 results. The requested variation procedure proposed amendments to the SmPC, PIL and RMP
MAH(s): Takeda Pharma A/S
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.9. Alogliptin, pioglitazone – INCRESYNC (CAP)
alogliptin, metformin – VIPDOMET (CAP)

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

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/002178/WS0519/0003, EMEA/H/C/002654/WS0519/0003
Procedure scope: Update of SmPC sections 4.4, 4.8, and 5.1 in order to reflect the results of study 402 (phase IIIb, randomised, double-blind, placebo-controlled, event-driven study, designed to demonstrate that no excess risk of a major adverse cardiovascular event (MACE) exists following treatment with alogliptin compared with placebo when added to standard of care in adults with T2DM and acute coronary syndrome (ACS). The MAH took this opportunity to propose amendments to the RMP in order to reflect study 402 results as well updating its structure according to the new European Union (EU) template for RMPs. The requested worksharing procedure proposed amendments to the SmPC and RMP
MAH(s): Takeda Pharma A/S
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.10. 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/0039, *Orphan*
Procedure scope: Update of SmPC section 4.4 in relation to the current recommendations for liver function and SmPC section 5.1 of with data on aminotransferase abnormalities from an analysis of the clinical study reports (CSR) for PASS 'AMB110094 (VOLT)'. The current 'Health care Professional information' in Annex II has been updated accordingly as well as the package leaflet and RMP
MAH(s): Glaxo Group Ltd
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.11. Bosentan – TRACLEER (CAP)

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

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/C/000401/II/0066
Procedure scope: Extension of indication to include the treatment of symptomatic pulmonary arterial hypertension in paediatric patients aged from 3 months to 18 years. The SmPC has been updated in order to include the data from studies conducted according to the agreed paediatric investigation plan (PIP) for bosentan (EMEA-000425-PIP02-10-M04). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2, 5.3 and 6.6 have been updated. The Package Leaflet has been updated accordingly. In addition, taking into account the new data in the paediatric population, an updated version of the RMP (version 5) has been provided
MAH(s): Actelion Registration Ltd.
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.12. Deferiprone – FERRIPROX (CAP)

- Evaluation of an RMP in the context of a variation

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/C/000236/II/0089/G
Procedure scope: Update of SmPC section 4.5 regarding combination of deferiprone with other iron chelators further to request of the PRAC in the assessment of the PSUR (PSUV/083). Update of section 5.1 of the SmPC and the RMP with the results of Study LA37-111 conducted to evaluate the effect of deferiprone on cardiac QT and QT_C interval duration
MAH(s): Apotex Europe BV
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.13. Denosumab – PROLIA (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/001120/II/0036
Procedure scope: Update of SmPC section 4.4 upon request by PRAC following the assessment of PSU/027, to revise the warnings on osteonecrosis of the jaw (ONJ)
MAH(s): Amgen Europe B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.14. Denosumab – PROLIA (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/001120/II/0037
Procedure scope: Update of the SmPC, upon request by PRAC following the assessment of PSU 027, to refine the warnings on hypocalcaemia including a description of the clinical manifestations of severe symptomatic hypocalcaemia and increases in parathyroid hormone in sections 4.4 and 4.8, and to add musculoskeletal pain as an identified risk in section 4.8 further to post-marketing experience
MAH(s): Amgen Europe B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.15. Denosumab – XGEVA (CAP)

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

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

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

Administrative details:
Procedure number(s): EMEA/H/C/002173/II/0016
Procedure scope: Extension of indication to add treatment of giant cell tumour of bone in adults or skeletally mature adolescents. As a consequence, it is proposed to update SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2
MAH(s): Amgen Europe B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.16. Denosumab – XGEVA (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/002173/II/0027
Procedure scope: Update of the SmPC, upon request by PRAC following the assessment of PSU/014, to revise the warnings in section 4.4 on osteonecrosis of the jaw (ONJ), and to add information in sections 4.4 and 4.8 on the incidence of ONJ based on duration of exposure
MAH(s): Amgen Europe B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.17. Denosumab – XGEVA (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/002173/II/0028
Procedure scope: Update of the SmPC, upon request by PRAC following the assessment of PSU 014, to refine the warnings on hypocalcaemia including a description of the clinical manifestations of severe symptomatic hypocalcaemia and increases in parathyroid hormone in sections 4.4 and 4.8, and to add musculoskeletal pain as an identified risk in section 4.8 further to post-marketing experience. Further, sections 4.2 and 5.3 of the SmPC have been updated with respect to recommendations for monitoring of calcium levels, and information regarding patients with renal impairment
MAH(s): Amgen Europe B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.18. Dexamethasone – OZURDEX(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/001140/II/0015
Procedure scope: Update of SmPC section 4.1 to add a new indication for treatment of adult patients with diabetic macular oedema. Consequential updates were proposed for SmPC sections 4.2, 4.4, 4.8, 5.1 and 5.2. In addition, the MAH proposed to reduce and consolidate the current HCP leaflet, which is provided as a tear off section after the package leaflet
MAH(s): Allergan Pharmaceuticals Ireland
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.19. Dibotermin alfa – INDUCTOS (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/000408/II/0071

Procedure scope: Extension of indication to broaden the use of Inductos in interbody lumbar spine fusion
MAH(s): Medtronic BioPharma B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.20. Entecavir – BARACLUDE (CAP)

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

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

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

Administrative details:
Procedure number(s): EMEA/H/C/000623/II/0041
Procedure scope: Extension of indication to include treatment of chronic hepatitis B virus (HBV) infection in paediatric patients from 2 to <18 years of age with compensated liver disease and evidence of active viral replication and persistently elevated serum alanine transaminase (ALT) levels
MAH(s): Bristol-Myers Squibb Pharma EEIG
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.21. Enzalutamide – XTANDI (CAP)

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

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

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

Administrative details:
Procedure number(s): EMEA/H/C/002639/II/0008
Procedure scope: Extension of indication for the treatment of adult men with metastatic castration-resistant prostate cancer who are asymptomatic or mildly symptomatic after failure of androgen deprivation therapy in whom chemotherapy is not yet clinically indicated. Consequently, changes are proposed to SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2
MAH(s): Astellas Pharma Europe B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.22. Infliximab – REMICADE (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/000240/II/0179
Procedure scope: Update of SmPC section 4.8 of to add intestinal obstruction based on the data available from clinical trials, post-marketing experience and from registries in adult Crohn's disease
MAH(s): Janssen Biologics B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.23. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP)

- Evaluation of an RMP in the context of a variation

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

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

Administrative details:
Procedure number(s): EMEA/H/C/002617/II/0020
Procedure scope: Seasonal update of the composition of the strains to those officially recommended by WHO and CHMP for the season 2014/2015
MAH(s): MedImmune LLC
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

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

- Evaluation of an RMP in the context of a variation

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/000966/II/0026, EMEA/H/C/000957/II/0029
Procedure scope: Update of the product information to reflect that the strains are in accordance with the WHO recommendation and the EU decision for the 2014/2015 season. There is no change in the strains selected for the composition of the influenza vaccines compared to the previous season and the variation is therefore limited to an administrative update of the product information and a stability data update. In addition an update of the RMP to include an enhanced safety surveillance plan is provided
MAH(s): Sanofi Pasteur, Sanofi Pasteur MSD SNC
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.25. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) – OPTAFLU (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/000758/II/0069
Procedure scope: Update of the product information to reflect that the strains are in accordance with the WHO recommendation and the EU decision for the 2014/2015 season. There is no change in the strains selected for the composition of the influenza vaccines compared to the previous season and the variation is therefore limited to an administrative update of the product information and a stability data update. In line with the adopted interim guidance on safety surveillance for seasonal influenza vaccines in the EU, an updated RMP including an enhanced safety surveillance plan is submitted
MAH(s): Novartis Vaccines and Diagnostics GmbH
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.26. Insulin lispro – **HUMALOG** (CAP), **LIPROLOG** (CAP)

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

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

Regulatory details:
PRAC Rapporteur: Julie Williams (UK)

Administrative details:
Procedure number(s): EMEA/H/C/000088/X/0125, EMEA/H/C/000393/X/092
Procedure scope: Addition of a new strength (200 U/ml KwikPen resentation)
MAH(s): Eli Lilly Nederland B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.27. Interferon beta-1a – **REBIF** (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/000136/II/0106
Procedure scope: Update of the SmPC sections 4.4 and 4.8 to include class labelling information on thrombotic microangiopathy (TMA), thrombotic thrombocytopenic purpura (TTP) and haemolytic uraemic syndrome (HUS). In addition the RMP is being updated to version 7.0
MAH(s): Merck Serono Europe Limited
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

See also 10.1.2.

5.2.28. Lenalidomide – **REVLIMID** (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: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/C/000717/X/0073/G
Procedure scope: Grouping of type II variations to add the following indication: continuous treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant and a line extension application to add the following strength: 20 mg (21 capsules pack)
MAH(s): Celgene Europe Limited
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.29. Liraglutide – **VICTOZA** (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/001026/II/0028
Procedure scope: Update of SmPC sections 4.2, 4.8 and 5.1 to reflect data from study NN2211-3916 (efficacy and safety of liraglutide as add-on to existing diabetes medications in patients with type 2 diabetes mellitus and moderate renal impairment). The Package Leaflet has been updated accordingly as well as the RMP (revised version 4 provided). In addition, the MAH takes the opportunity to update the instructions for use in the Package Leaflet to comply with EN ISO14971:2012 (application of risk management to medical devices) and to reflect residual risk mitigations
MAH(s): Novo Nordisk A/S
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.30. Pasireotide – SIGNIFOR (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: Qun-Ying Yue (SE)

Administrative details:
Product number(s): EMEA/H/C/002052/X/0010
Procedure scope: Line extension application to add 20mg, 40mg and 60mg powder and solvent for suspension for injection in the treatment of adult patients with acromegaly for whom surgery is not an option or has not been curative, or who are inadequately controlled on treatment with other somatostatin analogues
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.31. Posaconazole – NOXAFIL (CAP)

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

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

Regulatory details:
PRAC Rapporteur: Rafe Suvarna (UK)

Administrative details:
Procedure number(s): EMEA/H/C/000610/X/0033
Procedure scope: Line extension to add Noxafil 18mg/ml concentrate for solution for infusion
MAH(s): Merck Sharp & Dohme Limited
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.32. Ranibizumab – LUCENTIS (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/000715/II/0047
Procedure scope: Update of SmPC section 4.2 to harmonise the administration instructions for Lucentis across indications in line with the available clinical evidence, relevant guidelines and treatment recommendations as well as clinical practice. The proposed posology recommendations for diabetic macular oedema are further supported by the final report of the RETAIN study. In addition, SmPC sections 4.5 and 5.1 were proposed to be updated to reflect RETAIN study data including data on the concomitant treatment with thiazolidinediones. The information in SmPC section 5.1 on the RESTORE study were also proposed to be updated with data from the 2-year extension phase as previously requested by the CHMP in the context of post-authorisation procedure MEA 034
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.33. Saxagliptin – KOMBOGLYZE (CAP)
saxagliptin, metformin – ONGLYZA (CAP)

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

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/002059/WS0529/0014/G, EMEA/H/C/001039/WS0529/0024/G
Procedure scope: Update of SmPC sections 4.2, 4.4, 4.5, 4.8 and 5.1 of Onglyza and Komboglyze, respectively, with regard to information from the results from study D1680C00003 (SAVOR), a cardiovascular outcome study, and study D1680L00002 (GENERATION), a study comparing saxagliptin with glimepiride in elderly patients
MAH(s): Bristol-Myers Squibb/AstraZeneca EEIG
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.34. Telithromycin – KETEK (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/000354/II/0062
Procedure scope: Update of SmPC sections 4.4 and 4.8 with new adverse events on ventricular arrhythmias, convulsions and tremor following a request from the CHMP
MAH(s): Aventis Pharma S.A.
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.35. Tocilizumab – ROACTEMRA (CAP)

- Evaluation of an RMP in the context of a variation

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

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

Administrative details:
Procedure number(s): EMEA/H/C/000955/II/0032
Procedure scope: Update of SmPC sections 4.1 and 5.1 and consequential changes to section 1 of the Package Leaflet in order to extend the indication to the treatment in combination with methotrexate (MTX) of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX
MAH(s): Roche Registration Ltd
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

5.2.36. Ustekinumab – STELARA (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/000958/II/0041
Procedure scope: Update of SmPC section 4.8 to add the adverse reactions of skin exfoliation and erythrodermic psoriasis further to the request of the CHMP to implement the outcome of a PRAC signal recommendation
MAH(s): Janssen-Cilag International N.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.37. Zoledronic acid – ZOLEDRONIC ACID TEVA (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: Ulla Wändel Liminga (SE)

Administrative details:
Product number(s): EMEA/H/C/002439/X/0008
Procedure scope: Line extension to include a new pharmaceutical form, solution for infusion. The new pharmaceutical form has three new presentations
MAH(s): Teva Pharma B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

RMP evaluated in the context of a PSUR procedure

See also Besilesomab – SCINTIMUN 6.1.6. , C1 inhibitor, human – CINRYZE 6.1.8. , Canakinumab – ILARIS 6.1.10. , Eptacog alfa (activated) – NOVOSEVEN 6.1.15. , Roflumilast – DALIRESP, DAXAS, LIBERTEK 6.1.30.

RMP evaluated in the context of PASS results

See also Dabigatran – PRADAXA 7.4.1. , Dolutegravir – TIVICAY 7.4.3. , Human rotavirus, live attenuated – ROTARIX 7.4.4.

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

5.2.38. Alendronic acid, colecalciferol – VANTAVO (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: Julie Williams (UK)

Administrative details:
Procedure number(s): EMEA/H/C/001180/R/0019 (with RMP version 7.0)
MAH(s): Merck Sharp & Dohme Limited
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.39. Amifampridine – FIRDAPSE (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: Julie Williams (UK)

Administrative details:
Procedure number(s): EMEA/H/C/001032/R/0029 (with RMP version 5.0)
MAH(s): BioMarin Europe Ltd
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.40. Dronedarone – MULTAQ (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: Menno van der Elst (NL)

Administrative details:
Product number(s): EMEA/H/C/001043/R/0030 (with RMP version 9.0)
Applicant: Sanofi-aventis groupe
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.41. Sevelamer – RENAGEL (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: Terhi Lehtinen (FI)

Administrative details:
Product number(s): EMEA/H/C/000254/R/0100 (with RMP version 6.0)
Applicant: Genzyme Europe BV
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

5.2.42. Silodosin – **SILODYX** (CAP), **UROREC** (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: Julie Williams (UK)

Administrative details:
Product number(s): EMEA/H/C/001209/R/0016 (with RMP version 11.0), EMEA/H/C/001092/R/0016 (with RMP version 11.0)
Applicant: Recordati Ireland Ltd
Documents:
For adoption: PRAC RMP AR, PRAC RMP Assessment overview and Advice

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

5.2.43. Sulfur hexafluoride – **SONOVUE** (CAP)

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

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/C/000303/LEG
Procedure scope: Subsequently to the CHMP positive adoption of variation II-25, review of a DHPC to inform of the deletion of a contraindication for use of Sonovue in patients with acute coronary syndrome or clinically unstable ischaemic cardiac disease and the new contraindication in combination with dobutamine in patients with conditions suggesting cardiovascular instability due to the risk of severe cardiac arrhythmia (5 cases reports) and the need to update the educational material to reflect these changes
MAH(s): Bracco International B.V.
Documents:
For adoption: PRAC RMP AR, PRAC RMP assessment overview and advice

6. Periodic Safety Update Reports (PSURs)

6.1. Evaluation of PSUR procedures[3]

6.1.1. Abatacept – **ORENCIA** (CAP)

- Evaluation of a PSUR procedure

[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

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

Regulatory details:
PRAC Rapporteur: Kirsti Villikka (FI)

Administrative details:
Procedure number(s): EMEA/H/C/000701/PSUV/0079
MAH(s): Bristol-Myers Squibb Pharma EEIG
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.2. Ambrisentan – VOLIBRIS (CAP)

- Evaluation of a PSUR 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/000839/PSUV/0037
MAH(s): Glaxo Group Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.3. Amifampridine – FIRDAPSE (CAP)

- Evaluation of a PSUR 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/001032/PSUV/0028
MAH(s): BioMarin Europe Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.4. Avanafil – SPEDRA (CAP)

- Evaluation of a PSUR 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/002581/PSUV/0005
MAH(s): Menarini International Operations Luxembourg S.A.
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.5. Belatacept – NULOJIX (CAP)

- Evaluation of a PSUR 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/002098/PSUV/0021
MAH(s): Bristol-Myers Squibb Pharma EEIG
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.6. Besilesomab – SCINTIMUN (CAP)

- Evaluation of a PSUR 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/001045/PSUV/0004 (with RMP version 11.0)
MAH(s): Cis Bio International
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.7. Bromelain enriched proteolytic enzyme preparation from ananas comosus – NEXOBRID (CAP)

- Evaluation of a PSUR 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/002246/PSUV/0011
MAH(s): MediWound Germany GmbH
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.8. C1 inhibitor, human – CINRYZE (CAP)

- Evaluation of a PSUR 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/001207/PSUV/0023 (with RMP version 9.0)
MAH(s): ViroPharma SPRL
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.9. Cabazitaxel – **JEVTANA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/C/002018/PSUV/0023
MAH(s): Sanofi-Aventis Groupe
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.10. Canakinumab – **ILARIS** (CAP)

- Evaluation of a PSUR 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/001109/PSUV/0032 (with RMP version 8.0)
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.11. Clopidogrel – **PLAVIX** (CAP), CAP, NAP
clopidogrel, acetylsalicylic acid – DUOCOVER (CAP), **DUOPLAVIN** (CAP)

- Evaluation of a PSUSA[4] procedure

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

Regulatory details:
PRAC Rapporteur: Margarida Guimarães (PT)

Administrative details:
Procedure number(s): EMEA/H/C/PSUSA/00000820/201311
MAH(s): Sanofi Clir SNC (Plavix), Sanofi-aventis groupe (DuoCover), Sanofi Pharma Bristol-Myers Squibb SNC (DuoPlavin), various
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.12. Darunavir – **PREZISTA** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Sabine Straus (NL)

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

Administrative details:
Procedure number(s): EMEA/H/C/000707/PSUV/0066
MAH(s): Janssen-Cilag International N.V.
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.13. Dextromethorphan, quinidine – NUEDEXTA (CAP)

- Evaluation of a PSUR 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/002560/PSUV/0003
MAH(s): Jenson Pharmaceutical Services Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.14. Enzalutamide – XTANDI (CAP)

- Evaluation of a PSUR 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/PSUV/0009
MAH(s): Astellas Pharma Europe B.V.
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.15. Eptacog alfa (activated) – NOVOSEVEN (CAP)

- Evaluation of a PSUR 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/000074/PSUV/0080 (with RMP version 1.0)
MAH(s): Novo Nordisk A/S
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.16. Ferumoxytol – RIENSO (CAP)

- Evaluation of a PSUR 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/002215/PSUV/0014
MAH(s): Takeda Pharma A/S
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.17. Human hepatitis B immunoglobulin – ZUTECTRA (CAP), NAP

- Evaluation of a PSUSA[5] 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/PSUSA/00001631/201311
MAH(s): Biotest Pharma GmbH, various
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.18. Hydrocortisone – PLENADREN (CAP)

- Evaluation of a PSUR procedure

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

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

Administrative details:
Procedure number(s): EMEA/H/C/002185/PSUV/0013
MAH(s): ViroPharma SPRL
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.19. Influenza vaccine (live attenuated, nasal) – FLUENZ (CAP), FLUENZ TETRA (CAP)

- Evaluation of a PSUR procedure

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

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

Administrative details:
Procedure number(s): EMEA/H/C/001101/PSUV/0060, EMEA/H/C/002617/PSUV/0016
MAH(s): MedImmune LLC
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.20. Lenalidomide – REVLIMID (CAP)

- Evaluation of a PSUR procedure

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

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/C/000717/PSUV/0074
MAH(s): Celgene Europe Limited
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.21. Lutropin alfa – LUVERIS (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Torbjörn Callréus (DK)

Administrative details:
Procedure number(s): EMEA/H/C/000292/PSUV/0062
MAH(s): Merck Serono Europe Limited
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.22. Methylthioninium – METHYLTHIONINIUM CHLORIDE PROVEBLUE (CAP), NAP

- Evaluation of a PSUSA[6] procedure

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

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

Administrative details:
Procedure number(s): EMEA/H/C/PSUSA/00002029/201311
MAH(s): Provepharm, various
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.23. Nepafenac – NEVANAC (CAP)

- Evaluation of a PSUR 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/000818/PSUV/0024
MAH(s): Alcon Laboratories (UK) Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

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

6.1.24. Nitric oxide – INOMAX (CAP), NAP

- Evaluation of a PSUSA[7] 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/PSUSA/00002172/201312
MAH(s): Linde Healthcare AB, various
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.25. Omalizumab – XOLAIR (CAP)

- Evaluation of a PSUR procedure

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

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

Administrative details:
Procedure number(s): EMEA/H/C/000606/PSUV/0052
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.26. Pertuzumab – PERJETA (CAP)

- Evaluation of a PSUR 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/002547/PSUV/0008
MAH(s): Roche Registration Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.27. Plerixafor – MOZOBIL (CAP)

- Evaluation of a PSUR 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/001030/PSUV/0021
MAH(s): Genzyme Europe BV

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

Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

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

- Evaluation of a PSUR procedure

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

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

Administrative details:
Procedure number(s): EMEA/H/C/000973/PSUV/0077
MAH(s): GlaxoSmithKline Biologicals S.A.
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.29. Ponatinib – ICLUSIG (CAP)

- Evaluation of a PSUR 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/002695/PSUV/0009
MAH(s): Ariad Pharma Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.30. Roflumilast – DALIRESP (CAP), DAXAS (CAP), LIBERTEK (CAP)

- Evaluation of a PSUR 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/002398/PSUV/0016 (with RMP version 13.0), EMEA/H/C/001179/PSUV/0020 (with RMP version 13.0), EMEA/H/C/002399/PSUV/0016 (with RMP version 13.0)
MAH(s): Takeda GmbH
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.31. Saquinavir – INVIRASE (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Harald Herkner (AT)

Administrative details:
Procedure number(s): EMEA/H/C/000113/PSUV/0108
MAH(s): Roche Registration Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.32. Ticagrelor – **BRILIQUE** (CAP)

- Evaluation of a PSUR 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/001241/PSUV/0023
MAH(s): AstraZeneca AB
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.33. Tobramycin – **TOBI PODHALER** (CAP)

- Evaluation of a PSUR 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/002155/PSUV/0021
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.34. Ustekinumab – **STELARA** (CAP)

- Evaluation of a PSUR 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/000958/PSUV/0040
MAH(s): Janssen-Cilag International N.V.
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.35. Verteporfin – **VISUDYNE** (CAP)

- Evaluation of a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number(s): EMEA/H/C/000305/PSUV/0085
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.1.36. Ziconotide – **PRIALT** (CAP)

- Evaluation of a PSUR procedure

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

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

Administrative details:
Procedure number(s): EMEA/H/C/000551/PSUV/0044
MAH(s): Eisai Ltd
Documents:
For adoption: PRAC PSUR AR, PRAC recommendation

6.2. Follow-up to PSUR procedures[8]

6.2.1. Cabecitabine – **XELODA** (CAP)

- Evaluation of a follow-up to a PSUR procedure

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

Regulatory details:
PRAC Rapporteur: Martin Huber (DE)

Administrative details:
Procedure number(s): EMEA/H/C/000316/LEG 027.2
Procedure scope: MAH's response to PSU-027 (PSUR#10) as adopted in May 2013
MAH(s): Roche Registration Ltd
Documents:
For adoption: Updated PRAC Rapp AR

6.2.2. Eculizumab – **SOLIRIS** (CAP)

- Evaluation of a follow-up to a PSUR procedure

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/000791/LEG 055
Procedure scope: MAH's response to PSUR#10 as adopted in April 2014
MAH(s): Alexion Europe SAS
Documents:
For adoption: Updated PRAC Rapp AR

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

6.2.3. Ruxolitinib – JAKAVI (CAP)

- Evaluation of a follow-up to a PSUR procedure

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/002464/LEG 011
Procedure scope: MAH's response to PSUV/0011 (PSUR#2) RSI as adopted in March 2014
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: Updated PRAC Rap AR

7. Post-authorisation Safety Studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[9]

7.1.1. Autologous peripheral-blood mononuclear cells activated with prostatic acid phosphatase granulocyte-macrophage colony factor (Sipuleucel-T) - PROVENGE (CAP)

- Evaluation of an imposed PASS protocol

Status: *for decision*

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

Administrative details:
Procedure number: EMEA/H/C/002513/ANX 001
Procedure scope: Evaluation of a PASS protocol to establish and keep an observational EU-based registry of male patients with mCRPC (therapy in men with metastatic castrate-resistant prostate cancer) to evaluate overall survival, the risk of ischemic stroke or myocardial infarction following treatment with Provenge and other identified and potential risks (observational study P13-1)
MAH(s): Dendreon UK Ltd
Documents:
For adoption: PRAC AR, Letter of endorsement/objection/notification that study is a clinical trial

7.1.2. Deferasirox - EXJADE (CAP)

- Evaluation of an imposed PASS protocol

Status: *for decision*

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure number: EMEA/H/C/000670/ANX/038.4
Procedure scope: Evaluation of MAH's response to ANX 038.3 as adopted by PRAC on 10 April 2014 including a revised PASS protocol for study CICL670E2422: observational cohort study in paediatric non transfusion dependant-thalassaemia (NTDT) patients over 10 years
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: PRAC AR, Letter of endorsement/objection/notification that study is a clinical trial

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

7.1.3. **Ethinylestradiol, chlormadinone** (NAP)

- Evaluation of an imposed PASS protocol

Status: *for decision*

Regulatory details:
PRAC Rapporteur: Valerie Strassmann (DE)

Administrative details:
Procedure scope: Evaluation of a joint PASS protocol (following conclusion of Art.31 referral procedure for combined hormonal contraceptives with CHMP opinion adopted in November 2013) to study the risk of venous thromboembolism (VTE) associated with chlormadinone/ethinylestradiol (CMA/EE) containing products
MAH(s): Gideon Richter, various
Documents:
For adoption: PRAC AR, Letter of endorsement/objection/notification that study is a clinical trial

7.1.4. **Ethinylestradiol, gestodene** transdermal patch (NAP)

- Evaluation of an imposed PASS protocol

Status: *for decision*

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure scope: Evaluation of a PASS protocol on the European active surveillance study comparing regimens of application in combined hormonal contraception (EURAS-CORA)
MAH(s): Bayer (Apleek)
Documents:
For adoption: PRAC AR, Letter of endorsement/objection/notification that study is a clinical trial

7.1.5. **Hydroxyethyl starch (HES)** (NAP)

- Evaluation of an imposed PASS protocol

Status *for appointment of Rapporteur and agreement of timetable*

Regulatory details:
PRAC Rapporteur: *to be appointed*

Administrative details:
Procedure scope: Evaluation of a PASS protocol (Drug utilisation study) to assess the effectiveness of the risk minimisation taken following EC decision dated 19 December 2013 on a referral procedure (EMEA/H/A-107I/1376)
MAH(s): B. Braun Melsungen AG (Tetraspan, Venofundin), Fresenius Kabi Deutschland GmbH (Volulyte, Voluven Fresenius, Voluven, HyperHAES, HAES-steril), Serumwerk Bernburg AG (VitaHES, Vitafusal, Plasma Volume Redibag, PlasmaHES Redibag, Hesra, Hesra infuusioneste)
Documents:
For adoption: Procedure timetable

7.1.6. **Modified vaccinia Ankara virus - IMVANEX** (CAP)

- Evaluation of an imposed PASS protocol

Status: *for decision*

Regulatory details:
PRAC Rapporteur: Rafe Suvarna (UK)

Administrative details:
Procedure number: EMEA/H/C/002596/SOB 002
Procedure scope: Evaluation of PASS protocols: 1) POX-MVA-038: observational, non-interventional post-authorisation safety study for the prophylactic vaccination with Imvanex in adults; 2) POX-MVA-039: observational, non-interventional post-authorisation safety and efficacy study for the prophylactic vaccination with Imvanex following re-emergence of circulating smallpox infections
MAH(s): Bavarian Nordic A/S
Documents:
For adoption: PRAC AR, Letter of endorsement/objection/notification that study is a clinical trial

7.1.7. Solutions for parenteral nutrition, combination - NUMETA G16%E EMULSION FOR INFUSION and associated names (NAP)

- Evaluation of an imposed PASS protocol

Status: *for decision*

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

Administrative details:
Procedure scope: Evaluation of a PASS protocol (following conclusion of 107i Referral) on a multicentre, non-interventional, uncontrolled, open-label, observational study in children to evaluate serum mg levels associated with the intake of Numeta G 16% E
MAH(s): Baxter
Documents:
For adoption: PRAC AR, Letter of endorsement/objection/notification that study is a clinical trial

7.1.8. Sodium, magnesium, potassium sulphates for bowel preparation (NAP)

- Evaluation of an imposed PASS protocol

Status: *for decision*

Regulatory details:
PRAC Rapporteur: Isabelle Robine (FR)

Administrative details:
Procedure scope: Evaluation of a PASS 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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[10]

7.2.1. Telaprevir – INCIVO (CAP)

- Evaluation of a PASS protocol

[10] 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: Qun-Ying Yue (SE)

Administrative details:
Procedure number(s): EMEA/H/C/002313/MEA 016.1
Procedure scope: Evaluation of MAH's response to MEA 016 [study report of study VX-950-C219] as adopted at CHMP in April 2013
MAH(s): Janssen-Cilag International N.V.
Documents:
For adoption: PRAC advice

7.3. Results of PASS imposed in the marketing authorisation(s)[11]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[12]

7.4.1. **Dabigatran – PRADAXA** (CAP)

- Evaluation of PASS results

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

Regulatory details:
PRAC Rapporteur: Torbjörn Callréus (DK)

Administrative details:
Procedure number(s): EMEA/H/C/000829/II/0066 (with RMP version 28.6)
Procedure scope: Submission of the 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 (version 28.6)
MAH(s): Boehringer Ingelheim International GmbH
Documents:
For adoption: PRAC AR

7.4.2. **Denosumab – PROLIA** (CAP)

- Evaluation of PASS results

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

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

Administrative details:
Procedure number(s): EMEA/H/C/001120/II/0040 (without RMP)
Procedure scope: Submission of the results of a category 3 PASS - study 20090695: post-marketing observational study to estimate off-label use in selected EU Member States
MAH(s): Amgen Europe B.V.
Documents:
For adoption: PRAC AR

[11] In accordance with Article 107p-q of Directive 2001/83/EC
[12] 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/0001 (with RMP version 2.0)
Procedure scope: Submission of data from a physiologically-based pharmacokinetic model in fulfilment of MEA 4 regarding the potential for a drug-drug interaction with midazolam
MAH(s): ViiV Healthcare
Documents:
For adoption: PRAC AR

7.4.4. 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 version 10.0)
Procedure scope: Submission of the final report of genetic stability study EPI-ROTA-014 VS BE – 112560 that addresses the post-approval measure ME2 005.2 in which the MAH commits to monitor 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

7.5. 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[13]

7.5.1. Betaine anhydrous – CYSTADANE (CAP)

- Evaluation of interim PASS results

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

Regulatory details:
PRAC Rapporteur: Valerie Strassmann (DE)

Administrative details:
Procedure number(s): EMEA/H/C/000678/MEA 018.3
Procedure scope: Submission of the first progress report of Cystadane surveillance PASS protocol (in collaboration with E-HOD) registry, replacing the ROCH registry. Final study report of the ROCH registry is submitted in parallel
MAH(s): Orphan Europe S.A.R.L.
Documents:
For adoption: PRAC advice

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

7.5.2. Exenatide – BYDUREON (CAP)

- Evaluation of interim PASS results

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/002020/MEA 011.2
Procedure scope: First annual report on an epidemiologic study using one or more European databases to identify possible cases of thyroid neoplasms among type 2 diabetes mellitus patients who initiate exenatide once weekly (study B017)
MAH(s): Bristol-Myers Squibb/AstraZeneca EEIG
Documents:
For adoption: PRAC advice

7.5.3. Ulipristal – ESMYA (CAP)

- Evaluation of interim PASS results

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

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

Administrative details:
Procedure number(s): EMEA/H/C/002041/MEA 003.2
Procedure scope: Second annual progress report on a prospective multicentre non-interventional study of women treated with Esmya (ulipristal acetate) as pre-operative treatment of moderate to severe symptoms of uterine fibroids
MAH(s): Gedeon Richter Plc.
Documents:
For adoption: PRAC advice

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

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. **Basiliximab – SIMULECT** (CAP)

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

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/000207/II/0078
Procedure scope: Update of SmPC sections 4.1 and 4.4 with information on the lack of efficacy of Simulect for the prophylaxis of acute rejection in recipients of other solid organ allografts following a recommendation by the PRAC
MAH(s): Novartis Europharm Ltd
Documents:
For adoption: PRAC advice

10.1.2. **Interferon beta-1a – AVONEX** (CAP)
Interferon beta-1b – BETAFERON (CAP), **EXTAVIA** (CAP)

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

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

Regulatory details:
PRAC Rapporteurs: Dolores Montero Corominas (ES), Julie Williams (UK)

Administrative details:
Procedure number(s): EMEA/H/C/000102/II/0143, EMEA/H/C/000081/II/0095, EMEA/H/C/000933/II/0064
Procedure scope: Update of the SmPC Sections 4.4 and 4.8 to include class labelling wording on thrombotic microangiopathy (TMA), thrombotic thrombocytopenic purpura (TTP) and haemolytic uraemic syndrome (HUS). The Package leaflet has been updated accordingly
MAH(s): Biogen Idec (Avonex), Bayer Pharma AG (Betaferon), Novartis Europharm Ltd (Extavia)
Documents:
For adoption: PRAC advice

See also 5.2.27.

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); **cobicistat – TYBOST** (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); **enfuvirtide – FUZEON** (CAP); **etravirine – INTELENCE** (CAP); **fosamprenavir – TELZIR** (CAP); **indinavir – CRIXIVAN** (CAP); **lamivudine – EPIVIR** (CAP); **lamivudine, zidovudine – COMBIVIR** (CAP); **lopinavir, ritonavir – KALETRA** (CAP); **maraviroc – CELSENTRI** (CAP); **nevirapine – VIRAMUNE** (CAP); **raltegravir – ISENTRESS** (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

Status: *for discussion*

Regulatory details:
PRAC Rapporteur (lead): Qun-Ying Yue (SE)
PRAC Co-Rapporteur: Isabelle Robine (FR), Julie Williams (UK)

Administrative details:
Procedure number(s): N/A
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. (Fuzeon, Invirase), ViiV Healthcare UK Limited (Celsentri, Combivir, Epivir, Kivexa, Telzir, Trizivir, Ziagen)
Documents:
For adoption: PRAC advice

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: Isabelle Robine (FR), Dolores Montero Corominas (ES)

Administrative details:
Procedure scope: Erythropoiesis-stimulating agents: outcome of statistical analysis of clinical trial data in chronic kidney disease (CKD) patients on dialysis/not on dialysis (treatment of anaemia)
Procedure number(s): EMEA/H/C/000332/LEG 083.3 (Aranesp), EMEA/H/C/000727/LEG 023.3 (Abseamed), EMEA/H/C/000725/LEG 022.3 (Binocrit), EMEA/H/C/000726/LEG 023.3 (epoetin Alfa Hexal), EMEA/H/C/000739 LEG 032.3 (Mircera), EMEA/H/C/000116/LEG 049.3 (NeoRecormon), EMEA/H/C/001036/LEG 019.3 (Biopoin), EMEA/H/C/001033/LEG 019.3 (Eporatio), EMEA/H/C/000872/LEG 036.3 (Retacrit), EMEA/H/C/000760/LEG 035.3 (Silapo)
Scope: Erythropoiesis-Stimulating Agents (ESA): 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. **Influenza vaccine (inactivated, split-virion trivalent)** (NAP)

- PRAC consultation on a safety-related variations upon CHMP request, upon Member State's request

Status: *for discussion and agreement of PRAC advice*

Regulatory details:
Lead member: Isabelle Robine (FR)

Administrative details:
Procedure number: FR/H/0122/001/II/68, FR/H/0121/001/II/72, FR/H/0139/001/II/46
Procedure scope: Consultation on safety variations on annual enhanced active safety surveillance for the 2014-2015 influenza vaccination campaign
MAH(s): Sanofi Pasteur, Sanofi Pasteur MSD (Mutagrip, Vaxigrip, Vaxigrip Enfants)
Documents:
For adoption: PRAC advice

11.2. Renewals of the Marketing Authorisation

None

11.3. Other requests

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

- PRAC consultation on risk of accidental exposure, upon Member State's request

Status: *for discussion and agreement of PRAC advice*

Regulatory details:
Lead member: Sabine Straus (NL)

Administrative details:
Procedure scope: Consultation on MAH's proposal to improve patch visibility and timelines for implementation
MAH(s): Janssen-Cilag (Duragesic)
Documents:
For adoption: PRAC advice

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Pharmacovigilance audits and inspections

12.2.1. **Pharmacovigilance Systems and their Quality Systems**

- Update on the Pharmacovigilance Programme

***Status**: for information*

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

- Update on the PSUR repository Project

***Status:** for discussion and agreement*

12.3.3. Union Reference Date List

- Consultation on the draft List, version July 2014

***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*

12.5. Adverse Drug Reactions reporting and additional reporting

12.5.1. Management and Reporting of Adverse Reactions to Medicinal Products

- Guideline on good pharmacovigilance practices (GVP) Module VI on management and reporting of adverse reactions to medicinal products: Revision of the post-authorisation studies reporting requirements

***Status**: for agreement*

Documents:
For adoption: Revised GVP Module VI

12.5.2. Additional Monitoring

None

12.5.3. List of Product under Additional Monitoring

- Consultation on the draft List, version July 2014

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

None

12.6.2. Changes to EudraVigilance Database and functional specifications

- Project plan on EudraVigilance auditable requirements

Status*: for discussion*

12.6.3. Others

- Revision of the EudraVigilance Access Policy in accordance with Regulation 726/2004

Status*: for discussion*

12.7. Risk Management Plans and Effectiveness of risk Minimisations

12.7.1. Risk Management Systems

None

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

None

12.8. Post-authorisation Safety Studies

12.8.1. Post-Authorisation Safety Studies

None

12.9. Community Procedures

12.9.1. Referral Procedures for Safety Reasons

None

12.10. Risk communication and Transparency

12.10.1. Public Participation in Pharmacovigilance

- Draft rules of procedure on the organisation and conduct of public hearings

***Status**: for discussion and agreement*

Documents:
For discussion: draft rules of procedure for consultation

12.10.2. Safety Communication

None

12.11. Continuous pharmacovigilance

None

12.11.1. Incident Management

None

12.12. Interaction with EMA Committees and Working Parties

12.12.1. Committees

None

12.12.2. Working Parties

None

12.13. Interaction within the EU regulatory network

None

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

- EU Post-Authorisation Studies (PAS) Register - Feedback on Member States' experience

***Status**: for discussion*

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

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

None

12.15. Others

None

13. Any other business

13.1. Regulation on Pharmacovigilance Fees

***Status:** for information*