8 February 2016
EMA/PRAC/94187/2016
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 February 2016

Chair: June Raine – Vice-Chair: Almath Spooner

08 February 2016, 13:00 – 19:00, room 3/A

09 February 2016, 08:30 – 19:00, room 3/A

10 February 2016, 08:30 – 19:00, room 3/A

11 February 2016, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

25 February 2016, 10:00 - 12:00, room 7/B, via Adobe Connect

Health and safety information

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

Disclaimers

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

Of note, this agenda is a working document primarily designed for PRAC members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of 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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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 08-11 February 2016. See February month 2016 PRAC minutes (to be published post March 2016 PRAC meeting).

1.2. Agenda of the meeting of 08-11 February 2016

Action: For adoption

1.3. Minutes of the previous meeting on 11-14 January 2016

Action: For adoption

2. EU referral procedures for safety reasons: urgent EU procedures

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

2.4. Planned public hearings

None

3. EU referral procedures for safety reasons: other EU referral procedures

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

3.3.1. Fusafungine (NAP), nasal and oral solution - EMEA/H/A-31/1420

Applicant: Les Laboratoires Servier, various

PRAC Rapporteur: Julia Pallos; PRAC Co-rapporteur: Jana Mladá

Scope: Review of the benefit-risk balance following notification by Italy of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data
Action: For adoption of a recommendation to CMDh

3.3.2. Natalizumab – TYSABRI (CAP) - EMEA/H/A-20/1416

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski; PRAC Co-rapporteur: Carmela Macchiarulo

Scope: 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
Action: For adoption of a recommendation to CHMP

3.3.3. Sodium-glucose co-transporter-2 (SGLT2) inhibitors: canagliflozin – INVOKANA (CAP); canagliflozin, metformin – VOKANAMET (CAP); dapagliflozin – FORXIGA (CAP); dapagliflozin, metformin – XIGDUO (CAP); empagliflozin - JARDIANCE (CAP); empagliflozin, metformin – SYNJARDY (CAP) - EMEA/H/A-20/1419

Applicant: AstraZeneca AB (Forxiga, Xigduo), Boehringer Ingelheim International GmbH (Jardiance, Synjardy), Janssen-Cilag International N.V. (Invokana, Vokanamet)

PRAC Rapporteur: Menno van der Elst; PRAC Co-rapporteurs: Valerie Strassmann, Qun-Ying Yue

Scope: Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data
Action: For adoption of a recommendation to CHMP

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

None

3.5. Others

None

4. Signals assessment and prioritisation[1]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Rivaroxaban - XARELTO (CAP)

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of spontaneous spinal haematoma
Action: For adoption of PRAC recommendation
EPITT 18606 – New signal
Lead Member State: SE

4.1.2. Sofosbuvir – SOVALDI (CAP)

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Signal of hepatitis B reactivation
Action: For adoption of PRAC recommendation
EPITT 18607– New signal
Lead Member State: UK

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab – HUMIRA (CAP) - EMEA/H/C/000481/SDA/089

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of autoimmune haemolytic anaemia (AIHA) and haemolytic anaemia (HA)
Action: For adoption of PRAC recommendation
EPITT 18447– Follow-up to October 2015

4.3.2. Alogliptin – VIPIDIA (CAP) - EMEA/H/C/0002182/SDA/010; alogliptin, metformin – VIPDOMET (CAP); alogliptin, pioglitazone – INCRESYNC (CAP); linagliptin – TRAJENTA (CAP) - EMEA/H/C/002110/SDA/015; linagliptin, metformin – JENTADUETO (CAP) - EMEA/H/C/002279/SDA/009

Applicant: Boehringer Ingelheim International (Jentadueto, Trajenta), Takeda Pharma A/S (Incresync, Vipdomet, Vipidia)

PRAC Rapporteur: Menno van der Elst

[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

Scope: Signal of arthralgia
Action: For adoption of PRAC recommendation
EPITT 18489 – Follow-up to October 2015

4.3.3. Carbidopa, levodopa (NAP)

Applicant: AbbVie Ltd, various

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of intussusception
Action: For adoption of PRAC recommendation
EPITT 18424 – Follow-up to October 2015

4.3.4. Mitotane – LYSODREN (CAP) – EMEA/H/C/000521/SDA/023

Applicant: Laboratoire HRA Pharma, SA

PRAC Rapporteur: Dolores Montero Corominas

Scope: Signal of sex hormone disturbances and development of ovarian macrocysts
Action: For adoption of PRAC recommendation
EPITT 18301 – Follow-up to October 2015

4.3.5. Peginterferon alfa-2a – PEGASYS (CAP) - EMEA/H/C/000395/SDA/055

Applicant: Roche Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of acquired haemophilia
Action: For adoption of PRAC recommendation
EPITT 18476 – Follow-up to October 2015

4.3.6. Tyrosine kinase inhibitors (TKI): bosutinib – BOSULIF (CAP) -EMEA/H/C/002373/SDA/012; dasatinib - SPRYCEL (CAP) - EMEA/H/C/000709/SDA/042; imatinib – GLIVEC (CAP) - EMEA/H/C/000406/SDA/196; nilotinib – TASIGNA (CAP) - EMEA/H/C/000798/SDA/049; ponatinib – ICLUSIG (CAP) - EMEA/H/C/002695/SDA/013

Applicant: Bristol-Myers Squibb Pharma EEIG (Sprycel), Novartis Europharm Ltd (Glivec, Tasigna), Pfizer Limited (Bosulif), Ariad Pharma Ltd (Iclusig)

PRAC Rapporteur: Dolores Montero Corominas

Scope: Signal of hepatitis B virus (HBV) reactivation
Action: For adoption of PRAC recommendation
EPITT 18405 – Follow-up to September 2015

4.3.7. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/SDA/043

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Signal of pemphigoid
Action: For adoption of PRAC recommendation
EPITT 18469 – Follow-up to October 2015

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Albutrepenonacog alfa - EMEA/H/C/003955, Orphan

Applicant: CSL Behring GmbH

Scope: Prophylaxis and treatment of bleeding in all patients with haemophilia B5.1 RMP - Medicines in pre-authorisation phase
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.2. Amikacin - EMEA/H/C/003936, Orphan

Applicant: Insmed Limited

Scope: Treatment of nontuberculous mycobacterial lung infection
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.3. Autologous CD34$^+$ enriched cell fraction that contains CD34$^+$ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) cDNA sequence - EMEA/H/C/003854, Orphan

Applicant: GlaxoSmithKline Trading Services, ATMP[2]

Scope: Treatment of severe combined immunodeficiency
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.4. Chenodeoxycholic acid - EMEA/H/C/004061, Orphan

Applicant: Sigma-tau Arzneimittel GmbH

Scope: Treatment of inborn errors of primary bile acid synthesis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.5. Chlorhexidine - EMEA/H/W/003799

Scope: Prophylaxis of omphalitis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.6. Ceftazidime, avibactam - EMEA/H/C/004027

Scope: Treatment of complicated intra-abdominal infections (cIAI), complicated urinary-tract infections (cUTI) and nosocomial pneumonia
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.7. Daclizumab - EMEA/H/C/003862

Scope: Treatment of multiple sclerosis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.8. Grazoprevir, elbasivir - EMEA/H/C/004126

Scope: Treatment of chronic hepatitis C (CHC) in adults

[2] Advanced-therapy medicinal product

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.9. Infliximab - EMEA/H/C/004020

Scope: Treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, psoriasis and ulcerative colitis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.10. Irinotecan - EMEA/H/C/004125, Orphan

Applicant: Baxter Innovations GmbH

Scope: Treatment of pancreatic cancer
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.11. Lutetium (^{177}Lu) chloride - EMEA/H/C/003999

Scope: Radiolabelling of carrier molecules specifically developed for radiolabelling with this radionuclide
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.12. Opicapone - EMEA/H/C/002790

Scope: Treatment of Parkinson's disease and motor fluctuations
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.13. Palonosetron - EMEA/H/C/004129

Scope: Prevention of nausea and vomiting associated with cancer chemotherapy
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.14. Palonosetron - EMEA/H/C/004069

Scope: Prevention of nausea and vomiting associated with cancer chemotherapy
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.15. Pancreas powder - EMEA/H/C/002070

Scope: Treatment in exocrine pancreatic insufficiency
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.16. Saxagliptin, dapagliflozin - EMEA/H/C/004057

Scope: Treatment of type 2 diabetes
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.17. Trifluridine, tipiracil - EMEA/H/C/003897

Scope: Treatment of colorectal cancer
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.2. Medicines in the post-authorisation phase – PRAC-led procedures

5.2.1. Bosentan – STAYVEER (CAP) - EMEA/H/C/002644/WS/0899/G; TRACLEER (CAP) - EMEA/H/C/000401/WS/0899/G

Applicant: Marklas Nederlands BV (Stayveer), Actelion Registration Ltd (Tracleer)

PRAC Rapporteur: Isabelle Robine

Scope: Revised RMP in order to align the additional risk minimisation measures of three safety concerns ('pulmonary oedema associated with veno-occlusive disease', 'interaction with sildenafil' and 'interaction with antiretrovirals'), with the requirements defined in Annex II of the Marketing Authorisation. In addition, the RMP is updated in line with the outcome of previous procedures and other corrections
Action: For adoption of PRAC AR

5.2.2. Efavirenz, emtricitabine, tenofovir disoproxil – ATRIPLA (CAP) - EMEA/H/C/000797/WS/0860/G emtricitabine – EMTRIVA (CAP) - EMEA/H/C/000533/WS/0860/G emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA (CAP) - EMEA/H/C/002312/WS/0860/G

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd (Atripla), Gilead Sciences International Ltd (Emtriva, Eviplera)

PRAC Rapporteur: Rafe Suvarna

Scope: Revised RMP following the PRAC review on the 'comprehensive analysis of existing data on lipodystrophy (updated literature data on non-clinical and clinical aspects)' and 'comprehensive analysis of existing data on lactic acidosis (updated literature data on non-clinical and clinical aspects)'
Action: For adoption of PRAC AR

5.2.3. Emtricitabine, tenofovir disoproxil – TRUVADA (CAP) - EMEA/H/C/000594/WS/0903/G tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/WS/0903/G

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Revised RMP to remove 'lactic acidosis with severe hepatomegaly with steatosis' as an important identified risk following the PRAC outcome whereby the warning statements regarding lactic acidosis have been removed from the product information for emtricitabine and tenofovir disoproxil-containing products. In addition, the RMP is revised to remove 'lipodystophy' as an important identified risk following the PRAC outcome on lipodystrophy whereby the warning statements regarding lipodystrophy have been removed from the product information for antiretroviral products. Furthermore, the RMP is amended with the due date for submission of GS-US-236-0103 Week 192 clinical study report from 'Q3 2015' to 'Q1 2016'
Action: For adoption of PRAC AR

5.2.4. Liraglutide – SAXENDA (CAP) - EMEA/H/C/003780/WS/0892; VICTOZA (CAP) - EMEA/H/C/001026/WS/0892

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Revised RMP to change the due date submission of the final study report for the Optum database study (study NN2211-3784) from 'January 2016' to 'August 2016'
Action: For adoption of PRAC AR

5.2.5. Orlistat – ALLI (CAP) - EMEA/H/C/000854/II/0052

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Revised RMP in order to update the safety concerns, pharmacovigilance plan and risk minimisations measures and replace PASS study RH01159 (survey based on the use of a questionnaire handed out by pharmacists at the point of sale) with PASS study 204675 (study comprising an online questionnaire on a series of virtual customers to include both customers who are suitable and unsuitable for alli)
Action: For adoption of PRAC AR

5.2.6. Pertuzumab – PERJETA (CAP) - EMEA/H/C/002547/II/0021/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Revised RMP in order to update the length of the follow-up period of the PERUSE study from 45 to 60 months. Consequently, the due date for study completion is amended to September 2020. Annex II of the product information is updated accordingly. In addition, further to the outcome of PSUSA/10125/201412 procedure concluding on the inclusion of diarrhoea management in the product information, the RMP is updated accordingly
Action: For adoption of PRAC AR

5.2.7. Posaconazole – NOXAFIL (CAP) - EMEA/H/C/000610/II/0040

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Revised RMP (version 12.0) in order to reflect the study results showing a lack of interaction effect of OATP1B1 and OATP1B3 substrates and inhibitors
Action: For adoption of PRAC AR

5.2.8. Velaglucerase alfa – VPRIV (CAP) - EMEA/H/C/001249/II/0029

Applicant: Shire Pharmaceuticals Ireland Ltd.

PRAC Rapporteur: Valerie Strassmann

Scope: Revised RMP (version 9.0) in order to include an additional risk minimisation measure to mitigate the risk of serious infusion related reactions and hypersensitivity reactions in the home setting, such as educational material for healthcare professionals and patients/caregivers and questionnaire (testing request form)
Action: For adoption of PRAC AR

5.2.9. Zoledronic acid – ACLASTA (CAP) - EMEA/H/C/000595/II/0056

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Revised RMP (version 11.0) in order to introduce a patient reminder card as an additional risk minimisation measure for the existing identified risk of osteonecrosis of the

jaw (ONJ) and to propose indicators to measure the effectiveness of this new measure. Furthermore, the clinical trial exposure data from the Aclasta study ZOL446H2301E2 has been updated
Action: For adoption of PRAC AR

5.2.10. Zoledronic acid – ZOMETA (CAP) - EMEA/H/C/000336/II/0069

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Revised RMP in order to reflect the PSUR data approved in procedure EMEA/H/C/PSUSA/00003149/201408 and to introduce a patient reminder card in osteonecrosis of the jaw (ONJ) as an additional risk minimisation measure as well as to propose indicators to measure its effectiveness . The MAH has also taken the opportunity to add to the RMP the targeted follow-up checklist for the identified risk of hypocalcaemia
Action: For adoption of PRAC AR

5.3. Medicines in the post-authorisation phase – CHMP-led procedures

5.3.1. Abatacept – ORENCIA (CAP) - EMEA/H/C/000701/II/0097

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Extension of indication in combination with methotrexate (MTX) in the treatment of adults with rheumatoid arthritis (RA) who have highly active disease with poor prognostic factors not previously treated with MTX. As a consequence, sections 4.1 and 5.1 of the SmPC are updated based on results from the AVERT study (IM101226). The Package Leaflet is updated accordingly. Moreover, the updated RMP version 20 has been submitted
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.2. Afatinib – GIOTRIF (CAP) - EMEA/H/C/002280/II/0012

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) of squamous histology progressing on or after platinum-based chemotherapy for Giotrif. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. Aflibercept – EYLEA (CAP) - EMEA/H/C/002392/II/0027/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Isabelle Robine

Scope: Grouped variations to include: 1) 3-year data of the pivotal trials VIVID-DME and VISTA-DME; 2) protocol T data with a consequential update to section 5.1 of the SmPC . Furthermore, the MAH took the opportunity to condense the SmPC section 4.8 text relating to antiplatelet trialists' collaboration (APTC) as recommended by EMA during II/0018 variation (diabetic macular oedema (DME) 2 year data), to shorten SmPC section 5.1 as committed by the MAH during II/0021 variation (indication myopic choroidal neovascularisation (mCNV)), to align the annexes with the latest QRD templates (version 9.1, June 2015) and to implement minor changes within age-related macular degeneration (AMD) and DME posology sections

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.4. Brentuximab vedotin – ADCETRIS (CAP) - EMEA/H/C/002455/II/030/G

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Update of section 4.4 of the SmPC in order to add a warning on hepatotoxicity, further to the outcome of PSUSA/00010039/201502. The Package Leaflet and RMP are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Update of section 4.4 of the SmPC in order to add a warning on gastrointestinal complications. The Package Leaflet and RMP are updated accordingly. Update of section 4.4 of the SmPC in order to update a warning on pulmonary toxicity, providing examples of pulmonary toxicity diagnoses. The Package Leaflet and RMP are updated accordingly. Update of section 4.8 of the SmPC in order to implement data from the pivotal phase II studies. The RMP is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.5. Cobimetinib – COTELLIC (CAP) - EMEA/H/C/003960/II/0001/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2, 4.8, 5.2 of the SmPC to reflect the results of GP29342, with recommendations for patients with hepatic impairment. In addition, the MAH took the opportunity to correct an alternative use of 'CYP3A' and 'CYP3A4' in sections 4.4, 4.5 of the SmPC in line with previous recommendations. The Package Leaflet is updated accordingly. Furthermore, the MAH submitted results of the in vitro CYP time-dependent inhibition study (study 15-1983)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.6. Conestat alfa – RUCONEST (CAP) - EMEA/H/C/001223/II/0032

Applicant: Pharming Group N.V

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to remove the requirement for testing all new patients for immunoglobulin E (IgE) antibodies against rabbit epithelium (dander) prior to initiation of treatment and the requirement for repeat testing of IgE antibodies to rabbit dander. The Package Leaflet is updated accordingly. Annex II is updated to reflect changes to the educational material. Furthermore, the RMP is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. Empagliflozin – JARDIANCE (CAP) - EMEA/H/C/002677/II/0014

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Miguel-Angel Macia

Scope: Extension of indication to include the prevention of cardiovascular events, based on the final data of the cardiovascular safety phase III clinical trial EMPA-REG OUTCOME. As a consequence, section 4.1 of the SmPC is updated in order to add safety information on this study. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.8. Epoetin alfa – ABSEAMED (CAP) - EMEA/H/C/000727/WS/0877; BINOCRIT (CAP) - EMEA/H/C/000725/WS/0877; EPOETIN ALFA HEXAL (CAP) - EMEA/H/C/000726/WS/0877

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG (Abseamed), Sandoz GmbH (Binocrit), Hexal AG (Epoetin alfa Hexal)

PRAC Rapporteur: Isabelle Robine

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to add a subcutaneously (SC) route of administration in addition to the intravenous route in the treatment of anaemia in patients with chronic renal failure based on clinical study HX575-308 (SENSE) to address MEA 024.1. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make minor editorial changes in the SmPC and to update the list of local representatives in Greece in the Package Leaflet and to bring the product information in line with the latest QRD template version 9.1. Moreover, the RMP (version 15) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.9. Everolimus – AFINITOR (CAP) - EMEA/H/C/001038/II/0048

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the treatment of unresectable or metastatic, well-differentiated non-functional neuroendocrine tumours of gastrointestinal or lung origin in adults with progressive disease for Afinitor. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. Furthermore, the product information is brought in line with the latest QRD template version 9.1
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.10. Everolimus – VOTUBIA (CAP) - EMEA/H/C/002311/II/0039

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 (for dispersible tablets) and section 4.8 and 5.2 (for tablets) of the SmPC in order to update the safety and efficacy information with the data from the final clinical study report (CSR) comprising the extension phase of study M2302 in fulfilment of ANX 027. The Annex II and Package Leaflet are updated accordingly. In addition, update of section 4.2 and 4.4 of the SmPC in order to align the wording with the product information of Afinitor. Furthermore, the MAH took the opportunity to bring the PI in line with the latest QRD template version 9.1. Moreover, the RMP (version 11.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.11. Evolocumab – REPATHA (CAP) - EMEA/H/C/003766/X/0002

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Addition of a new strength of 420 mg (120 mg/mL) for evolocumab solution for injection in cartridge, for subcutaneous (SC) administration by an automated mini-doser device
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.12. Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) – GARDASIL (CAP) - EMEA/H/C/000703/WS/0908; SILGARD (CAP) - EMEA/H/C/000732/WS/0908

Applicant: Sanofi Pasteur MSD SNC (Gardasil), Merck Sharp & Dohme Limited (Silgard)

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 5.1 of the SmPC with long-term data based on the final clinical study report (CSR) for study P018-11, in fulfilment of Article 46 and post-authorisation measures MEA 020.6 and MEA 020.7, as well as interim reports for studies P015-21, P019-21 and P020-21. In addition, the MAH took the opportunity to implement changes related to the latest QRD template v 9.1, in particular, the MAH has combined the SmPC of the pre-filled syringe and the vial presentations, Annex II and labelling. The RMP (version 10.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.13. Ibrutinib – IMBRUVICA (CAP) - EMEA/H/C/003791/II/0013

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Update of SmPC sections 4.8 and 4.9 of the SmPC with information on hepatic failure and hepatotoxicity. The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.14. Ibrutinib – IMBRUVICA (CAP) - EMEA/H/C/003791/II/0017/G

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information following the conclusion of studies MCL 3001 and CLL 3001. Annex II has been updated to remove the obligation to submit the final clinical study report (CSR) of study MCL 3001. The Package Leaflet and RMP are updated accordingly. In addition, the final CSRs for studies MCL 2001 and 1117 are provided in fulfilment of post-authorisation measures. Furthermore, data from two other trials are included in support of the use of ibrutinib in combination with other agents in subjects with relapsed/refractory chronic lymphocytic leukaemia (CLL)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.15. Idelalisib – ZYDELIG (CAP) - EMEA/H/C/003843/II/0011

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Extension of indication to include the combination of idelalisib with ofatumumab. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.16. Idelalisib – ZYDELIG (CAP) - EMEA/H/C/003843/II/0018

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information regarding Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) based on post marketing experience. The Package Leaflet and the RMP (version 1.5) are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.17. Iloprost – VENTAVIS (CAP) - EMEA/H/C/000474/II/0051/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Isabelle Robine

Scope: Grouped variations to introduce an additional nebulizer 'FOX Bavent' for application of Ventavis 10 µg/ mL and Ventavis 20 µg/mL solution, a change of pack sizes within the range of current approved pack sizes as well as consequential changes to SmPC sections 4.2, 4.4, 6.5 and 8, to the labelling and Package Leaflet. In addition, the MAH took the opportunity to delete reference in the product information to nebulizers which are no longer available by the device manufacturer (ProDose and HaloLite), to merge the texts for Ventavis 10 µg/ mL and Ventavis 20 µg/ mL,nebulizer solution into one SmPC and one Package Leaflet text, to update the list of local representatives in the Package Leaflet, to implement minor editorial changes in the annexes and to bring the annexes in line with the latest QRD template version 9.1. The RMP (version 7.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.18. Lumacaftor, ivacaftor – ORKAMBI (CAP) - EMEA/H/C/003954/II/0002

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Update of sections 4.4, 4.8 and 5.1 of SmPC to add information regarding increase of blood pressure and decrease of heart rate following the review of clinical safety data. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.19. Maraviroc – CELSENTRI (CAP) - EMEA/H/C/000811/II/0045/G

Applicant: ViiV Healthcare Uk Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the 148 week final clinical study report (CSR) for study A4001098, a multicentre, randomized, blinded, placebo-controlled study to evaluate the safety of maraviroc in combination with other antiretroviral agents in HIV-1-infected subjects co-infected with Hepatitis C and/or Hepatitis B virus. The RMP (version 10.0) is updated to add information related to study A4001098 and to include modifications requested during variation II/41 (i.e. to remove the associations between study A4001098 and the safety concern 'potential to alter immune function: infection since this concern is not addressed by the study). Moreover, the RMP contains also information on ongoing studies (studies A4001067, POEM and WS324148/CRT115653, CADIRIS). In addition, the due dates for A4001067 (category 3 study) are amended in the RMP
Action: For adoption of PRAC Assessment Report

5.3.20. Olaparib – LYNPARZA (CAP) - EMEA/H/C/003726/II/0001/G

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.4, 4.5 and 4.6 of the SmPC in order to include further information related to pharmacokinetic interactions based on the in vivo interaction study D0816C00008, three in vitro interaction studies (studies ADME-AZS-Wave3-140714, ADME-AZS-Wave3-140725 and 140483) and data from previously submitted interaction studies. The provision of the final clinical study report (CSR) for study D0816C00008 addresses the post-authorisation measure MEA 004. Furthermore, the MAH provided the study report of in vitro study 8305083. In addition, the MAH took the opportunity to add the published ATC code in section 5.1 of the SmPC, and to implement minor editorial changes in the SmPC, labelling and Package Leaflet. The RMP (version 6) is updated accordingly. Further, the MAH is taking the opportunity to update the due dates for the provision of the final study reports of the category 3 studies D0816C00005 and D0816C00006, and to add the new category 3 study D0816C00010
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.21. Panobinostat – FARYDAK (CAP) - EMEA/H/C/003725/II/0001

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of section 5.1 of the SmPC in order to update the safety information with regards to the key secondary endpoint of overall survival in study D2308 to fulfil a post authorisation measure (ANX 001). The Annex II of the product information is updated accordingly to remove the specific obligations. The RMP (version 2.2) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.22. Panobinostat – FARYDAK (CAP) - EMEA/H/C/003725/II/0003

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of section 4.6 of the SmPC in order to update the safety information with a recommendation for pregnancy testing prior to treatment with Farydak, as a cautionary measure. The RMP (version 2.3) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.23. Pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/II/0002

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC with safety and pharmacokinetic (PK) data based on the clinical study report (CSR) of study P006v01. Furthermore, the adverse drug reaction (ADR) Guillain-Barré Syndrome (GBS) is added to sections 4.4 and 4.8 of the SmPC. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to revise the text referring to fatal cases of pneumonitis in section 4.4 of the SmPC, to implement minor editorial changes in the annexes, to align the SmPC, Annex II, labelling and Package Leaflet with the latest QRD template version 9.1, and to update the contact details of the local representative in Luxemburg in the Package Leaflet. The RMP (version 2.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.24. Regorafenib – STIVARGA (CAP) - EMEA/H/C/002573/II/0015/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

Scope: Update of SmPC section 5.1 based on the results from study 15967 (CONSIGN), a phase 3b trial in patients with metastatic colorectal cancer. In addition, the MAH took the opportunity to provide long-term results from study 14874 (GRID addendum clinical study report (CSR)), a pivotal phase 3 trial in patients with gastrointestinal stromal tumour (GIST). The RMP (version 4.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.25. Thiotepa – TEPADINA (CAP) - EMEA/H/C/001046/II/0026

Applicant: Adienne S.r.l. S.U.

PRAC Rapporteur: Corinne Fechant

Scope: Update of section 4.8 of the SmPC in order to update the safety information on leukoencephalopathy. The Package Leaflet is updated accordingly.
In addition, the MAH took the opportunity to make editorial changes in the PI.
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.26. Trastuzumab emtansine – KADCYLA (CAP) - EMEA/H/C/002389/II/0019/G

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Grouped variation to amend Annex II of the product information to delete the obligation regarding the EMILIA (TDM4370g/BO21977) study (ANX 006). Furthermore, update of section 4.8 of the SmPC in order to update frequency of adverse drug reaction as a result of a pool data analysis from several clinical studies. The RMP is updated accordingly, including also changes related to inclusion and deletion of safety concerns in the RMP (enhanced pregnancy programme, evaluation of cardiac safety in patients with baseline left ventricular ejection fraction and efficacy of monotherapy versus trastuzumab associated to docetaxel). In addition, changes of the final clinical study report (CSR) due dates for the KRISTINE study (study BO28408) and the KAMILLA study (study mo28231) have been introduced. The MAH also took the opportunity to update the RMP following requests from previously assessed procedures (MEA 011.1 and ANX 007)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

6. Periodic safety update reports (PSURs)

6.1. PSUR procedures including centrally authorised products (CAPs) only

6.1.1. Aclidinium bromide – BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) - PSUSA/09005/201507

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.2. Aflibercept – ZALTRAP (CAP) - PSUSA/10019/201508

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Ulla Wändel Liminga

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.3. Agalsidase alfa – REPLAGAL (CAP) - PSUSA/00069/201508

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Sabine Straus

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.4. Aripiprazole – ABILIFY (CAP); ABILIFY MAINTENA (CAP) - PSUSA/00234/201507

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Leonor Chambel

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.5. Ataluren – TRANSLARNA (CAP) - PSUSA/10274/201507

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.6. Atazanavir – REYATAZ (CAP) - PSUSA/00258/201506

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Isabelle Robine

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.7. Catridecacog – NOVOTHIRTEEN (CAP) - PSUSA/10034/201507

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Isabelle Robine

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.8. Dapagliflozin, metformin – XIGDUO (CAP) - PSUSA/10294/201507

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.9. Dasabuvir – EXVIERA (CAP) - PSUSA/10363/201507

Applicant: AbbVie Ltd.

PRAC Rapporteur: Miguel-Angel Macia

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.10. Dolutegravir – TIVICAY (CAP); dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - PSUSA/10075/201507

Applicant: ViiV Healthcare (Tivicay), ViiV Healthcare UK Limited (Triumeq)

PRAC Rapporteur: Julie Williams

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.11. Efavirenz, emtricitabine, tenofovir – ATRIPLA (CAP) - PSUSA/01201/201507

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd.

PRAC Rapporteur: Martin Huber

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.12. Eliglustat – CERDELGA (CAP) - PSUSA/10351/201507

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.13. Icatibant – FIRAZYR (CAP) - PSUSA/01714/201507

Applicant: Shire Orphan Therapies GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.14. Idursulfase – ELAPRASE (CAP) - PSUSA/01722/201507

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Rafe Suvarna

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.15. Infliximab – INFLECTRA (CAP), REMSIMA (CAP) - PSUSA/10106/201507

Applicant: Hospira UK Limited (Inflectra), Celltrion Healthcare Hungary Kft. (Remsima)

PRAC Rapporteur: Rafe Suvarna

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.16. Ingenol mebutate – PICATO (CAP) - PSUSA/10035/201507

Applicant: Leo Pharma A/S

PRAC Rapporteur: Julie Williams

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.17. Lipegfilgrastim – LONQUEX (CAP) - PSUSA/10111/201507

Applicant: Sicor Biotech UAB

PRAC Rapporteur: Julie Williams

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.18. Lomitapide – LOJUXTA (CAP) - PSUSA/10112/201507

Applicant: Aegerion Pharmaceuticals Limited

PRAC Rapporteur: Menno van der Elst

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.19. Modified vaccinia ankara virus – IMVANEX (CAP) - PSUSA/10119/201507 (with RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Rafe Suvarna

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.20. Ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP) - PSUSA/10367/201507

Applicant: AbbVie Ltd.

PRAC Rapporteur: Miguel-Angel Macia

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.21. Peginterferon beta-1a – PLEGRIDY (CAP) - PSUSA/10275/201507

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Julie Williams

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.22. Perampanel – FYCOMPA (CAP) - PSUSA/09255/201507

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Julie Williams

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.23. Romiplostim – NPLATE (CAP) - PSUSA/02660/201507

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.24. Rotavirus vaccine live oral monovalent – ROTARIX (CAP) - PSUSA/02665/201507

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.25. Simoctocog alfa – NUWIQ (CAP) - PSUSA/10276/201507

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.26. Telithromycin – KETEK (CAP) - PSUSA/02881/201507

Applicant: Aventis Pharma S.A.

PRAC Rapporteur: Qun-Ying Yue

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.27. Tocofersolan – VEDROP (CAP) - PSUSA/02981/201507 (with RMP)

Applicant: Orphan Europe S.A.R.L.

PRAC Rapporteur: Julie Williams

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.28. Vismodegib – ERIVEDGE (CAP) - PSUSA/10140/201507

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.1.29. Vorapaxar – ZONTIVITY (CAP) - PSUSA/10357/201507

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.2. PSUR procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)

6.2.1. Ibandronic acid monosodium salt, monohydrate – BONDRONAT (CAP); BONVIVA (CAP); NAP - PSUSA/01702/201506

Applicant: Roche Registration Limited, various

PRAC Rapporteur: Doris Stenver

Scope of procedure: Evaluation of a PSUSA procedure
Action: Adoption of recommendation to CHMP

6.3. PSUR procedures including nationally authorised products (NAPs) only

6.3.1. Aciclovir (NAP) - PSUSA/00000048/201506

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.2. Alanine, arginine, aspartic acid, cysteine, glucose anhydrous, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, olive oil refined, ornithine, phenylalanine, proline, serine, sodium chloride, sodium glycerophosphate hydrated, soya bean oil refined, taurine, threonine, tryptophan, tyrosine, valine, potassium acetate, calcium chloride dihydrate, magnesium acetate tetrahydrate (NAP) - PSUSA/00010190/201506

Applicant: various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.3. Bemetizide, triamterene (NAP) - PSUSA/00009076/201506

Applicant: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.4. Cefepime (NAP) - PSUSA/00000593/201506

Applicant: various

PRAC Lead: Margarida Guimarães

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.5. Clonazepam (NAP) - PSUSA/00000812/201506

Applicant: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.6. Daunorubicin (NAP) - PSUSA/00000936/201506

Applicant: various

PRAC Lead: Marianne Lunzer

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.7. Dexchlorpheniramine (NAP) - PSUSA/00000989/201506

Applicant: various

PRAC Lead: Leonor Chambel

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.8. Dihydroergocryptine (NAP) - PSUSA/00001074/201507

Applicant: various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.9. Ethinylestradiol, etonogestrel (NAP) - PSUSA/00001307/201507

Applicant: various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.10. Glibenclamide, metformin hydrochloride (NAP) - PSUSA/00002002/201506

Applicant: various

PRAC Lead: Corinne Fechant

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.11. Human fibrinogen (NAP) - PSUSA/00001624/201506

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.12. Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/201507

Applicant: various

PRAC Lead: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.13. Magnesium sulfate (NAP) - PSUSA/00009225/201506

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.14. Manidipine (NAP) - PSUSA/00001932/201506

Applicant: various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.15. Misoprostol (gastrointestinal indication) (NAP) - PSUSA/00010291/201506

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.16. Nimesulide (systemic formulations) (NAP) - PSUSA/00009236/201506

Applicant: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.17. Nimesulide (topical formulations) (NAP) - PSUSA/00002165/201506

Applicant: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.18. Rabbit anti-human thymocyte (concentrate for solution for infusion) (NAP) - PSUSA/00010252/201506

Applicant: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.19. Rabbit anti-human thymocyte (powder for solution for infusion) (NAP) - PSUSA/00010184/201506

Applicant: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.20. Rupatadine (NAP) - PSUSA/00002673/201506

Applicant: various

PRAC Lead: Miguel-Angel Macia

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.21. Salmon calcitonin, synthetic analogue of eel calcitonin (NAP) - PSUSA/00000494/201506

Applicant: various

PRAC Lead: Miguel-Angel Macia

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.22. Sertindole (NAP) - PSUSA/00002695/201507

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Solifenacin, tamsolusin (NAP) - PSUSA/00010285/201507

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.24. Tiagabine (NAP) - PSUSA/00002942/201506

Applicant: various

PRAC Lead: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.25. Tianeptine (NAP) - PSUSA/00002943/201506

Applicant: various

PRAC Lead: Isabelle Robine

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.26. Urapidil (NAP) - PSUSA/00003078/201507

Applicant: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Botulinum b toxin – NEUROBLOC (CAP) - EMEA/H/C/000301/LEG 062.1

Applicant: Eisai Ltd

PRAC Rapporteur: Leonor Chambel

Scope: MAH's responses to LEG 062 [MAH's response to PSUSA/00000428/201406 following PRAC outcome in February 2015] as adopted in September 2015
Action: For adoption of advice to CHMP

6.4.2. Pregabalin – LYRICA (CAP) - EMEA/H/C/000546/LEG 050; PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/LEG 003

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: MAH's responses to the request included in the recommendation of PSUSA/00002511/201501 adopted in September 2015: on positive de-challenge or re-challenge and temporal association between pregabalin use and the occurrence of hyponatraemia/syndrome of inappropriate antidiuretic hormone (SIADH)
Action: For adoption of advice to CHMP

6.4.3. Repaglinide – NOVONORM (CAP) - EMEA/H/C/000187/LEG 018; PRANDIN (CAP) - EMEA/H/C/000362/LEG 018

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to the request included in the recommendation of PSUSA/00002618/201412 adopted in September 2015 on the interaction between repaglinide and clopidogrel
Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[3]

7.1.1. Dexamfetamine (NAP) - EMEA/H/N/PSP/0018.2

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG.

PRAC Rapporteur: Julie Williams

Scope: Revised protocol for a PASS to evaluate the long-term safety profile of dexamfetamine in children with attention deficit hyperactivity disorder (ADHD), specifically targeting key issues such as cardiovascular events, growth and psychiatric related adverse events
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.2. Dinutuximab – UNITUXIN (CAP) - EMEA/H/C/PSP/0035

Applicant: United Therapeutics Europe Limited

PRAC Rapporteur: Sabine Straus

Scope: Protocol for a PASS registry to evaluate the long-term safety outcomes of dinutuximab in high-risk neuroblastoma patients (including central and peripheral nervous system, prevalence of organ dysfunction, long-term effects on growth and endocrine development, hearing loss, cardiac toxicity and survival data)
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.3. Sebelipase alfa – KANUMA (CAP) - EMEA/H/C/PSP/0036

Applicant: Alexion Europe SAS

PRAC Rapporteur: Qun-Ying Yue

Scope: Protocol for a PASS: a non-interventional, multicentre, prospective disease and clinical outcome registry of patients with lysosomal acid lipase deficiency (LAL-D) to further understand the disease, its progression and any associated complication, and to evaluate the long-term efficacy (normalisation of hepatic function) and safety of Kanuma (in

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

particular hypersensitivity reactions, including anaphylaxis, and anti-drug antibodies development potentially impacting response to drug)
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[4]

7.2.1. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/003718/MEA/005.1

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Updated PASS protocol for a knowledge survey to assess the effectiveness of educational materials among healthcare professionals who prescribe alemtuzumab
Action: For adoption of advice to CHMP

7.2.2. Alglucosidase alfa – MYOZYME (CAP) - EMEA/H/C/000636/MEA/053.2

Applicant: Genzyme Europe BV

PRAC Rapporteur: Isabelle Robine

Scope: MAH's responses to MEA 053.1 [PASS study ALGMYC07390 protocol 'prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reaction'] as per the request for supplementary information (RSI) as adopted in December 2015
Action: For adoption of advice to CHMP

7.2.3. Apremilast – OTEZLA (CAP) - EMEA/H/C/003746/MEA/006.1

Applicant: Celgene Europe Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to MEA 006 [revised PASS protocol for CPRD (UK) data analysis for PsA and psoriasis] as per the request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.2.4. Eliglustat – CERDELGA (CAP) - EMEA/H/C/003724/MEA/005.2

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's revised protocol and responses to MEA 005.1 [PASS protocol for the drug utilisation study (DUS) of eliglustat for the treatment of Gaucher disease in Europe using electronic healthcare records] to address the PRAC's request for supplementary information (RSI) adopted in September 2015
Action: For adoption of advice to CHMP

7.2.5. Eliglustat – CERDELGA (CAP) - EMEA/H/C/003724/MEA/006.1

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

[4] 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

Scope: MAH's revised protocol and responses to MEA 006 [PASS protocol for the drug utilisation study (DUS) of eliglustat for the treatment of Gaucher disease in the US population using MarketScan database] to address the PRAC's request for supplementary information (RSI) adopted in September 2015
Action: For adoption of advice to CHMP

7.2.6. Fenofibrate, simvastatin – CHOLIB (CAP) - EMEA/H/C/002559/MEA/002.2

Applicant: BGP Products Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 002.1 [revised PASS protocol for study ABT285.E.001: a drug utilisation research (DUR) study on the use of fenofibrate and simvastatin fixed combination: a European multinational study using secondary health records databases], as per the request for supplementary information (RSI) as adopted in October 2014
Action: For adoption of advice to CHMP

7.2.7. Human normal immunoglobulin – HYQVIA (CAP) - EMEA/H/C/002491/MEA/004.2

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's responses to MEA 004 [Pregnancy registry PASS protocol (study 161301)] as per the request for supplementary information (RSI) as adopted in September 2013
Action: For adoption of advice to CHMP

7.2.8. Hydrocortisone – PLENADREN (CAP) - EMEA/H/C/002185/MEA/005.2

Applicant: Shire Services BVBA

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's responses to MEA 005.1 [PASS protocol for study SWE-DUS, study no.: 10918 -404 (SHP617-404): a Swedish, retrospective, study progress reports to be provided on a yearly basis evaluating the pattern of Plenadren use from as part of the PSURs Swedish quality registries], as per the request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.2.9. Liraglutide – SAXENDA (CAP) - EMEA/H/C/003780/MEA/014.1

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 014 [Drug utilisation study (DUS) protocol (study NN8022-4241): in-market utilisation of liraglutide used for weight management in Europe: a retrospective medical record review study], as per the request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.2.10. Liraglutide – SAXENDA (CAP) - EMEA/H/C/003780/MEA/015.1

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 015 [Drug utilisation study (DUS) protocol (study NN8022-4246): in-market utilisation of liraglutide used for weight management in the UK: a study in the CPRD primary care database], as per the request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.2.11. Olaparib – LYNPARZA (CAP) - EMEA/H/C/003726/MEA/011.2

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Revised protocol for a PASS to collect and/or retrieve prospective data from sizeable patient cohorts with ovarian cancer] following MAH's responses to MEA 011.1 request for supplementary information (RSI) as adopted in November 2015
Action: For adoption of advice to CHMP

7.2.12. Rituximab – MABTHERA (CAP) - EMEA/H/C/000165/MEA/093.1

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Revised PASS registry protocol for a long-term surveillance study of rituximab (Mabthera)-treated patients with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) following MAH's responses to MEA 093 request for supplementary information (RSI)
Action: For adoption of advice to CHMP

7.2.13. Sonidegib – ODOMZO (CAP) - EMEA/H/C/002839/MEA/021

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Protocol for study CLDE225A2404: a non-interventional, multi-national, multi-centre PASS to assess the long-term safety and tolerability of Odomzo (sonidegib) administered in patients with locally advanced basal cell carcinoma (laBCC)
Action: For adoption of advice to CHMP

7.2.14. Tenofovir disoproxil– VIREAD (CAP) - EMEA/H/C/000419/MEA/273.1

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Isabelle Robine

Scope: MAH's responses to MEA 0273 [draft protocol for PASS study GS-EU-174-1846: a multicentre, non-interventional, retrospective cohort study of patients with chronic hepatitis B and with moderate or severe renal impairment treated with Viread], as per the request for supplementary information (RSI) as adopted in December 2015
Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[5]

7.3.1. Trimetazidine (NAP) - EMEA/H/N/PSR/0001

Applicant: Les Laboratoires Servier

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

PRAC Rapporteur: Dolores Montero Corominas

Scope: Results of a drug utilisation study (DUS) in five European countries, using cross sectional analysis, to assess the extent of prescriptions of trimetazidine for its withdrawn ophthalmological and/or ear, nose and throat (ENT) indications among general practitioners, ophthalmologists and ENT specialists
Action: For adoption of a recommendation to CMDh

7.3.2. Trimetazidine (NAP) - EMEA/H/N/PSR/0002

Applicant: Lupin (Europe) Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Results of a drug utilisation study (DUS): a joint PASS survey among healthcare professionals to assess knowledge and attitudes on prescribing conditions of trimetazidine in Bulgaria, Czech Republic, Estonia, France, Hungary, Latvia, Lithuania, Poland, Portugal, Romania, Slovakia, and Spain; results of a database DUS: trimetazidine drug utilization study in European countries using databases – analysis for France, Hungary, Romania and Spain
Action: For adoption of a recommendation to CMDh

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

7.4.1. Agomelatine – THYMANAX (CAP) - EMEA/H/C/000916/II/0028

Applicant: Servier (Ireland) Industries Ltd.

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Submission of the final report of PASS study CLE-20098- 068: an 'observational cohort study to evaluate the safety of agomelatine in standard medical practice in depressed patients: a prospective, observational (non-interventional), international, multicentre cohort study' to fulfil a post-authorisation measure (MEA 06)
Action: For adoption of PRAC Assessment Report

7.4.2. Agomelatine – VALDOXAN (CAP) - EMEA/H/C/000915/II/0030

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Submission of results from an observational cohort study to evaluate the safety of agomelatine in standard medical practice in depressed patients, to fulfil a post-authorisation measure agreed in the RMP (MEA 006)
Action: For adoption of PRAC Assessment Report

7.4.3. Anidulafungin – ECALTA (CAP) - EMEA/H/C/000788/II/0030

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of final results of study A8851030: a retrospective cohort study of the risk of severe hepatic injury in hospitalised patients treated with echinocandins for candida infections, to fulfil a post-authorisation measure (MEA 023.10)
Action: For adoption of PRAC Assessment Report

[6] 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

7.4.4. Dabigatran etexilate – PRADAXA (CAP) - EMEA/H/C/000829/II/0091/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of a group of variations containing 1) the final clinical study report (CSR) for 1160.118: an 'observational cohort study to evaluate the safety and efficacy of switching from Lovenox (enoxaparin) 40 mg to Pradaxa (dabigatran etexilate) 220 mg in patients undergoing elective total hip or knee replacement surgery' and consequent update of the RMP and 2) update of the timeline for availability of study 1160.144 report
Action: For adoption of PRAC Assessment Report

7.4.5. Ipilimumab – YERVOY (CAP) - EMEA/H/C/002213/II/0038

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Submission of the final study report for study CA184242: risk minimisation tool effectiveness evaluation survey. The RMP (version 12) is updated accordingly
Action: For adoption of PRAC Assessment Report

7.4.6. Memantine – AXURA (CAP) - EMEA/H/C/000378/WS/0804; EBIXA (CAP) - EMEA/H/C/000463/WS/0804; MEMANTINE MERZ (CAP) - EMEA/H/C/002711/WS/0804

Applicant: Merz Pharmaceuticals GmbH (Axura, Memantine Herz), H. Lundbeck A/S (Ebixa)

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final results of a non-interventional PASS to examine the use of memantine and risk of prostate cancer (nationwide case-control studies in Denmark and Sweden) in order to fulfil MEA 031.5. The RMP (version 8.0) has been updated to: 1) delete the important potential risk 'prostate cancer' based on the results of case control studies, 2) delete the important identified risk 'overdose with pump device' based on the PSUR#16 PRAC outcome and 3) update clinical trial exposure and post-authorisation experience
Action: For adoption of PRAC Assessment Report

7.4.7. Pioglitazone – ACTOS (CAP) - EMEA/H/C/000285/WS/0827; GLUSTIN (CAP) - EMEA/H/C/000286/WS/0827
pioglitazone, glimepiride – TANDEMACT (CAP) - EMEA/H/C/000680/WS/0827
pioglitazone, metformin – COMPETACT (CAP) - EMEA/H/C/000655/WS/0827; GLUBRAVA (CAP) - EMEA/H/C/000893/WS/0827

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Submission of the final results from observational study PROactive together with post-hoc analysis of Kaiser Permanente Northern California (KPNC) and comprehensive review of the data on prostate cancer risk. The RMP is updated accordingly
Action: For adoption of PRAC Assessment Report

7.4.8. Temozolomide – TEMODAL (CAP) - EMEA/H/C/000229/II/0075

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final results from study MK 7365-295: an observational PASS regarding Temodal and severe acute liver injury in brain cancer patient
Action: For adoption of PRAC Assessment Report

7.4.9. Ticagrelor – BRILIQUE (CAP) - EMEA/H/C/001241/II/0031

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Submission of a final study report for a drug utilisation study (DUS) to fulfil a post-authorisation measure (MEA 008): detailed description of patients who are prescribed ticagrelor for the first time and comparison with patients who are prescribed clopidogrel and prasugrel for the first time, with an estimation of the potential off-label use of ticagrelor. The study also aims to ascertain incident cases and estimate the crude incidence rate of selected safety outcomes among new users in the three cohorts of ticagrelor, clopidogrel and prasugrel
Action: For adoption of PRAC Assessment Report

7.5. Interim results of imposed and non-imposed PASS submitted before the entry into force of the revised variation regulation[7]

7.5.1. Aflibercept – ZALTRAP (CAP) - EMEA/H/C/002532/MEA/003.3

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second status report of PASS study AFLIBC06660: a drug utilisation study (DUS) to address potential for off-label use and particularly intravitreal off-label use using European databases
Action: For adoption of advice to CHMP

7.5.2. Apixaban – ELIQUIS (CAP) - EMEA/H/C/002148/MEA/012.4

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 012.3 [second interim report on a drug utilisation study (DUS) to monitor the potential off label use with apixaban: study of the utilisation patterns in Sweden (study B066017) and in the Netherlands (study B066018)] as per the request for supplementary information (RSI) as adopted at CHMP in September 2015
Action: For adoption of advice to CHMP

7.5.3. Canagliflozin – INVOKANA (CAP) - EMEA/H/C/002649/MEA/005.4

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: MAH's responses to MEA 005.2 [canagliflozin independent data monitoring committee (IDMC) status reports for the DIA3008 CANVAS study], as per the request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

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

7.5.4. Canagliflozin – INVOKANA (CAP) - EMEA/H/C/002649/MEA/005.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: MAH's responses to MEA 005.3 [six-monthly status report of the canagliflozin independent data monitoring committee (IDMC) for the DIA3008 CANVAS study as requested in the RMP additional pharmacovigilance activity], as per the request for supplementary information (RSI) adopted in September 2015
Action: For adoption of advice to CHMP

7.5.5. Canagliflozin – INVOKANA (CAP) - EMEA/H/C/002649/MEA/006.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: MAH's responses to MEA 006 [first status report of the canagliflozin independent data monitoring committee (IDMC) for the NE-3001 CREDENCE study as requested in the RMP additional pharmacovigilance activity], as per the request for supplementary information (RSI) adopted in September 2015
Action: For adoption of advice to CHMP

7.5.6. Canagliflozin, metformin – VOKANAMET (CAP) - EMEA/H/C/002656/MEA/004.4

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 004.2 [canagliflozin independent data monitoring committee (IDMC) status reports for the DIA3008 CANVAS study], as per the request for supplementary information (RSI) adopted in September 2015
Action: For adoption of advice to CHMP

7.5.7. Canagliflozin, metformin – VOKANAMET (CAP) - EMEA/H/C/002656/MEA/004.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 004.3 [Six-monthly status report of the canagliflozin independent data monitoring committee (IDMC) for the DIA3008 CANVAS study as requested in the RMP additional pharmacovigilance activity], as per the request for supplementary information (RSI) adopted in September 2015
Action: For adoption of advice to CHMP

7.5.8. Canagliflozin, metformin – VOKANAMET (CAP) - EMEA/H/C/002656/MEA/005.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 005 [first status report of the canagliflozin independent data monitoring committee (IDMC) for the NE-3001 CREDENCE study as requested in the RMP additional pharmacovigilance activity], as per request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.5.9. Efavirenz – SUSTIVA (CAP) - EMEA/H/C/000249/MEA/079.3

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Margarida Guimarães

Scope: MAH's responses to MEA 079.2 [second annual report for malignant events associated with efavirenz: diagnostic consulting network (DCN) report dated June 2015] as per the request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.5.10. Efavirenz, emtricitabine, tenofovir disoproxil – ATRIPLA (CAP) - EMEA/H/C/000797/MEA/039.3

Applicant: Bristol-Myers Squibb and Gilead Sciences Ltd.

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 039.2 [second annual report for malignant events associated with efavirenz: diagnostic consulting network (DCN) report dated June 2015] as per the request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.5.11. Etanercept – ENBREL (CAP) - EMEA/H/C/000262/MEA/166

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Interim analysis report of study B1801023: an open-label extension study to assess the long-term safety and clinical benefit of etanercept in children and adolescents with extended oligoarticular juvenile idiopathic arthritis, enthesitis-related arthritis, or psoriatic arthritis who were previously enrolled in protocol 0881A1-3338-WW (B1801014)
Action: For adoption of advice to CHMP

7.5.12. Filgrastim – FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA/007.1; ZARZIO (CAP) - EMEA/H/C/000917/MEA/007.1

Applicant: Sandoz GmbH

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 007 [Submission of fourth interim report of study EP06-501 after four years of treatment: a non-interventional, prospective, long-term observational study to assess the safety and effectiveness of Zarzio/Filgrastim Hexal administered to healthy unrelated stem cell donors for peripheral blood progenitor cell mobilisation], as per the request for supplementary information (RSI) as adopted in September 2015
Action: For adoption of advice to CHMP

7.5.13. Filgrastim – RATIOGRASTIM (CAP) - EMEA/H/C/000825/MEA/019.2

Applicant: Ratiopharm GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Third annual report on safety data concerning suspected cases of immunogenicity including adverse drug reaction data from all sources including spontaneous reports and reports from the severe chronic neutropenia international registry (SCNIR)
Action: For adoption of advice to CHMP

7.5.14. Filgrastim – TEVAGRASTIM (CAP) - EMEA/H/C/000827/MEA/019.2

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Third annual report on safety data concerning suspected cases of immunogenicity including adverse drug reaction data from all sources including spontaneous reports and reports from the severe chronic neutropenia international registry (SCNIR)
Action: For adoption of advice to CHMP

7.5.15. Somatropin – OMNITROPE (CAP) - EMEA/H/C/000607/MEA/012.1

Applicant: Sandoz GmbH

PRAC Rapporteur: Sabine Straus

Scope: Interim report for study EP00-502 – PATRO Adults: a non-interventional post-marketing surveillance in adult patients with growth hormone deficiency treated with Omnitrope within routine clinical practice in Europe
Action: For adoption of advice to CHMP

7.5.16. Strontium ranelate – OSSEOR (CAP) - EMEA/H/C/000561/ANX/039; PROTELOS (CAP) - EMEA/H/C/000560/ANX/039

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: First annual report for an imposed non-interventional safety study to evaluate the effectiveness of the applied risk minimisation measures, including a description of the treated patient population in everyday clinical practice (reference to EMEA/H/C/PSP/j/0013.1 – ANX 034)
Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Pegaptanib sodium – MACUGEN (CAP) - EMEA/H/C/000620/LEG 049

Applicant: PharmaSwiss Ceska Republika s.r.o

PRAC Rapporteur: Jean-Michel Dogné

Scope: Cumulative review of the available data for systemic exposure and adverse events with Macugen [from R/62]
Action: For adoption of advice to CHMP

7.6.2. Vernakalant – BRINAVESS (CAP) - EMEA/H/C/001215/LEG 025.1

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to LEG 025 [From II/09: requirement to promptly inform the CHMP of any future serious cases of hypotension, with or without fatal outcome. Such case reports will be accompanied by a causality assessment. With this LEG the MAH provides the details including the causality assessment of a hypotension case related to Brinavess], request for supplementary information (RSI) as adopted in July 2015
Action: For adoption of advice to CHMP

7.7. New Scientific Advice

Disclosure of information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

7.8. Ongoing Scientific Advice

Disclosure of information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

7.9. Final Scientific Advice (Reports and Scientific Advice letters)

Disclosure of information related to this section cannot be released at the present time as it is deemed to contain commercially confidential information.

8. Renewals of the marketing authorisation, conditional renewal and annual reassessments

8.1. Annual reassessments of the marketing authorisation

8.1.1. Anagrelide – XAGRID (CAP) - EMEA/H/C/000480/S/0072 (without RMP)

Applicant: Shire Pharmaceutical Contracts Ltd

PRAC Rapporteur: Corinne Fechant

Scope: Annual reassessment of the marketing authorisation
Action: For adoption of advice to CHMP

8.1.2. Antithrombin alfa – ATRYN (CAP) - EMEA/H/C/000587/S/00026 (without RMP)

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Isabelle Robine

Scope: Annual reassessment of the marketing authorisation
Action: For adoption of advice to CHMP

8.1.3. Histamine dihydrochloride – CEPLENE (CAP) - EMEA/H/C/000796/S/0026 (without RMP)

Applicant: Meda AB

PRAC Rapporteur: Almath Spooner

Scope: Annual reassessment of the marketing authorisation
Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

None

8.3. Renewals of the marketing authorisation

8.3.1. Antithrombin alfa – ATRYN (CAP) - EMEA/H/C/000587/R/0024 (without RMP)

Applicant: GTC Biotherapeutics UK Limited

PRAC Rapporteur: Isabelle Robine

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.2. Deferasirox – EXJADE (CAP) - EMEA/H/C/000670/R/0047 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Corinne Fechant

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.3. Entacapone – ENTACAPONE ORION (CAP) - EMEA/H/C/002440/R/00011 (without RMP)

Applicant: Orion Corporation

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.4. Ibandronic acid – IBANDRONIC ACID SANDOZ (CAP) - EMEA/H/C/002367/R/0017 (with RMP)

Applicant: Sandoz GmbH

PRAC Rapporteur: Doris Stenver

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.5. Ipilimumab – YERVOY (CAP) - EMEA/H/C/002213/R/0035 (with/without RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.6. Levetiracetam – LEVETIRACETAM RATIOPHARM (CAP) - EMEA/H/C/002244/R/0014 (without RMP)

Applicant: Ratiopharm GmbH

PRAC Rapporteur: Veerle Verlinden

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.7. Natalizumab – TYSABRI (CAP) - EMEA/H/C/000603/R/0091 (with RMP)

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.8. Nomegestrol, estradiol – ZOELY (CAP) - EMEA/H/C/001213/R/0032 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Corinne Fechant

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.9. Pioglitazone, metformin – COMPETACT (CAP) - EMEA/H/C/000655/R/0057 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.10. Temozolomide – TEMOZOLOMIDE SUN (CAP) - EMEA/H/C/002198/R/0019 (without RMP)

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

None

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

None

10.3. Other requests

None

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

11.2.1. Bosentan - NL/H/3407/001-2/DC, NL/H/3421/001-2/DC, NL/H/3422/001-2/DC

Applicant: Welding GmbH & Co

PRAC Lead: Menno van der Elst

Scope: PRAC consultation on the evaluation of initial marketing authorisation applications under the decentralised procedure for a generic medicinal product in order to consider the need for additional pharmacovigilance activities to reduce the number of new digital ulcers in patients with systemic sclerosis and ongoing digital ulcer disease
Action: For adoption of advice to Member States

11.2.2. Iron for intravenous (IV) use (NAP)

Applicant: various

PRAC Lead: Corinne Fechant

Scope: PRAC consultation on the evaluation of a PASS feasibility study: evaluation of European databases for studies evaluating the risk of hypersensitivity reactions in users of intravenous iron compounds (database feasibility evaluation report), literature review of ferumoxytol and other IV iron containing medicinal products and hypersensitivity reactions, annual cumulative reviews of hypersensitivity reactions for IV iron-containing medicinal products
Action: For adoption of advice to Member States

11.2.3. Trimetazidine (NAP)

Applicant: Les Laboratoires Servier (Vastarel)

PRAC Lead: Dolores Montero Corominas

Scope: PRAC consultation on the: 1) evaluation of interim study results for a nested case-control study based on data from the registry of the European Society of Cardiology to evaluate of the risk of extra-pyramidal syndrome (EPS) in patients with a chronic ischemic cardiovascular disease (CICD) taking trimetazidine; 2) feasibility study report using the SIDIAP[8] database to assess the feasibility for a PASS on the potential association of extrapiramidal symptoms with trimetazidine
Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh

None

12.3. Coordination with EMA Working Parties/Working Groups/Drafting Groups

12.3.1. EMA workshop on the role of pharmacokinetic and pharmacodynamic measurements in the use of direct oral anticoagulants (DOAC) held on 23 November 2015 – feedback

PRAC lead: Jean-Michel Dogné
Action: For discussion

12.3.2. Enhanced early dialogue to foster development and facilitate accelerated assessment: PRIME project

Action: For discussion

12.3.3. Scientific Advice Working Party (SAWP) – consultation procedure: criteria and process

Action: For discussion

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

None

[8] Information system for the development of primary care research

12.6. Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee

12.6.1. Innovative Medicines Initiative (IMI)2 Patient Preferences in benefit risk assessment during the life cycle – potential for PRAC participation

Action: For discussion

12.7. PRAC work plan

12.7.1. PRAC work plan 2016

Action: For adoption

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

12.10. Periodic safety update reports (PSURs) & Union reference date (EURD) list

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst; Margarida Guimarães
Action: For discussion

12.10.3. PSURs repository

None

12.10.4. Union reference date list – consultation on the draft list

Action: For adoption of the revised list

12.10.5. Project and Maintenance Group (PMG) 2 - common understanding on EU PSUR single assessment: Joint PRAC/CMDh recommendation paper - draft

PRAC lead: Margarida Guimarães; Menno van der Elst; Jolanta Gulbinovic
Action: For discussion

12.11. Signal management

12.11.1. Signal management – feedback from Signal Management Review Technical (SMART) Working Group

PRAC lead: Sabine Straus
Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

12.12.3. List of products under additional monitoring – consultation on the draft list

Action: For adoption of the list

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality - EudraVigilance auditable requirement project update – external testing plan

Action: For adoption

12.13.1. EudraVigilance – annual report 2015

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

12.14.2. Risk Management Plan (RMP) revised assessment process for initial marketing authorisation(s) - performance indicators

Action: For discussion

12.14.3. Tools, educational materials and effectiveness measurement of risk minimisations

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Direct oral anticoagulants (DOACs) – proposal for an EMA funded study on the risk of major bleeding

Action: For discussion

See also under 12.3.1.

12.15.2. Post-authorisation Safety Studies – imposed PASS

None

12.15.3. Post-authorisation Safety Studies – non-imposed PASS

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Effects tables in selected important benefit/risk reviews

PRAC lead: Rafe Suvarna
Action: For discussion

12.19.2. Incident management

None

12.20. Others

12.20.1. Initial marketing authorisation(s) - revised accelerated assessment procedural timetables – follow up

PRAC lead: Ulla Wändel Liminga
Action: For discussion

12.20.2. Pharmacovigilance operation and implementation - streamlined governance structure - finalisation

Action: For adoption

12.20.3. Strategy on impact of pharmacovigilance - PRAC interest group (IG) mandate

Action: For adoption

13. Any other business

14. 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/