08 June 2015
EMA/PRAC/386470/2015
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 June 2015

Chair: June Raine – Vice-Chair: Almath Spooner

08 June 2015, 13:00 – 19:00, room 3/A

09 June 2015, 08:30 – 19:00, room 3/A

10 June 2015, 08:30 – 19:00, room 3/A

11 June 2015, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

25 June 2015, 10:00 – 12:00, room 6/B, via teleconference

Health and safety information

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

Disclaimers

Some of the information contained in this agenda is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scopes listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also 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.

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 8-11 June 2015. See (current) June 2015 PRAC minutes (to be published post July 2015 PRAC meeting).

1.2. Adoption of agenda of the meeting of 8-11 June 2015

1.3. Adoption of minutes of the previous meeting of 4-7 May 2015

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

2.4. Planned public hearings

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Inhaled corticosteroids (ICS)-containing medicinal products indicated in the treatment of chronic obstructive pulmonary disease: beclomethasone (NAP); beclomethasone, formoterol (NAP); budesonide (NAP); budesonide, formoterol – BIRESP SPIROMAX (CAP); BUDESONIDE FORMOTEROL TEVA (CAP); DUORESP SPIROMAX (CAP); VYALER SPIROMAX (CAP); flunisolide, salbutamol (NAP); fluticasone (NAP); fluticasone, salmeterol (NAP); fluticasone, vilanterol – RELVAR ELLIPTA (CAP); REVINTY ELLIPTA (CAP) – EMEA/H/A-31/1415

Applicant: Glaxo Group Ltd, Teva Pharma B.V., Teva Pharmaceuticals Europe, various

PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Jan Neuhauser

Scope: Review of the benefit-risk balance following notification by the European Commission of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data
Action: For discussion of a MAH's request for extension of timetable

3.3. Procedures for finalisation

None

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

None

3.5. Others

None

4. Signals assessment and prioritisation[1]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Anakinra - KINERET (CAP)

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Torbjorn Callreus

Scope: Signal of thrombocytopenia
Action: For adoption of PRAC recommendation
EPITT 18337 – New signal
Lead Member State: DK

4.1.2. Boceprevir – VICTRELIS (CAP)

Applicant: Merck Sharp & Dohme Limited

[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

PRAC Rapporteur: Isabelle Robine

Scope: Signal of hyponatraemia
Action: For adoption of PRAC recommendation
EPITT 18350 – New signal
Lead Member State: FR

4.1.3. Canagliflozin – INVOKANA (CAP); canagliflozin, metformin – VOKANAMET (CAP); dapagliflozin – FORXIGA (CAP); dapagliflozin, metformin – XIGDUO (CAP); empagliflozin - JARDIANCE (CAP); empagliflozin, metformin – SYNJARDY (CAP)

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

PRAC Rapporteur: To be appointed

Scope: Signal of diabetic ketoacidosis
Action: For adoption of PRAC recommendation
EPITT 18375 – New signal
Lead Member States: DE, ES, SE

4.1.4. Enfuvirtide – FUZEON (CAP)

Applicant: Roche Registration Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of amyloidosis
Action: For adoption of PRAC recommendation
EPITT 18347– New signal
Lead Member State: SE

4.1.5. HMG-CoA reductase inhibitors: Atorvastatin (NAP); fluvastatin (NAP); lovastatin (NAP); pitavastatin (NAP); pravastatin (NAP); pravastatin, fenofibrate - PRAVAFENIX (CAP); rosuvastatin (NAP); simvastatin (NAP); simvastatin, fenofibrate - CHOLIB (CAP)

Applicant: BGP Products Ltd (Cholib), Laboratoires SMB S.A. (Pravafenix), various

PRAC Rapporteur: To be appointed

Scope: Signal of lichenoid drug eruption
Action: For adoption of PRAC recommendation
EPITT 18299 – New signal
Lead Member States: CZ, DE, ES, FR, IE, NL, UK

4.1.6. Nalmefene - SELINCRO (CAP)

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Martin Huber

Scope: Signal of suicidal ideation
Action: For adoption of PRAC recommendation
EPITT 18333 – New signal
Lead Member State: DE

4.1.7. Oxybutynin – KENTERA (CAP)

Applicant: Nicobrand Limited

PRAC Rapporteur: Veerle Verlinden

Scope: Signal of psychiatric disorders
Action: For adoption of PRAC recommendation
EPITT 18342 – New signal
Lead Member State: BE

4.1.8. Pertuzumab – PERJETA (CAP)

Applicant: Roche Registration Ltd

PRAC Rapporteur: Doris Stenver

Scope: Signal of acute renal failure
Action: For adoption of PRAC recommendation
EPITT 18322 – New signal
Lead Member State: DK

4.2. New signals detected from other sources

4.2.1. Pregabalin - LYRICA (CAP)

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Signal of hyponatremia and syndrome of inappropriate antidiuretic hormone (SIADH)
Action: For adoption of PRAC recommendation
EPITT 18334 – New signal
Lead Member States: NL

4.3. Signals follow-up and prioritisation

4.3.1. Clopidogrel – ISCOVER (CAP), PLAVIX (CAP); prasugrel – EFIENT (CAP)

Applicant: Eli Lilly Nederland B.V. (Efient), Sanofi-aventis groupe (Iscover), Sanofi Clir SNC (Plavix)

PRAC Rapporteur: Margarida Guimarães

Scope: Signal of safety of dual antiplatelet therapy
Action: For discussion
EPITT 18184 – Follow-up to January 2015

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

Applicant: Bayer, Sanofi, various

PRAC Rapporteur: Martin Huber
EMA resources: SML: Julie Durand, EPL: Not applicable

Scope: Signal of retinal detachment
Action: For adoption of PRAC recommendation
EPITT 15914 – Follow-up to June 2014

4.3.3. Hormone replacement therapy medicinal products containing oestrogens or oestrogens and progestogens in combination (NAP); bazedoxifene, oestrogens conjugated – DUAVIVE (CAP)

Applicant: Pfizer Limited (Duavive), various

PRAC Rapporteur: Menno van der Elst

Scope: Signal of increased risk of ovarian cancer
Action: For adoption of PRAC recommendation
EPITT 18258 – Follow-up to April 2015

4.3.4. Paliperidone – INVEGA (CAP) – EMEA/H/C/000746/SDA/023, XEPLION (CAP) - EMEA/H/C/0002105/SDA/012

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of acute renal failure
Action: For adoption of PRAC recommendation
EPITT 18102 – Follow-up to November 2014

4.3.5. Teriparatide – FORSTEO (CAP) – EMEA/H/C/000425/SDA/051

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Signal of angina pectoris
Action: For adoption of PRAC recommendation
EPITT 18203 – Follow-up to February 2015

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

Applicant: Insmed Limited

Scope: Treatment of nontuberculous mycobacterial (NTM) lung infections in adult patients and management of chronic pulmonary infections due to *Pseudomonas aeruginosa* in patients with cysticfibrosis (CF) aged 6 years and older
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.2. Amlodipine, valsartan - EMEA/H/C/004037, Generic

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

5.1.3. Aripiprazole - EMEA/H/C/004008, Generic

Scope: Treatment of schizophrenia and treatment and prevention of manic episodes in bipolar I disorder
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.4. Asfotase alfa - EMEA/H/C/003794

Scope: Treatment of paediatric-onset hypophosphatasia
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.5. Carfilzomib - EMEA/H/C/003790, Orphan

Applicant: Amgen Europe B.V.

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

5.1.6. Cobimetinib - EMEA/H/C/003960

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

5.1.7. Duloxetine - EMEA/H/C/003935, Generic

Scope: Treatment of depressive disorder, diabetic neuropathic pain, anxiety disorder
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.8. Glycerol phenylbutyrate - EMEA/H/C/003822, Orphan

Applicant: Horizon Therapeutics Limited

Scope: Treatment of patients with urea cycle disorders
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.9. Glycopyrronium bromide - EMEA/H/C/003883

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

5.1.10. Guanfacine - EMEA/H/C/003759

Scope: Treatment of attention deficit hyperactivity disorder (ADHD)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.11. Insulin human - EMEA/H/C/003858, Biosimilar

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

5.1.12. Idebenone - EMEA/H/C/003834, Hybrid

Scope: Treatment of Leber's hereditary optic neuropathy (LHON)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.13. Mercaptamine - EMEA/H/C/003769, Orphan

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

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

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

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

5.1.15. Pemetrexed - EMEA/H/C/004109, Hybrid

Scope: Treatment of malignant pleural mesothelioma and non-small cell lung cancer
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.16. Pemetrexed - EMEA/H/C/004011, Generic

Scope: Treatment of malignant pleural mesothelioma and non-small cell lung cancer
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.17. Sebelipase alfa - EMEA/H/C/004004, Orphan

Applicant: Synageva BioPharma Ltd

Scope: Treatment of enzyme replacement therapy (ERT)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.18. Sirolimus - EMEA/H/C/003978, Orphan

Applicant: Santen Oy

Scope: Treatment of chronic non-infectious uveitis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.19. Sonidegib - EMEA/H/C/002839

Scope: Treatment of basal cell carcinoma (BCC)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.20. Talimogene laherparepvec - EMEA/H/C/002771, ATMP

Scope: Treatment of adults with melanoma regionally or distantly metastatic
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. Eltrombopag – REVOLADE (CAP) - EMEA/H/C/001110/II/0026

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Following low number of eltrombopag users in registry, the MAH is proposing to terminate study WEUSKOP7134 and remove the post-approval measure MEA 026 from the RMP. An updated RMP version 30 has been provided accordingly

Action: For adoption of PRAC AR

5.2.2. Filgrastim – ACCOFIL (CAP) - EMEA/H/C/003956II/0002

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of the RMP following a product information update with regard to routine risk minimisation measures of for several safety concerns
Action: For adoption of PRAC AR

5.2.3. Influenza vaccine (split virion, inactivated) – IDFLU (CAP) - EMEA/H/C/000966/WS/0763; INTANZA (CAP) - EMEA/H/C/000957/WS/0763

Applicant: Sanofi Pasteur, Sanofi Pasteur MSD SNC

PRAC Rapporteur: Miguel-Angel Macia

Scope: Submission of a revised RMP (version 9.0) to update the strategy of the enhanced safety surveillance in EEA during 2015-2016 influenza season, the status of GID47 updated and details on clinical study report, results of THIN study and the table of risk minimisation measures updated according to the PRAC assessment report of the RMP 8.0
Action: For adoption of PRAC AR

5.2.4. Lapatinib – TYVERB (CAP) - EMEA/H/C/000795/II/0041/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a revised RMP in order to include general updates in the RMP regarding posology update, addition of some new studies to pharmacovigilance activities and addition of details on three newly available study reports. Timelines have been also changed for study EGF114299 and study EGF117165. The RMP and Annex II have been updated accordingly
Action: For adoption of PRAC AR

5.2.5. Liraglutide – SAXENDA (CAP) - EMEA/H/C/003780/WS0746/0001; VICTOZA (CAP) - EMEA/H/C/001026/WS0746/0031

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP for Victoza and Saxenda in order to change the due date for the pharmacovigilance activity relating to submission of a final report of the cardiovascular outcome study EX2211-3748 LEADER to November 2016
Action: For adoption of PRAC AR

5.2.6. Oseltamivir – TAMIFLU (CAP) - EMEA/H/C/000402/II/0114

Applicant: Roche Registration Ltd

PRAC Rapporteur: Kirsti Villikka

Scope: Proposal for a new and alternative study BV29684 assessing the safety of prenatal exposure to oseltamivir' as a category 3 study (MEA 099) to replace the agreed 2-year extension of the Danish-Swedish registry (NV25577)

Action: For adoption of PRAC AR

5.2.7. Rivastigmine – EXELON (CAP) - EMEA/H/C/000169/WS0743/0106; PROMETAX (CAP) - EMEA/H/C/000255/WS0743/0106

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Update of the RMP (version 8.1) including a proposal to remove the important potential risk 'acute renal failure' and the important identified risk 'dehydration', and to add the potential complications of gastro-intestinal symptoms as dehydration and renal failure. An updated protocol for CENA713D2409 is also proposed
Action: For adoption of PRAC AR

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

5.3.1. Adalimumab – HUMIRA (CAP) - EMEA/H/C/000481/II/0137

Applicant: AbbVie Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to the treatment of active moderate to severe hidradenitis suppurativa (acne inversa) in adult patients, including treatment of inflammatory lesions and prevention of worsening of abscesses and draining fistulas. Consequential changes are proposed for sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.2. Aflibercept – EYLEA (CAP) - EMEA/H/C/002392/II/0021

Applicant: Bayer Pharma AG

PRAC Rapporteur: Isabelle Robine

Scope: Extension of indication to the treatment in adults of visual impairment due to myopic choroidal neovascularisation (myopic CNV). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 are updated. The package leaflet is updated in accordance
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. Ambrisentan – VOLIBRIS (CAP) - EMEA/H/C/000839/II/0039

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of section 4.4 of the SmPC in relation to the current recommendations for liver function and section 5.1 of the SmPC with data on aminotransferase abnormalities from an analysis of the clinical study report 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 (revised version 6 provided)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.4. Ataluren – TRANSLARNA (CAP) - EMEA/H/C/002720/II/0005/G

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Submission of non-clinical study 100011749 (study of Ataluren (PTC124) and M4 metabolite in the β3 binding assay) and non-clinical study 100012124 (study of ataluren (PTC124) and M4 (PTC-0256858-04) functional activity in a beta-3 adrenergic cellular assay) in fulfilment of MEA 006. The results of these studies have no impact on the Translarna product information
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.5. Bosentan – STAYVEER (CAP) - EMEA/H/C/002644/II/0011

Applicant: Marklas Nederlands BV

PRAC Rapporteur: Isabelle Robine

Scope: Update of SmPC sections 4.2, 4.5, 4.6, 4.8, 5.1, 5.2 and 5.3 to reflect non-clinical and clinical data generated in studies conducted according to the agreed Paediatric Investigation Plan for bosentan (EMEA-000425-PIP02-10-M04) in line with the recently approved variation II/66 for Tracleer (bosentan). The Annex II and the package leaflet have been updated accordingly. Furthermore, the MAH took the opportunity to make editorial changes in the SmPC and to update the contact details of the local representatives in the package leaflet. In addition, taking into account the new data in the paediatric population, an updated version of the RMP (version 7) aligned with RMP version 7 for Tracleer was provided
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.6. Brentuximab – ADCETRIS (CAP) - EMEA/H/C/002455/II/0025

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include a new indication for Adcetris for the treatment of adult patients at increased risk of relapse or progression following autologous stem cell transplant. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. Cabozantinib – COMETRIQ (CAP) - EMEA/H/C/002640/II/0015

Applicant: TMC Pharma Services Ltd

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.8 and 5.1 of the SmPC following the results of study XL184-301. The RMP and the package leaflet are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.8. Ceftaroline fosamil – ZINFORO (CAP) - EMEA/H/C/002252/II/0021

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Submission of the final study report of the multicentre, randomised, double-blind, comparative study to evaluate the efficacy and safety of ceftaroline fosamil (600 mg every 8 hours) versus vancomycin plus aztreonam in the treatment of patients with complicated bacterial skin and soft tissue infections with evidence of systemic inflammatory response or underlying comorbidities. The RMP (version 14) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.9. Conestat alfa – RUCONEST (CAP) - EMEA/H/C/001223/R/0023

Applicant: Pharming Group N.V

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of the RMP in the context of a 5-year renewal of the marketing authorisation
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.10. Darbapoetin alfa – ARANESP (CAP) - EMEA/H/C/000332/II/0130

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Update of the SmPC section 4.2 to incorporate dosing recommendations for paediatric patients from 1 to < 11 years of age and to include updates to SmPC sections 4.8, 5.1 and 5.2 to reflect the available data in the paediatric population. The package leaflet has been revised accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.11. Denosumab – XGEVA (CAP) - EMEA/H/C/002173/II/0038

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC in order to update the safety information regarding the risk of osteonecrosis of the jaw (ONJ). In addition, the MAH took the opportunity to bring the SmPC in line with the package leaflet regarding typographical errors in section 4.2 of the SmPC
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.12. Eltrombopag – REVOLADE (CAP) - EMEA/H/C/001110/II/0019

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of section 4.8 of the SmPC to include the adverse drug reaction 'thrombotic microangiopathy (TMA) with acute renal failure'. The package leaflet has been updated accordingly. In addition, the MAH took the opportunity to make a minor change to section 4.8 of the SmPC clarifying that the safety data included are derived both from studies and from post-marketing reports
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.13. Eltrombopag – REVOLADE (CAP) - EMEA/H/C/001110/II/0020

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication: Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to add a new indication for the treatment of adult patients with severe aplastic anaemia (SAA) who have had an insufficient response to immunosuppressive therapy. The package leaflet is updated accordingly. In addition, the MAH has corrected the acronym used for full blood counts (FBC) in the SmPC, Annex II and package leaflet
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.14. Eltrombopag – REVOLADE (CAP) - EMEA/H/C/001110/X/0022/G

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication for paediatric (age 1 year and above) chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients who had an insufficient response to other treatments (e.g. corticosteroids, immunoglobulins). Grouping with line extension for one new tablet strength (12.5mg) and a new powder for oral suspension formulation (25mg)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.15. Etanercept – ENBREL (CAP) - EMEA/H/C/000262/II/0184

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Update of section 4.6 of the SmPC in order to update the information on the effects of etanercept on pregnancy and lactation. The package leaflet and the RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.16. Human normal immunoglobulin – HYQVIA (CAP) - EMEA/H/C/002491/II/0013

Applicant: Baxter Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.4, 4.6 and 5.3 of the SmPC in order to update the safety information regarding pregnancy, fertility and lactation following new additional preclinical data. The package leaflet is updated accordingly. Furthermore, Annex II has been revised to remove educational material based on the availability of additional new data. An updated RMP (version 7.0) has been submitted accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.17. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) – CERVARIX (CAP) - EMEA/H/C/000721/II/0067

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include prevention against premalignant anal lesions and anal cancer as of 9 years of age for Cervarix. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to update the RMP (version 11.0) including the new indication
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.18. Ingenol mebutate – PICATO (CAP) - EMEA/H/C/002275/II/0012

Applicant: Leo Pharma A/S

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC to provide new efficacy and safety data supporting a labelling update that introduces repeat treatment of Picato gel (150 mcg/g and 500 mcg/g), based on study LP0041-22. The package leaflet is updated accordingly

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

5.3.19. Interferon alfa-2b – INTRONA (CAP) - EMEA/H/C/000281/WS0611/0099 peginterferon alfa-2B – PEGINTRON (CAP) - EMEA/H/C/000280/WS0611/0119; VIRAFERONPEG (CAP) - EMEA/H/C/000329/WS0611/0112

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 4.4 of the SmPC to include updated information on homicidal ideation and for patients with decompensated liver disease, and update of section 4.8 of the SmPC to add pulmonary fibrosis as a post-marketing adverse drug reaction. The package leaflet have been revised accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.20. Ivacaftor – KALYDECO (CAP) - EMEA/H/C/002494/II/0027

Applicant: Vertex Pharmaceuticals (U.K.) Ltd

PRAC Rapporteur: Miguel-Angel Macia

Scope: Extension of indication to include the treatment of cystic fibrosis in patients aged 18 years and older who have a R117H mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Consequently, changes are proposed to sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and to the package leaflet
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.21. Levetiracetam – KEPPRA (CAP) - EMEA/H/C/000277/R/0154

Applicant: UCB Pharma SA

PRAC Rapporteur: Veerle Verlinden

Scope: Evaluation of the RMP in the context of a 5-year renewal of the marketing authorisation
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.22. Macitentan – OPSUMIT (CAP) - EMEA/H/C/002697/II/0007/G

Applicant: Actelion Registration Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of final study report for studies AC-055C301/DUAL-1 and AC-055C302/DUAL-2, two completed Phase 3 studies in patients with digital ulcers associated with systemic sclerosis. An updated RMP has been submitted accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.23. Natalizumab – TYSABRI (CAP) - EMEA/H/C/000603/II/0077

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adults with highly active relapsing remitting multiple sclerosis with high disease activity despite treatment with at least one modifying therapy (DMT). As a consequence, sections 4.1 and 4.4 of the SmPC are updated in order to provide physicians with more options for treating relapsing remitting multiple

sclerosis (RRMS) patients with high disease activity who fail an initial disease modifying therapy (DMT). Consequential changes to SmPC sections 4.2, 4.3, 5.1 and package leaflet sections 2 and 3 are submitted accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.24. Nilotinib – TASIGNA (CAP) - EMEA/H/C/000798/II/0075

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Update of section 5.3 of the SmPC in order to update the safety information based on the results from a 26-week oral gavage carcinogenicity study in 001178 T
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.25. Nonacog alfa – BENEFIX (CAP) - EMEA/H/C/000139/II/0133

Applicant: Pfizer Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.8 of the SmPC in order to revise adverse event frequencies based on all-causality data set. In addition, the MAH took the opportunity to update SmPC sections 4.1, 4.2, 4.4, 4.5, 4.7, 4.8 and 4.9 in line with the latest revision of the Core SmPC for factor IX Products. The package leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.26. Ramucirumab – CYRAMZA (CAP) - EMEA/H/C/002829/II/0004

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include a new indication for Cyramza, in combination with FOLFIRI (irinotecan, folinic acid, and 5-fluorouracil), for the treatment of adult patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin and a fluoropyrimidine. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.27. Regorafenib – STIVARGA (CAP) - EMEA/H/C/002573/II/0011

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

Scope: Submission of study results from retrospective biomarker analyses from the pivotal GRID trial (study 14874) in order to fulfil ANX 003.2
Action: For adoption of PRAC Assessment Report

5.3.28. Rilpivirine – EDURANT (CAP) - EMEA/H/C/002264/II/0017/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of antiretroviral treatment-naïve paediatric patients aged 12 to <18 years of age based on the results of the 48-week data of study TMC278-TiDP38-C213 (PAINT), undertaken to evaluate the pharmacokinetics, safety/

tolerability, and efficacy of rilpivirine 25 mg qd in combination with an investigator-selected background regimen containing 2 nucleoside (nucleotide) reverse transcriptase inhibitors (NRTIs) in this adolescent population. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC have been updated and the package leaflet has been updated accordingly. A revised RMP (version 6.0) is submitted accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.29. Ritonavir – NORVIR (CAP) - EMEA/H/C000127/X/0127

Applicant: AbbVie Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Line extension of a new oral powder formulation of Norvir (ritonavir) as a replacement for the currently marketed Norvir oral solution for a more suitable ritonavir formulation for the paediatric population
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.30. Secukinumab – COSENTYX (CAP) - EMEA/H/C/003729/II/0001/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication to include a new indication for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate as monotherapy or in combination with methotrexate (MTX). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, and 5.2 of the SmPC are updated in order to update the safety and efficacy information. The package leaflet is updated in accordance
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.31. Secukinumab – COSENTYX (CAP) - EMEA/H/C/003729/II/0002

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication to the treatment of severe active ankylosing spondylitis in adults who have responded inadequately to conventional therapy. Consequently SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, and 5.2 have been revised to include new efficacy and safety information. The package leaflet and RMP have been updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.32. Sodium oxybate – XYREM (CAP) - EMEA/H/C/000593/R/0054

Applicant: UCB Pharma Ltd

PRAC Rapporteur: Magda Pedro

Scope: Evaluation of the RMP in the context of a 5-year renewal of the marketing authorisation
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.33. Telaprevir - INCIVO (CAP) - EMEA/H/C/002313/II/0035

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of SmPC section 4.2 to provide posology information for the special population of liver transplant patients without cirrhosis and of SmPC section 4.4 to add a warning for organ transplant patients, as part of the RMP commitments to address the missing information in the liver post-transplant population and based on the submission of the study report for phase 3b study HPC3006. SmPC section 4.5, 4.8 and 5.1 and the package leaflet are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.34. Thalidomide – THALIDOMIDE CELGENE (CAP) - EMEA/H/C/000823/II/0043

Applicant: Celgene Europe Limited

PRAC Rapporteur: Corinne Féchant

Scope: Update of sections 4.2 and 4.8 of the SmPC in order to add new dosing information for elderly patients (>75 years) with untreated multiple myeloma receiving thalidomide in combination with melphalan and prednisone (MPT). In addition the MAH is updating the posology with the recommended starting doses for melphalan and prednisone for completeness. The package leaflet is being updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.35. Trametinib – MEKINIST (CAP) - EMEA/H/C/002643/II/0006/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.5 and 5.2 of the SmPC in order to update the safety information based on new preclinical data provided to fulfil 4 nonclinical Post-authorisation measures (REC 001, MEA 004, MEA 005 and MEA 006). Moreover, an updated RMP (version 10) has been submitted
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.36. Trametinib – MEKINIST (CAP) - EMEA/H/C/002643/II/0007

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.2 and 5.3 of the SmPC in order to update the safety information based on new preclinical data from an oral juvenile toxicity study in rats. Moreover, an updated RMP (version 10) has been submitted
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.37. Trastuzumab – HERCEPTIN (CAP) - EMEA/H/C/000278/II/0093

Applicant: Roche Registration Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 5.1 of the SmPC in order to reflect the safety information of Herceptin 600 mg solution for injection (EU/1/00/145/002 and EU/1/00/145/003) in line with the interim report of study MO28048 (SafeHER). The RMP is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.38. Umeclidinium bromide – INCRUSE (CAP) - EMEA/H/C/002809/ WS0723/0004/G umeclidinium bromide, vilanterol – ANORO (CAP) - EMEA/H/C/002751/WS0723/0004/G; LAVENTAIR (CAP) - EMEA/H/C/003754/WS0723/0004/G

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Submission of two non-clinical studies (2014N214514 and 2014N214870) regarding in-vitro investigations to determine the potential for drug-drug interactions in fulfilment of MEA 003 for Anoro and Laventair and MEA 002 for Incruse. The RMP is updated accordingly. In addition the MAH take the occasion to include minor routine updates in the RMP and to include in the MA for Anoro and Laventair report 2012N156532 on results of physiologically based PK modelling and simulation already assessed during the initial marketing authorisation application procedure
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.39. Vemurafenib – ZELBORAF (CAP) - EMEA/H/C/002409/II/0023

Applicant: Roche Registration Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.5 of the SmPC in order to update the drug-drug interaction information following finalisation of study GO28394 (phase I, open-label, multicentre, 3-period, fixed sequence study to investigate the effect of vemurafenib on the pharmacokinetics of a single dose of digoxin in patients with BRAFV600 mutation-positive metastatic malignancy – MEA 013). The MAH took the opportunity to introduce editorial changes to improve clarity and consistency in the SmPC and package leaflet
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. Aflibercept – EYLEA (CAP) - PSUSA/10020/201411

Applicant: Bayer Pharma AG

PRAC Rapporteur: Isabelle Robine

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

6.1.2. Apixaban – ELIQUIS (CAP) - PSUSA/00226/201411

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

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

6.1.3. Boceprevir – VICTRELIS (CAP) - PSUSA/09081/201411

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Isabelle Robine

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

6.1.4. Canagliflozin– INVOKANA (CAP) canagliflozin, metformin – VOKANAMET (CAP) - PSUSA/10077/201411

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

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

6.1.5. Darbepoetin alfa – ARANESP (CAP) - PSUSA/00932/201410

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Valerie Strassmann

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

6.1.6. Diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rdna), poliomyelitis (inact.) And haemophilus type b conjugate vaccine (adsorbed) – INFANRIX HEXA (CAP) - PSUSA/01122/201410

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

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

6.1.7. Erlotinib – TARCEVA (CAP) - PSUSA/01255/201411

Applicant: Roche Registration Ltd

PRAC Rapporteur: Doris Stenver

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

6.1.8. Ethinylestradiol, norelgestromin – EVRA (CAP) - PSUSA/01311/201411

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

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

6.1.9. Fidaxomicin – DIFICLIR (CAP) - PSUSA/01390/201411

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Qun-Ying Yue

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

6.1.10. Flutemetamol (^{18}F) – VIZAMYL (CAP) - PSUSA/10293/201410

Applicant: GE Healthcare Ltd

PRAC Rapporteur: Julie Williams

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

6.1.11. Fluticasone furoate, vilanterol – RELVAR ELLIPTA (CAP); REVINTY ELLIPTA (CAP) - PSUSA/10099/201411

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Miguel-Angel Macia

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

6.1.12. Fondaparinux – ARIXTRA (CAP) - PSUSA/01467/201412

Applicant: Aspen Pharma Trading Limited

PRAC Rapporteur: Qun-Ying Yue

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

6.1.13. Fosamprenavir – TELZIR (CAP) - PSUSA/01470/201410

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Isabelle Robine

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

6.1.14. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) – CERVARIX (CAP) - PSUSA/09175/201411

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

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

6.1.15. Insulin detemir – LEVEMIR (CAP) - PSUSA/01750/201410

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

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

6.1.16. Lidocaine, prilocaine – FORTACIN (CAP) - PSUSA/10110/201411

Applicant: Plethora Solutions Ltd.

PRAC Rapporteur: Miguel-Angel Macia

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

6.1.17. Metformin, saxagliptin – KOMBOGLYZE (CAP) - PSUSA/02686/201411

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

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

6.1.18. Nelarabine – ATRIANCE (CAP) - PSUSA/02132/201410

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

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

6.1.19. Pandemic influenza vaccine (H1N1) (whole virion, inactivated, prepared in cell culture) – CELVAPAN (CAP) - PSUSA/02280/201410

Applicant: Baxter AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.1.20. Pixantrone dimaleate – PIXUVRI (CAP) - PSUSA/09261/201411

Applicant: CTI Life Sciences Limited

PRAC Rapporteur: Rafe Suvarna

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

6.1.21. Pneumococcal polysaccharide conjugate vaccine, 10 valent adsorbed – SYNFLORIX (CAP) - PSUSA/09262/201412

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Qun-Ying Yue

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

6.1.22. Radium-223 – XOFIGO (CAP) - PSUSA/10132/201411

Applicant: Bayer Pharma AG

PRAC Rapporteur: Rafe Suvarna

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

6.1.23. Rilpivirine – EDURANT (CAP) - PSUSA/09282/201411

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Sabine Straus

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

6.1.24. Rituximab – MABTHERA (CAP) - PSUSA/02652/201411

Applicant: Roche Registration Ltd

PRAC Rapporteur: Doris Stenver

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

6.1.25. Rotavirus vaccine (live, oral) – ROTATEQ (CAP) - PSUSA/02666/201411

Applicant: Sanofi Pasteur MSD SNC

PRAC Rapporteur: Rafe Suvarna

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

6.1.26. Sapropterin – KUVAN (CAP) - PSUSA/02683/201412

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Almath Spooner

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

6.1.27. Saquinavir – INVIRASE (CAP) - PSUSA/02684/201412

Applicant: Roche Registration Ltd

PRAC Rapporteur: Marianne Lunzer

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

6.1.28. Shingles (herpes zoster) vaccine (live) – ZOSTAVAX (CAP) - PSUSA/09289/201411

Applicant: Sanofi Pasteur MSD SNC

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.1.29. Simeprevir – OLYSIO (CAP) - PSUSA/10255/201411

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

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

6.1.30. Sofosbuvir – SOVALDI (CAP) - PSUSA/10134/201412

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

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

6.1.31. Stiripentol – DIACOMIT (CAP) - PSUSA/02789/201411

Applicant: Biocodex

PRAC Rapporteur: Julie Williams

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

6.1.32. Vedolizumab – ENTYVIO (CAP) - PSUSA/10186/201411

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

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. Bosentan – STAYVEER (CAP); TRACLEER (CAP) - PSUSA/00425/201411

Applicant: Actelion Registration Ltd., Marklas Nederlands BV, various

PRAC Rapporteur: Isabelle Robine

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

6.2.2. Insulin human, isophane insulin – ACTRAPHANE (CAP); ACTRAPID (CAP); INSULATARD (CAP); INSULIN HUMAN WINTHROP (CAP); INSUMAN (CAP); MIXTARD (CAP); PROTAPHANE (CAP); NAP - PSUSA/01753/201410

Applicant: Novo Nordisk A/S, various

PRAC Rapporteur: Doris Stenver

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

6.2.3. Sevelamer – RENAGEL (CAP), RENVELA (CAP); NAP - PSUSA/02697/201410

Applicant: Genzyme Europe BV, various

PRAC Rapporteur: Veerle Verlinden

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

6.2.4. Sodium oxybate – XYREM (CAP); NAP - PSUSA/02757/201410

Applicant: UCB Pharma Ltd., various

PRAC Rapporteur: Magda Pedro

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

6.2.5. Tadalafil – ADCIRCA (CAP), CIALIS (CAP); NAP - PSUSA/02841/201410

Applicant: Eli Lilly Nederland B.V., various

PRAC Rapporteur: Miguel-Angel Macia

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

6.2.6. Toremifene – FARESTON (CAP); NAP - PSUSA/02999/201409

Applicant: Orion Corporation, various

PRAC Rapporteur: Corinne Féchant

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

6.3. PSUR procedures including nationally authorised products (NAPs)

6.3.1. Betamethasone, tetryzoline (NAP) - PSUSA/00010072/201409

Applicant: various

PRAC lead: Viola Macolić Šarinić

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

6.3.2. Calcium carbonate, famotidine, magnesium hydroxide (NAP) - PSUSA/00001351/201409

Applicant: various

PRAC lead: Isabelle Robine

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

6.3.3. Cefuroxime sodium (for intracameral use) (NAP) - PSUSA/00010206/201411

Applicant: various

PRAC lead: Maia Uusküla

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

6.3.4. Corticorelin (NAP) - PSUSA/00000876/201410

Applicant: various

PRAC lead: Jan Neuhauser

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

6.3.5. Desflurane (NAP) - PSUSA/00000958/201409

Applicant: various

PRAC lead: Julie Williams

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

6.3.6. Etifoxine (NAP) - PSUSA/00001321/201410

Applicant: various

PRAC lead: Maria Popova-Kiradjieva

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

6.3.7. Famotidine (NAP) - PSUSA/00001350/201409

Applicant: various

PRAC lead: Carmela Macchiarulo

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

6.3.8. Fluticasone, salmeterol (NAP) - PSUSA/00001455/201410

Applicant: various

PRAC lead: Qun-Ying Yue

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

6.3.9. Human von Willebrand factor (NAP) - PSUSA/00001642/201409

Applicant: various

PRAC lead: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.10. Hydroxyzine chloride, hydroxyzine pamoate and all fixed combination; hydroxyzine (NAP) - PSUSA/00001696/201411

Applicant: various

PRAC lead: Isabelle Robine

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

6.3.11. Idebenone (NAP) - PSUSA/00001721/201409

Applicant: various

PRAC lead: Amy Tanti

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

6.3.12. Insulin porcine (NAP) - PSUSA/00001756/201410

Applicant: various

PRAC lead: Julie Williams

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

6.3.13. Isoniazid (NAP) - PSUSA/00001789/201411

Applicant: various

PRAC lead: Qun-Ying Yue

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

6.3.14. Ketotifen (oral formulations) (NAP) - PSUSA/00001813/201410

Applicant: various

PRAC lead: Carmela Macchiarulo

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

6.3.15. Letrozole (NAP) - PSUSA/00001842/201410

Applicant: various

PRAC lead: Isabelle Robine

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

6.3.16. Miconazole; hydrocortisone, miconazole nitrate; miconazole nitrate, zinc oxide (NAP) - PSUSA/00002052/201410

Applicant: various

PRAC lead: Ulla Wändel Liminga

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

6.3.17. Pramiracetam (NAP) - PSUSA/00002492/201409

Applicant: various

PRAC lead: Zane Neikena

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

6.3.18. Prulifloxacin (NAP) - PSUSA/00002569/201410

Applicant: various

PRAC lead: Carmela Macchiarulo

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

6.3.19. Sumatriptan (NAP) - PSUSA/00002832/201409

Applicant: various

PRAC lead: Sabine Straus

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

6.3.20. Tapentadol (NAP) - PSUSA/00002849/201411

Applicant: various

PRAC lead: Martin Huber

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

6.3.21. Tetrabenazine (NAP) - PSUSA/00002911/201410

Applicant: various

PRAC lead: Almath Spooner

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

6.3.22. Vigabatrin (NAP) - PSUSA/00003112/201409

Applicant: various

PRAC lead: Kirsti Villikka

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

6.4. Follow-up to PSUR procedures

6.4.1. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - EMEA/H/C/002617/LEG 007

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to PSUV/0023
Action: For adoption of advice to CHMP

6.4.2. Methoxypolyethylene glycol-epoetin beta – MIRCERA (CAP) - EMEA/H/C/000739/LEG 037

Applicant: Roche Registration Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to PSUSA/00002017/201407 - PSUR#9
Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[2]

7.1.1. Cholic acid– KOLBAM (CAP) - EMEA/H/C/PSP/0017

Applicant: ASK Pharmaceuticals GmbH

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PASS protocol for a patient registry to monitor the long term safety and efficacy in patients treated with cholic acid FGK
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

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

7.1.2. Ivabradine – CORLENTOR (CAP), PROCOLORAN (CAP) - EMEA/H/C/PSP/0019.1

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a revised DUS protocol for a multinational, retrospective, observational study to assess effectiveness of risk-minimisation measures
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.3. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSP/0020

Applicant: Celgene Europe Limited

PRAC Rapporteur: Corinne Féchant

Scope: Evaluation of a PASS protocol for study CC-5013-MM-034, a lenalidomide product registry of previously untreated adult multiple myeloma patients who are not eligible for transplant
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.4. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSP/0025

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a protocol for a pharmacoepidemiological study of rivaroxaban use and potential adverse outcomes in routine clinical practice in Germany, Netherlands, UK and Sweden
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.5. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSP/0026

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a protocol for an observational post-authorisation Safety Specialist Cohort Event Monitoring study (SCEM) to monitor the safety and utilisation of rivaroxaban initiated in secondary care for the prevention of atherothrombotic events in patients who have had acute coronary syndrome in England and Wales.
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.6. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSP/0027

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a revised protocol for an observational post-authorisation modified prescription-event monitoring safety study (M-PEM) to monitor the safety and utilisation of rivaroxaban for the prevention of stroke in patients with atrial fibrillation (AF), treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE following an acute DVT in the primary care setting in England – including an extension to the rivaroxaban M-PEM study to include acute coronary syndrome patients
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.7. Teicoplanin (NAP) - EMEA/H/N/PSP/0011.3

Applicant: Sanofi

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a revised protocol for a prospective observational cohort, non-comparative study describing the safety profile of the higher recommended teicoplanin loading dose of 12 mg/kg twice a day
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[3]

7.2.1. Alglucosidase alfa – MYOZYME (CAP) - EMEA/H/C/000636/MEA 053

Applicant: Genzyme Europe BV

PRAC Rapporteur: Isabelle Robine

Scope: Evaluation of a PASS protocol for an epidemiology study ALGMYC07390: Prevalence of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions
Action: For adoption of advice to CHMP

7.2.2. Canakinumab – ILARIS (CAP) - EMEA/H/C/001109/MEA 037.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a MAH's responses to a request for supplementary information for MEA 037.1 [non-interventional study collecting safety and efficacy data from systemic juvenile idiopathic arthritis (SJIA) patients enrolled in Pharmachild JIA registry, protocol, Study no. CACZ885G2401] adopted in September 2014
Action: For adoption of advice to CHMP

7.2.3. Delamanid – DELTYBA (CAP) - EMEA/H/C/002552/MEA 002.2

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a MAH's responses to a request for supplementary information for MEA 002.1 [PASS study 242-120402] as adopted in February 2015
Action: For adoption of advice to CHMP

7.2.4. Elvitegravir – VITEKTA (CAP) - EMEA/H/C/002577/MEA 007.1

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a MAH's responses to a request for supplementary information for MEA 007 [Feasibility Study / Drug Utilisation Study (DUS) GS-EU-183-1335] as adopted in February 2014
Action: For adoption of advice to CHMP

[3] 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

7.2.5. Exenatide – BYDUREON (CAP) - EMEA/H/C/002020/MEA 011.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of MAH's responses to a request for supplementary information for MEA 011.3 [annual report of study B017] as adopted in January 2015
Action: For adoption of advice to CHMP

7.2.6. Human normal immunoglobulin – HYQVIA (CAP) - EMEA/H/C/002491/MEA 004.1

Applicant: Baxter Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Revised pregnancy registry PASS protocol [study 161301]
Action: For adoption of advice to CHMP

7.2.7. Insulin lispro – HUMALOG (CAP) - EMEA/H/C/000088/MEA 025.1, LIPROLOG (CAP) - EMEA/H/C/000393/MEA 108.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of MAH's responses to a request for supplementary information for MEA 025 [Protocol synopsis for PASS study examining the effectiveness of risk minimisation on 200 units strength] as adopted in January 2015

Action: For adoption of advice to CHMP

7.2.8. Olaparib – LYNPARZA (CAP) - EMEA/H/C/003726/MEA 011

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Synopsis protocol for a study to collect and/or retrieve prospective data from sizeable patient cohorts with ovarian cancer, representing real world evidence from relevant countries
Action: For adoption of advice to CHMP

7.2.9. Ramucirumab – CYRAMZA (CAP) - EMEA/H/C/002829/MEA 001.1

Applicant: Elli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Revised PASS protocol for a prospective observational registry of safety and effectiveness of ramucirumab in patients with advanced gastric cancer in the European Union and North America (I4T-MC-JVDD)

Action: For adoption of advice to CHMP

7.2.10. Secukinumab –COSENTYX (CAP) - EMEA/H/C/003729/MEA 002

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Protocol for a non-interventional, non-imposed PASS to study the comparative safety of approved psoriasis therapies in a national cohort of psoriasis subjects treated by dermatologists
Action: For adoption of advice to CHMP

7.2.11. Telavancin – VIBATIV (CAP) - EMEA/H/C/001240/ANX 007.3

Applicant: Clinigen Healthcare Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of the MAH's responses to a request for supplementary information for ANX 007.2 (Pregnancy Exposure Registry study 9809-CL-1409) adopted in October 2014
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.3. Results of PASS imposed in the marketing authorisation(s)[4]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[5]

7.4.1. Dabigatran – PRADAXA (CAP) - EMEA/H/C/000829/II/0079/G (with RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of the final clinical study report (CSR) for study 1160.84: observational cohort study undertaken to evaluate the safety and efficacy of Pradaxa in patients with moderate renal impairment (creatinine clearance 30-50 ml/min) undergoing elective total hip replacement surgery or total knee replacement surgery. The provision of the CSR addresses the post-authorisation measure MEA 010.1. The application includes an updated RMP version 31.0, which includes changes pertaining to the study report of study 1160.84, the update of due dates in the RMP for the provision of 14 study reports, and the inclusion of the outcome of 2 phase I studies (studies 1160.141 and 1160.142) following the CHMP assessment of variations II/46 and II/61
Action: For adoption of PRAC Assessment Report

7.4.2. Epoetin theta – BIOPOIN (CAP) - EMEA/H/C/001036/II/0023 (without RMP)

Applicant: Teva GmbH

PRAC Rapporteur: Isabelle Robine

Scope: Submission of a PASS final report relating to epoetin theta in patients with chronic kidney disease to assess the incidence and severity of predefined cardiovascular events including ischaemic stroke, and to detect and describe any adverse drug reaction including pure red cell aplasia (PASS XM01-30)
Action: For adoption of PRAC Assessment Report

7.4.3. Epoetin theta – EPORATIO (CAP) - EMEA/H/C/001033/II/0022 (without RMP)

Applicant: Ratiopharm GmbH

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

PRAC Rapporteur: Isabelle Robine

Scope: Submission of a PASS final report relating to epoetin theta in patients with chronic kidney disease to assess the incidence and severity of predefined cardiovascular events including ischaemic stroke, and to detect and describe any adverse drug reaction including pure red cell aplasia (PASS XM01-30)
Action: For adoption of PRAC Assessment Report

7.4.4. Ribavirin – REBETOL (CAP) - EMEA/H/C/000246/II/0076 (with RMP)

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Isabelle Robine

Scope: Submission of a final study report for study MK-8908-060 assessing the utilisation of ribavirin in paediatric patients with hepatitis C virus. A revised RMP has been submitted with this procedure
Action: For adoption of PRAC Assessment Report

7.4.5. Rotavirus vaccine, live – ROTARIX (CAP) - EMEA/H/C/000639/II/0062 (with RMP)

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

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 for the potential occurrence of genetic drifts and shifts in the vaccine strain in post-marketing settings
Action: Preliminary discussion

7.4.6. Rotigotine – LEGANTO (CAP) - EMEA/H/C/002380/WS0751/0018/G (with RMP); NEUPRO (CAP) - EMEA/H/C/000626/WS0751/0068/G (with RMP)

Applicant: UCB Manufacturing Ireland Ltd

PRAC Rapporteur: Magda Pedro

Scope: Submission of two final study reports for PASS studies which investigated the potential risk of cardiovalvular fibrosis in Parkinson's disease patients treated with rotigotine and other anti-Parkinson's drugs. The RMP is updated accordingly
Action: For adoption of PRAC Assessment Report

7.4.7. Sofosbuvir – SOVALDI (CAP) - EMEA/H/C/002798/II/0015 (with RMP)

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Submission of the final study report to investigate the safety and efficacy of GS-7977 and ribavirin for 24 weeks in subjects with recurrent chronic HCV post liver transplant (GS-US-334-0126). This submission fulfils MEA 005. An updated RMP (version 3.0) is proposed accordingly
Action: For adoption of PRAC Assessment Report

7.4.8. Tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/WS0731/0147 (with RMP)
tenofovir disoproxil, emtricitabine – EVIPLERA (CAP) - EMEA/H/C/002312/WS0731/0056 (with RMP); TRUVADA (CAP) -

EMEA/H/C/000594/WS0731/0113 (with RMP)
tenofovir disoproxil, emtricitabine, efavirenz – ATRIPLA (CAP) - EMEA/H/C/000797/WS0731/0101 (with RMP)
tenofovir disoproxil, emtricitabine, elvitegravir, cobicistat – STRIBILD (CAP) - EMEA/H/C/002574/WS0731/0044 (with RMP)

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Submission of the final clinical study report for Viread study GS-US-104-0423 'phase 4 cross-sectional study of bone mineral density in HIV-1 infected subjects' in fulfilment of a post-authorisation measure (PAM) for Viread, Truvada, Eviplera, Stribild and Atripla (category 3 additional pharmacovigilance activity for Viread, Truvada, Eviplera and Stribild, and category 4 for Atripla). An updated RMP for each product is proposed accordingly
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[6]

7.5.1. Adalimumab – HUMIRA (CAP) - EMEA/H/C/000481/MEA 066.4

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of safety data from the clinical use of adalimumab from the national registry activities that are ongoing in Germany, Sweden and the UK
Action: For adoption of advice to CHMP

7.5.2. Critozinib – XALKORI (CAP) - EMEA/H/C/002489/MEA 011.2

Applicant: Pfizer Limited

PRAC Rapporteur: Corinne Féchant

Scope: Report for PASS study A8081038 to estimate the incidence rate and incidence proportion over a 3-year period of observation for hepatotoxicity, pneumonitis/interstitial lung disease (ILD), QTc prolongation related events, bradycardia, and visual disorder among lung cancer patients receiving crizotinib prescriptions
Action: For adoption of advice to CHMP

7.5.3. Eliglustat – CERDELGA (CAP) - EMEA/H/C/003724/MEA 005

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: Pilot study report for a drug utilisation study of eliglustat in Europe using electronic healthcare records
Action: For adoption of advice to CHMP

7.5.4. Entecavir – BARACLUDE (CAP) - EMEA/H/C/000626/MEA 026.7

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Qun-Ying Yue

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

Scope: Eighth annual report on a large prospective, observational study including 12,500 patients with chronic hepatitis B virus (HBV) infection randomised to either entecavir (ETV) or to another standard-of-care nucleos(t)ide analogue, including cancer surveillance
Action: For adoption of advice to CHMP

7.5.5. Exenatide – BYDUREON (CAP) - EMEA/H/C/002020/MEA 010.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of MAH's responses to a request for supplementary information for MEA 010.2 (modified prescription event monitoring (PEM) study H8O-MC-B016) as adopted in January 2015
Action: For adoption of advice to CHMP

7.5.6. Infliximab – REMICADE (CAP) - EMEA/H/C/000240/MEA 099.9

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Sixth interval report for a pregnancy registry study to gather birth outcome data for infants born to mothers exposed to infliximab, including follow-up of infants up to 1 year after birth
Action: For adoption of advice to CHMP

7.5.7. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA 004.2

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of MAH's responses to a request for supplementary information for MEA 004.1 [PASS study D2560C00008, first summary safety report] as adopted in February 2015
Action: For adoption of advice to CHMP

7.5.8. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA 006.1

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of MAH's responses to a request for supplementary information for MEA 006 [first annual report for an observational prospective cohort study MI-MA194] RSI as adopted in January 2015
Action: For adoption of advice to CHMP

7.5.9. Influenza vaccine (split virion, inactivated) – IDFLU (CAP) - EMEA/H/C/000966/MEA 032.1; INTANZA (CAP) – EMEA/H/C/000957/MEA 032.1

Applicant: Sanofi Pasteur

PRAC Rapporteur: Miguel-Angel Macia

Scope: Evaluation of a MAH's responses to a request for supplementary information for MEA 032 (from WS/638, enhanced safety surveillance for NH 2014-2015 campaign / intermediate results interventional studie s/ GID47 final report) as adopted in February 2015
Action: For adoption of advice to CHMP

7.5.10. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) – OPTAFLU (CAP) - EMEA/H/C/000758/LEG 050.1

Applicant: Novartis Influenza Vaccines Marburg GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to a request for supplementary information for LEG 050 [study No. V58_40OB surveillance report] as adopted in February 2015
Action: For adoption of advice to CHMP

7.5.11. Insulin lispro – HUMALOG (CAP) - EMEA/H/C/000088/MEA 028; LIPROLOG (CAP) - EMEA/H/C/000393/MEA 021

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Summary report on the analysis of the effectiveness of the US surveillance programme and how any limitations in the methodology will be addressed in the European programme
Action: For adoption of advice to CHMP

7.5.12. Ketoconazole – KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/MEA 004

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Viola Macolic Sarinic

Scope: First report on a named patient basis programme in France (ATU de cohorte) to further characterize the risk in terms of frequency, symptoms in a real life use, potential risk factors, and consequences
Action: For adoption of advice to CHMP

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Antithrombin alfa – ATRYN (CAP) - EMEA/H/C/000587/S/0021 (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

8.1.2. Idursulfase – ELAPRASE (CAP) - EMEA/H/C/000700/S/0055 (without RMP)

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Rafe Suvarna

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. Telmisartan, amlodipine – TWYNSTA (CAP) - EMEA/H/C/001224/R/0026 (without RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Valerie Strassmann

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

9.1.1. Risk-based programme for routine pharmacovigilance inspections of Marketing Authorisation Holders of Centrally Authorised Products for human use (first revision for 2015)

Action: For adoption

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

10.3.1. Naltrexone, bupropion – MYSIMBA (CAP) – EMEA/H/C/003687/ANX 001

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: PRAC consultation on a PASS protocol for a multicentre, randomised, double-blind, placebo-controlled, phase 4 study to assess the effect of naltrexone extended release (ER) /bupropion ER on the occurrence of major adverse cardiovascular events (MACE) in overweight and obese subjects
Action: For adoption of advice to CHMP

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. Ciprofloxacin for systemic use (NAP) – NO/H/PSUR/0010/002

Applicant: Bayer Health Care

PRAC lead: Ingebjørg Buajordet

Scope: PRAC consultation on a PSUR work-sharing procedure relating to signal of rhabdomyolysis and the need to request an interaction study with agomelatine
Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. Mandate of Chair and Vice-Chair

Action: For discussion

12.1.2. ORGAM: introduction of a topic request form

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

12.2.1. CHMP guidelines concerning tools for early access to medicines (accelerated assessment and conditional marketing authorisations): revision

Action: For discussion

12.2.2. PRAC lead variations: appointment of CHMP liaison persons

Action: For discussion

12.3. Coordination with EMA working parties / working groups / drafting groups

12.3.1. Scientific Advice Working Party (SAWP): call for PRAC members

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. EuroMediCAT: safety of medication use in pregnancy (7th Framework project) - conclusion

Action: For discussion

12.4.2. Strategy for EU medicines network to 2020

Action: For discussion

12.5. Cooperation with international regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2015

Action: For discussion

12.7.2. PRAC work plan: process and template

Action: For discussion

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. PSURs repository: update on the pilot and audit

Action: For discussion

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

Action: For adoption of the revised list (version June 2015)

12.11. Signal management

12.11.1. Electronic reaction monitoring reports (eRMR) pilot phase: specific consideration in signal detection

Action: For discussion

12.11.2. Screening of adverse drug reactions in EudraVigilance: draft guidance

Action: For discussion

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

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: Road map

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation safety studies – non-imposed PASS protocols: revised process

See under 12.3.1.

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

12.17.1. Five year-renewal procedure: revised assessment process

Action: For discussion

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. Incident management

None

12.19.2. Good pharmacovigilance practice GVP Module XV - communication and DHPC

Action: For discussion

12.20. Others

13. Any other business

13.1. Pharmacovigilance programme and revised implementation

Action: For discussion

13.2. Strategy on impact of pharmacovigilance

Action: For discussion

13.3. Type II variations: revised procedural timetables

Action: For discussion

Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

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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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