5 October 2015
EMA/PRAC/656971/2015
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 5-8 October 2015

Chair: June Raine – Vice-Chair: Almath Spooner

5 October 2015, 13:00 – 19:00, room 3/A

6 October 2015, 08:30 – 19:00, room 3/A

7 October 2015, 08:30 – 19:00, room 3/A

8 October 2015, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

22 October 2015, 10:00 – 12:00, room 6/B, via teleconference

Health and safety information

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

Disclaimers

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

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 5-8 October 2015. See October 2015 PRAC minutes (to be published post November 2015 PRAC meeting).

1.2. Adoption of agenda of the meeting on 5-8 October 2015

1.3. Adoption of the minutes of the previous meeting on 7-10 September 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. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) – CERVARIX (CAP)
Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) – GARDASIL (CAP), SILGARD (CAP)

Human papillomavirus vaccine [types 6, 11, 16, 18, 31, 33, 45, 52, 58] (recombinant, adsorbed) – GARDASIL 9 (CAP) - EMEA/H/A-20/1421

MAH(s): GlaxoSmithKline Biologicals S.A. (Cervarix), Sanofi Pasteur MSD SNC (Gardasil, Gardasil 9), Merck Sharp & Dohme Limited (Silgard)

PRAC Rapporteur: Julie Williams; PRAC Co-rapporteurs: Jean-Michel Dogné, Qun-Ying Yue

Scope: Review to further clarify the safety profile of human papillomavirus vaccines 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 list of questions to Scientific Advisory Group (SAG)

3.2.2. 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 discussion

3.2.3. 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 or a list of outstanding issues

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. Adalimumab – HUMIRA (CAP)

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– New signal
Lead Member State: SE

4.1.2. Carbidopa, levodopa (NAP)

Applicant: AbbVie Ltd, various

PRAC Rapporteur: To be appointed

Scope: Signal of intussusception
Action: For adoption of PRAC recommendation
EPITT 18424 – New signal
Lead Member State: SE

4.1.3. Ibrutinib – IMBRUVICA (CAP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Signal of peripheral neuropathy
Action: For adoption of PRAC recommendation
EPITT 18480 – New signal
Lead Member State: UK

4.1.4. Peginterferon alfa-2a – PEGASYS (CAP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of acquired haemophilia
Action: For adoption of PRAC recommendation
EPITT 18476 – New signal
Lead Member State: SE

4.1.5. Ustekinumab - STELARA (CAP)

Applicant: Janssen-Cilag International N.V.

[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: Julie Williams

Scope: Signal of pemphigoid
Action: For adoption of PRAC recommendation
EPITT 18469 – New signal
Lead Member State: UK

4.2. New signals detected from other sources

4.2.1. Alogliptin – VIPIDIA (CAP); alogliptin, metformin – VIPDOMET (CAP); alogliptin, pioglitazone – INCRESYNC (CAP) Linagliptin – TRAJENTA (CAP); linagliptin, metformin – JENTADUETO (CAP)

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

PRAC Rapporteur: To be appointed

Scope: Signal of arthralgia
Action: For adoption of PRAC recommendation
EPITT 18489 – New signal
Lead Member State: NL

4.3. Signals follow-up and prioritisation

4.3.1. Adalimumab – HUMIRA (CAP) – EMEA/H/C/00000481/SDA/0242

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of convulsion
Action: For adoption of PRAC recommendation
EPITT 18211 – Follow-up to July 2015

4.3.2. Anakinra - KINERET (CAP) - EMEA/H/C/000363/SDA/026

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Torbjorn Callreus

Scope: Signal of thrombocytopenia
Action: For adoption of PRAC recommendation
EPITT 18337 – Follow-up to June 2015

4.3.3. Boceprevir – VICTRELIS (CAP) - EMEA/H/C/002332/SDA/037

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Isabelle Robine

Scope: Signal of hyponatraemia
Action: For adoption of PRAC recommendation
EPITT 18350 – Follow-up to June 2015

4.3.4. 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: Valerie Strassmann

Scope: Signal of retinal detachment
Action: For adoption of PRAC recommendation
EPITT 15914 – Follow-up to June 2015

4.3.5. 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 May 2015

4.3.6. Sitagliptin - JANUVIA (CAP) - EMEA/H/C/000722/SDA/036, RISTABEN (CAP) - EMEA/H/C/001234/SDA/014, TESAVEL (CAP) - EMEA/H/C/000910/SDA/030, XELEVIA (CAP) - EMEA/H/C/000762/SDA/035 Sitagliptin, metformin – EFFICIB (CAP) - EMEA/H/C/000896/SDA/017, JANUMET (CAP) - EMEA/H/C/000861/SDA/017, RISTFOR (CAP) - EMEA/H/C/001235/SDA/013, VELMETIA (CAP) - EMEA/H/C/000862/SDA/017

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Signal of intestinal obstruction
Action: For adoption of PRAC recommendation
EPITT 18251 – Follow-up to April 2015

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Atazanavir - EMEA/H/C/004048

Generic

Scope: Treatment of human immunodefficiency virus (HIV)-1
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.2. Caspofungin - EMEA/H/C/004134

Generic

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

5.1.3. Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and haemophilus type b conjugate vaccine (adsorbed) - EMEA/H/C/003982

Scope: Vaccination against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and invasive diseases caused by Haemophilus influenzae type b (Hib)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.4. Human heterologous liver cells – HEPARESC (MAA) - EMEA/H/C/003750, Orphan

Applicant: Cytonet GmbH&Co KG

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

5.1.5. Insulin human - EMEA/H/C/003858

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

5.1.6. Lesinurad - EMEA/H/C/003932

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

5.1.7. Lopinavir, ritonavir - EMEA/H/C/004025

Generic

Scope: Treatment of human immunodeficiency virus (HIV-1) infected adults, adolescents and children above the age of 2 years
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.8. Migalastat - EMEA/H/C/004059, Orphan

Applicant: Amicus Therapeutics UK Ltd

Scope: Treatment of patients with Fabry desease
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.9. Osimertinib - EMEA/H/C/004124

Scope: Treatment of non-small-cell lung cancer (NSCLC)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.10. 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

5.1.11. Pitolisant - EMEA/H/C/002616, Orphan

Applicant: Bioprojet Pharma

Scope: Treatment of narcolepsy
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. Imatinib – GLIVEC (CAP) - EMEA/H/C/000406/II/0098/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of a revised RMP in order to exclude the potential drug interactions with acetaminophen/paracetamol and imatinib, exclude the elderly population as missing information. In addition, the RMP is updated with the safety actions taken since the last update including drug rash with eosinophilia and system symptoms, gastric antral vascular ectasia and chronic renal failure. Finally, the RMP is updated with amended due dates of final study reports for three category 3 studies: CSTI571A2405, CSTI571A2403 and CSTI571L2401
Action: For adoption of PRAC AR

5.2.2. Influenza vaccine (H1N1)v (split virion, inactivated, adjuvanted) – PANDEMRIX (CAP) - EMEA/H/C/000832/II/0079

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Rafe Suvarna

Scope: Update of Annex II of the product information in order to delete the obligation to perform non-clinical mechanistic studies in naïve or A(H1N1) pdm09 primed 4-week old female cotton rats to evaluate the potential disruption of blood-brain-barrier integrity and the potential CNS inflammation/damage following intramuscular administrations of *Pandemrix*, of non-adjuvanted H1N1 antigen and of AS03 adjuvant system
Action: For adoption of PRAC AR

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

5.3.1. 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

5.3.2. Ambrisentan – VOLIBRIS (CAP) - EMEA/H/C/000839/II/0041

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to include an expanded therapeutic indication for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1). In addition, the MAH took the opportunity to update Annex II to reflect a change in the PSUR cycle. The Package leaflet is proposed to be updated accordingly.
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. Bevacizumab – AVASTIN (CAP) - EMEA/H/C/000582/II/0086

Applicant: Roche Registration Ltd

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to extend the use of bevacizumab in combination with erlotinib for the first line treatment of patients with unresectable advanced, metastatic or recurrent non-squamous non-small lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) activating mutations. As a consequence sections 4.1, 4.2, 4.5, 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

5.3.4. Brentuximab vedotin – 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 brentuximab vedotin 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 accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.5. Brentuximab vedotin – ADCETRIS (CAP) - EMEA/H/C/002455/II/0028

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the 50mg powder for concentrate for solution SmPC in order to update the safety information based on study SGN35-006 part A to allow retreatment of adult patients who have responded to previous treatment with brentuximab vedotin under the existing indications of: 1) relapsed or refractory CD30+ Hodgkin lymphoma (HL) following autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option and for adult patients with or 2) relapsed or refractory systemic anaplastic large cell lymphoma (sALCL)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.6. Collagenase clostridium histolyticum – XIAPEX (CAP) - EMEA/H/C/002048/II/0059

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC to include information related to the treatment of Dupuytren's contracture with 2 concurrent injections of collagenase clostridium histolyticum. The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. Crizotinib – XALKORI (CAP) - EMEA/H/C/002489/II/0024

Applicant: Pfizer Limited

PRAC Rapporteur: Corinne Fechant

Scope: Extension of indication to the first-line treatment of anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC): update of section 4.1 of the SmPC. In addition update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC to include the results of the pivotal study A8081014: a multinational, multicentre, randomized, open-label, phase 3 study comparing the efficacy and safety of crizotinib to first-line chemotherapy (pemetrexed/cisplatin or pemetrexed/carboplatin) in patients with previously untreated ALK-positive advanced non-squamous NSCLC and updated safety results from studies A8081001, A8081005 and A8081007. In addition, section 5.1 of the SmPC was revised to include updated overall survival data from studies A8081001 and A8081005.
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.8. Daptomycin – CUBICIN (CAP) - EMEA/H/C/000637/II/0053/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to extend the age range for the indication 'complicated skin and soft-tissue infections' (cSSTI) to include paediatric patients from 1 to 17 years of age. As a consequence sections 4.1, 4.2, 4.4, 5.2 and 6.2 of the SmPC are being updated. The Package Leaflet is updated accordingly. Moreover, the updated RMP version 9.0 has been submitted accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.9. Empagliflozin, metformin – SYNJARDY (CAP) - EMEA/H/C/003770/WS/0800; linagliptin, metformin – JENTADUETO (CAP) - EMEA/H/C/002279/WS/0800

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.3, 4.4 and 4.5 of the SmPC in order to align it for Jentadueto and Synjardy to the recently modified SmPC for the UK metformin label (Glucophage). The RMPs (version 3.0 for Synjardy and version 11.0 for Jentadueto) have been updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.10. Empagliflozin – JARDIANCE (CAP) - EMEA/H/C/002677/WS/0801 empagliflozin, metformin – SYNJARDY (CAP) - EMEA/H/C/003770/WS/0801

Applicant: Boehringer Ingelheim International GmbH, Boehringer Ingelheim GmbH

PRAC Rapporteur: Miguel-Angel Macia

Scope: Update of sections 4.6 and 5.3 of the SmPC in order to update the renal development and maturation information after analysis of the non-clinical study 14R018 [n00231757] entitled '10-week toxicity study by oral gavage in the juvenile Wistar Han rat with a 13-week recovery'
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.11. Fingolimod – GILENYA (CAP) - EMEA/H/C/002202/II/0037

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Isabelle Robine

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information to include additional warning and guidance on progressive multifocal leukoencephalopathy (PML). The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.12. Human hepatitis B immunoglobulin – ZUTECTRA (CAP) - EMEA/H/C/001089/II/0024

Applicant: Biotest Pharma GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to the prevention of hepatitis B virus (HBV) re-infection in hepatitis B antigen (HBsAg) and HBV-DNA negative patients at least one week – instead of the approved at least 6 months - after liver transplantation for hepatitis B induced liver failure. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the rMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.13. Ibrutinib – IMBRUVICA (CAP) - EMEA/H/C/003791/II/0007/G

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Group of variations to submit several non-clinical studies reports. Accordingly, update of section 4.5 of the SmPC regarding BRCP inhibition, update of section 4.5 of the SmPC to delete the CYP3A4 inhibition statement, update of the wording regarding the co-administration with transport substrates/inhibitors in section 5.2 of the SmPC. The Package Leaflet and the RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Extension of indication to include a new indication for Zydelig 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

5.3.15. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/000717/II/0079

Applicant: Celgene Europe Limited

PRAC Rapporteur: Corinne Fechant

Scope: Extension of indication to add the treatment of adult patients with relapsed and/or refractory mantle cell lymphoma (MCL). As a consequence, SmPC sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 are updated. The Package Leaflet and RMP (version 25.0) are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.16. Measles, mumps, rubella and varicella vaccine (live) – PROQUAD (CAP) - EMEA/H/C/000622/R/0100

Applicant: Sanofi Pasteur MSD SNC

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

5.3.17. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/II/0002

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment as monotherapy of locally advanced or metastatic non-squamous non-small cell lung cancer (NSCLC) after prior chemotherapy in adults patients based on study CA209057. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC have been updated. Furthermore, SmPC section 4.8 has been revised with updated combined clinical trial exposure numbers to reflect inclusion of studies in non-squamous NSCLC and in nivolumab in combination with ipilimumab in advanced melanoma. The Package Leaflet and RMP (version 3.0) are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.18. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/II/0003

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment in combination with ipilimumab of advanced (unresectable or metastatic) melanoma in adults based on interim data from study CA209067 and the final clinical study report of study CA209069. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated. The Package Leaflet and RMP (version 3.0) are updated accordingly. The application includes a paediatric non-clinical biomarker study provided to fulfil paediatric requirements
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.19. Nivolumab – OPDIVO (CAP) - EMEA/H/C/003985/II/0004

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information on toxic epidermal necrolysis (TEN) and encephalitis. The Package Leaflet is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.20. Ofatumumab – ARZERRA (CAP) - EMEA/H/C/001131/II/0041

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Extension of indication to include the maintenance therapy in chronic lymphocytic leukemia (CLL). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordingly. The MAH is also taking the opportunity of this procedure to update the Annex II and combine the 2 SmPCs for the 100 mg an 1,000mg vials
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.21. Oritavancin – ORBACTIV (CAP) - EMEA/H/C/003785/II/0003

Applicant: The Medicines Company UK Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of sections 4.3, 4.4 and 4.5 of the SmPC in order to include information on the interaction potential between oritavancin and phospholipid-dependent and phospholipid-independent laboratory coagulation tests following the conclusion of two RMP category 3 studies. The Package Leaflet and RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.22. Regorafenib – STIVARGA (CAP) - EMEA/H/C/002573/II/0014/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

Scope: Update of section 4.4 of the SmPC in order to delete the warnings and precautions information on KRAS mutant tumours patients after analysis of the provided study report for the CONCUR study (15808) (ANX 002.4 and 002.3). In addition the MAH has submitted results of the CORRECT trial (14387) as final biomarker analysis of the study. The obligation to conduct post-authorisation measures in Annex II has been updated in line with the presented studies
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.23. Retigabine – TROBALT (CAP) - EMEA/H/C/001245/II/0037

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

Scope: Submission of a clinical study report (CSR) for the terminated post-authorisation efficacy study (PAES) PTG116878 entitled ‘a dose-optimization study of ezogabine/retigabine immediate release tablets versus placebo in the adjunctive treatment of subjects with partial-onset seizures’ in order to evaluate the efficacy of retigabine immediate release as an adjunctive treatment for partial-onset seizures in adults with epilepsy who have inadequate control of their seizures with a single antiepileptic drug. As a consequence a revised RMP (version 13.1) is submitted accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.24. Retigabine – TROBALT (CAP) - EMEA/H/C/001245/II/0038

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

Scope: Submission of a clinical study report (CSR) for the terminated post-authorisation efficacy study (PAES) RTG114855 entitled 'a randomised, double-blind, placebo-controlled, parallel-group, multicentre study to determine the efficacy and safety of 2 doses of retigabine immediate release (900 mg/day and 600 mg/day) used as adjunctive therapy in adult Asian subjects with drug-resistant partial-onset seizures' in order to investigate the efficacy, safety and tolerability and health outcomes of Asian subjects with drug-resistant partial onset seizures (POS). As a consequence, a revised RMP (version 13.2) is submitted accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.25. 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 (ARV) treatment-naïve paediatric patients aged 12 to <18 years 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 (RPV) 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. The Package Leaflet and RMP (version 6.0) are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.26. Ruxolitinib – JAKAVI (CAP) - EMEA/H/C/002464/II/0024

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC in order to add a warning on reported cases of Merkell cell carcinoma in patients treated with ruxolitinib. The RMP is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.27. Saquinavir – INVIRASE (CAP) - EMEA/H/C/000113/II/0115

Applicant: Roche Registration Ltd

PRAC Rapporteur: Marianne Lunzer

Scope: Update of section 4.5 the SmPC in order to update the drug-drug interaction information and to delete information regarding the use of unboosted invirase. The Package Leaflet is updated accordingly. The RMP is included as a consolidated version as requested as part of the last PSUR (PSUSA/00002684/201412)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.28. 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 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 and the RMP are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Extension of indication to add 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

5.3.30. Shingles (herpes zoster) vaccine (live) – ZOSTAVAX (CAP) - EMEA/H/C/000674/X/0085

Applicant: Sanofi Pasteur MSD SNC

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Line extension to add the 'intramuscular' route of administration for all presentations
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.31. Simeprevir – OLYSIO (CAP) - EMEA/H/C/002777/II/0015

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to amend the safety information regarding the use of simeprevir in interferon-free regimens, based on the primary analysis (SVR12) of studies HPC3017 and HPC3018. The Package Leaflet and Labelling are updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Celgene Europe Limited

PRAC Rapporteur: Corinne Fechant

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

5.3.33. Voriconazole – VFEND (CAP) - EMEA/H/C/000387/II/0110/G

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of the SmPC sections 4.4, 4.8 and 5.1 to reflect the safety and efficacy data from studies in paediatric population. The Package Leaflet and the RMP (version 4) are updated accordingly
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. Afatinib – GIOTRIF (CAP) - PSUSA/10054/201503

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.2. Albiglutide – EPERZAN (CAP) - PSUSA/10175/201503

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

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

6.1.3. Alemtuzumab – LEMTRADA (CAP) - PSUSA/10055/201503

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

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

6.1.4. Aminolevulinic acid – GLIOLAN (CAP) - PSUSA/00009/201503

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Margarida Guimarães

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

6.1.5. Apremilast – OTEZLA (CAP) - PSUSA/10338/201503

Applicant: Celgene Europe Limited

PRAC Rapporteur: Dolores Montero Corominas

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

6.1.6. Aprepitant – EMEND (CAP) - PSUSA/00229/201503

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.7. Atosiban – TRACTOCILE (CAP) - PSUSA/00264/201501

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Amelia Cupelli

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

6.1.8. Bedaquiline – SIRTURO (CAP) - PSUSA/10074/201503

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

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

6.1.9. Belimumab – BENLYSTA (CAP) - PSUSA/09075/201503

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.10. Canagliflozin – INVOKANA (CAP); canagliflozin, metformin – VOKANAMET (CAP) - PSUSA/10077/201503

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

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

6.1.11. Cholic acid – KOLBAM (CAP) - PSUSA/10182/201504

Applicant: Retrophin Europe Ltd

PRAC Rapporteur: Rafe Suvarna

Scope of procedure: Evaluation of a PSUSA procedure (MA withdrawal dated 11 June 2015)
Action: For information

6.1.12. Cholic acid - ORPHACOL (CAP) - PSUSA/10208/201503

Applicant: Laboratoires CTRS - Boulogne Billancourt

PRAC Rapporteur: Rafe Suvarna

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

6.1.13. Colesevelam – CHOLESTAGEL (CAP) - PSUSA/00864/201503

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

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

6.1.14. Dabigatran – PRADAXA (CAP) - PSUSA/00918/201503

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

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

6.1.15. Dexmedetomidine – DEXDOR (CAP) - PSUSA/00998/201503

Applicant: Orion Corporation

PRAC Rapporteur: Julie Williams

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

6.1.16. Dimethyl fumarate – TECFIDERA (CAP) - PSUSA/10143/201503

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

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

6.1.17. Dulaglutide – TRULICITY (CAP) - PSUSA/10311/201503

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

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

6.1.18. Emtricitabine – EMTRIVA (CAP) - PSUSA/01209/201504

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

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

6.1.19. Emtricitabine, tenofovir – TRUVADA (CAP) - PSUSA/01210/201504

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

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

6.1.20. Enfuvirtide – FUZEON (CAP) - PSUSA/01217/201503

Applicant: Roche Registration Ltd

PRAC Rapporteur: Qun-Ying Yue

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

6.1.21. Everolimus – AFINITOR (CAP) - PSUSA/10268/201503

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

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

6.1.22. Everolimus – VOTUBIA (CAP) - PSUSA/01343/201503

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

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

6.1.23. Exenatide – BYDUREON (CAP), BYETTA (CAP) - PSUSA/09147/201503

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

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

6.1.24. Fenofibrate, simvastatin – CHOLIB (CAP) - PSUSA/10096/201502

Applicant: BGP Products Ltd

PRAC Rapporteur: Julie Williams

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

6.1.25. Fosaprepitant – IVEMEND (CAP) - PSUSA/01471/201503

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.26. Glycopyrronium bromide, indacaterol – ULTIBRO BREEZHALER (CAP), ULUNAR BREEZHALER (CAP), XOTERNA BREEZHALER (CAP) - PSUSA/10105/201503

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

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

6.1.27. Influenza vaccine H1N1v (surface antigen, inactivated, adjuvanted) – FOCETRIA (CAP) - PSUSA/02278/201503

Applicant: Novartis Vaccines and Diagnostics S.r.l.

PRAC Rapporteur: Carmela Macchiarulo

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

6.1.28. Insulin degludec, liraglutide – XULTOPHY (CAP) - PSUSA/10272/201503

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

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

6.1.29. Ipilimumab – YERVOY (CAP) - PSUSA/09200/201503

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

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

6.1.30. Japanese encephalitis virus (inactivated) – IXIARO (CAP) - PSUSA/01801/201503

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.1.31. Lapatinib – TYVERB (CAP) - PSUSA/01829/201503 (with RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.32. Vildagliptin - GALVUS (CAP), JALRA (CAP), XILIARX (CAP); metformin, vildagliptin – EUCREAS (CAP), ICANDRA (CAP), ZOMARIST (CAP) - PSUSA/03113/201502

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

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

6.1.33. Methylnaltrexone bromide – RELISTOR (CAP) - PSUSA/02023/201503

Applicant: TMC Pharma Services Ltd

PRAC Rapporteur: Valerie Strassmann

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

6.1.34. Naloxegol – MOVENTIG (CAP) - PSUSA/10317/201503

Applicant: AstraZeneca AB

PRAC Rapporteur: Almath Spooner

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

6.1.35. Raltegravir –ISENTRESS (CAP); raltegravir, lamivudine - DUTREBIS (CAP) - PSUSA/02604/201503

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

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

6.1.36. Regorafenib – STIVARGA (CAP) - PSUSA/10133/201503

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

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

6.1.37. Retigabine – TROBALT (CAP) - PSUSA/02624/201503

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

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

6.1.38. Riociguat – ADEMPAS (CAP) - PSUSA/10174/201503

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

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

6.1.39. Rivaroxaban – XARELTO (CAP) - PSUSA/02653/201503

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

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

6.1.40. Tacrolimus – PROTOPIC (CAP) - PSUSA/02840/201503

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Almath Spooner

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

6.1.41. Telaprevir – INCIVO (CAP) - PSUSA/09306/201503

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Qun-Ying Yue

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

6.1.42. Telavancin – VIBATIV (CAP) - PSUSA/02879/201503

Applicant: Clinigen Healthcare Ltd

PRAC Rapporteur: Julie Williams

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

6.1.43. Teriflunomide – AUBAGIO (CAP) - PSUSA/10135/201503

Applicant: Sanofi-Aventis Groupe

PRAC Rapporteur: Martin Huber

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

6.1.44. Tolcapone – TASMAR (CAP) - PSUSA/02985/201503 (with RMP)

Applicant: Meda AB

PRAC Rapporteur: Almath Spooner

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

6.1.45. Trastuzumab – HERCEPTIN (CAP) - PSUSA/03010/201503

Applicant: Roche Registration Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.1.46. Vortioxetine – BRINTELLIX (CAP) - PSUSA/10052/201503 (with RMP)

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Veerle Verlinden

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

6.1.47. Zonisamide – ZONEGRAN (CAP) - PSUSA/03152/201503

Applicant: Eisai Ltd

PRAC Rapporteur: Almath Spooner

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. Cladribine – LITAK (CAP), NAP - PSUSA/00787/201502

Applicant: Lipomed GmbH, various

PRAC Rapporteur: Rafe Suvarna

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

6.2.2. Travoprost – IZBA (CAP), TRAVATAN (CAP), NAP - PSUSA/03011/201502

Applicant: Alcon Laboratories (UK) Ltd, various

PRAC Rapporteur: Dolores Montero Corominas

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

6.2.3. Voriconazole – VFEND (CAP), NAP - PSUSA/03127/201502

Applicant: Pfizer Limited, various

PRAC Rapporteur: Sabine Straus

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. Amitriptyline (NAP) - PSUSA/00168/201501

Applicant: various

PRAC Lead: Leonidas Klironomos

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

6.3.2. Amitriptyline, perphenazine (NAP) - PSUSA/00170/201501

Applicant: various

PRAC Lead: Leonidas Klironomos

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

6.3.3. Ampicillin, sulbactam (NAP) - PSUSA/00000197/201502

Applicant: various

PRAC Lead: Carmela Macchiarulo

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

6.3.4. Argatroban (NAP) - PSUSA/00009057/201501

Applicant: various

PRAC Lead: Qun-Ying Yue

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

6.3.5. Cilazapril, cilazapril hydrochlorothiazide (NAP) - PSUSA/00000749/201502

Applicant: various

PRAC Lead: Almath Spooner

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

6.3.6. Cilostazol (NAP) - PSUSA/00010209/201502

Applicant: various

PRAC Lead: Julie Williams

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

6.3.7. Clobetasol (NAP) - PSUSA/00000799/201502

Applicant: various

PRAC Lead: Veerle Verlinden

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

6.3.8. Fluocinolone acetonide (intravitreal implant in applicator) (NAP) - PSUSA/00010224/201502

Applicant: various

PRAC Lead: Margarida Guimarães

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

6.3.9. Iloprost (intravenous solution) (NAP) - PSUSA/00009190/201501

Applicant: various

PRAC Lead: Corinne Fechant

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

6.3.10. Lisdexamfetamine (NAP) - PSUSA/00010289/201502

Applicant: various

PRAC Lead: Julie Williams

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

6.3.11. Mesalazine (NAP) - PSUSA/00001990/201502

Applicant: various

PRAC Lead: Julie Williams

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

6.3.12. Methysergide (NAP) - PSUSA/00002030/201502

Applicant: various

PRAC Lead: Sabine Straus

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

6.3.13. Nafarelin (NAP) - PSUSA/00002105/201502

Applicant: various

PRAC Lead: Ingebjørg Buajordet

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

6.3.14. Nitrofurantoin, nifurtoinol (NAP) - PSUSA/00002174/201502

Applicant: various

PRAC Lead: Jolanta Gulbinovic

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

6.3.15. Nomegestrol (NAP) - PSUSA/00002181/201501

Applicant: various

PRAC Lead: Adam Przybylkowski

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

6.3.16. Olodaterol (NAP) - PSUSA/00010245/201503

Applicant: various

PRAC Lead: Sabine Straus

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

6.3.17. Ondansetron (NAP) - PSUSA/00002217/201502

Applicant: various

PRAC Lead: Milena Radoha-Bergoč

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

6.3.18. Potassium para aminobenzoate (NAP) - PSUSA/00010130/201502

Applicant: various

PRAC Lead: Martin Huber

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

6.3.19. Sevoflurane (NAP) - PSUSA/00002698/201501

Applicant: various

PRAC Lead: Almath Spooner

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

6.3.20. Tenonitrozole (NAP) - PSUSA/00003185/201502

Applicant: various

PRAC Lead: Nicolae Fotin

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

6.3.21. Tenoxicam (NAP) - PSUSA/00002893/201502

Applicant: various

PRAC Lead: Carmela Macchiarulo

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

6.3.22. Tiludronic acid (NAP) - PSUSA/00002959/201502

Applicant: various

PRAC Lead: Isabelle Robine

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

6.3.23. Vancomycin (NAP) - PSUSA/00003097/201501

Applicant: various

PRAC Lead: Torbjorn Callreus

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

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/LEG/050

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: From PSUSA/00002980/201410: Review of all cases of melanoma in association with tocilizumab that have become available since marketing approval and comparison of the (cumulative) incidence of melanomas (separated for skin and ocular melanoma) with background rates of melanomas in the target population (rheumatoid arthritis (RA), systemic juvenile idiopathic arthritis (SJIA)/polyarticular juvenile idiopathic arthritis (PJIA))
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. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSP/0020.1

Applicant: Celgene Europe Limited

PRAC Rapporteur: Corinne Fechant

Scope: Evaluation of a revised 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 advice to CHMP

7.1.2. Thiocolchicoside (NAP) - EMEA/H/N/PSP/j/0030

Applicant: Sanofi-Aventis Recherche & Développement and other companies involved in the consortium

PRAC Rapporteur: Amelia Cupelli

Scope: Drug utilisation study to characterise prescribing practices for the medicinal products during typical clinical use in representative groups of prescribers and to assess main reasons for prescription
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

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

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

7.2.1. Agomelatine – THYMANAX (CAP) - EMEA/H/C/000916/MEA/026, VALDOXAN (CAP) - EMEA/H/C/000915/MEA/026

Applicant: Servier (Ireland) Industries Ltd, Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: PASS protocol for study CLE-20098-96-096: a non-interventional post-authorisation safety study: agomelatine drug utilisation study (DUS) in selected European countries: a multinational, observational study to assess effectiveness of risk-minimisation measures
Action: For adoption of advice to CHMP

7.2.2. Albiglutide – EPERZAN (CAP) - EMEA/H/C/002735/MEA/002.2

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 002.1 (PASS protocol for an observational study of the risk of acute pancreatitis in subjects exposed to albiglutide, other GLP-1 agonists or DPP-4 inhibitors compared to other antidiabetic agents (protocol PRJ2335)) request for supplementary information (RSI) as adopted in April 2015
Action: For adoption of advice to CHMP

7.2.3. Albiglutide – EPERZAN (CAP) - EMEA/H/C/002735/MEA/003.2

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 003.1 (PASS protocol for a study to assess the risk of thyroid and pancreatic cancers, and malignancy when used in combination with insulins in observational databases of sufficient size that provides long term longitudinal follow up of patients (protocol PRJ2331)) request for supplementary information (RSI) as adopted in in April 2015
Action: For adoption of advice to CHMP

7.2.4. Albiglutide – EPERZAN (CAP) - EMEA/H/C/002735/MEA/004.2

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 004.1 (PASS protocol for a cohort study to investigate the prescribing of albiglutide among women of child bearing age who have type 2 diabetes (Protocol PRJ2376)) request for supplementary information (RSI) as adopted in April 2015
Action: For adoption of advice to CHMP

7.2.5. Albiglutide – EPERZAN (CAP) - EMEA/H/C/002735/MEA/005.2

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

[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

Scope: MAH's response to MEA 005.1 (PASS protocol for a retrospective cohort study to assess the utilisation of albiglutide among women of child bearing age in the U.S. (protocol PRJ2379)) request for supplementary information (RSI) as adopted in April 2015
Action: For adoption of advice to CHMP

7.2.6. Dasabuvir – EXVIERA (CAP) - EMEA/H/C/003837/MEA/001.1

Applicant: AbbVie Ltd.

PRAC Rapporteur: Miguel-Angel Macia

Scope: MAH's responses to MEA001 (PASS protocol for a prospective, observational cohort study utilising the Hepatitis C Therapeutic Registry and Research Network (HCV-TARGET) data to evaluate the clinical impact and real world frequency of Grade 3+ ALT elevations in patients being treated for hepatitis C with paritaprevir with ritonavir (paritaprevir/ritonavir), ombitasvir and dasabuvir (3 direct-acting antiviral (DAA) regimen) or paritaprevir/ritonavir and ombitasvir (2-DAA regimen) with or without ribavirin for hepatitis C infection (HCV) (SHORT – evaluation of the potential for and clinical impact of increased ALT in patients using the AbbVie 2-DAA or 3-DAA Regimens in a real world setting) as adopted in April 2015
Action: For adoption of advice to CHMP

7.2.7. Desloratadine – AERIUS (CAP) - EMEA/H/C/000313/MEA/065; AZOMYR (CAP) - EMEA/H/C/000310/MEA/065; NEOCLARITYN (CAP) - EMEA/H/C/000314/MEA/065

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of a new protocol for a PASS: 'association between use of desloratadine and risk of seizures, supraventricular tachycardia, and atrial fibrillation or flutter: A nordic register-based study', following procedure EMEA/H/C/xxxx/WS/0641
Action: For adoption of advice to CHMP

7.2.8. Edoxaban – LIXIANA (CAP) - EMEA/H/C/002629/MEA/005

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Drug utilisation of edoxaban (DUS), study No. DSE-EDO-01-14-EU: edoxaban prescription patterns in Europe: a retrospective drug utilisation chart review study
Action: For adoption of advice to CHMP

7.2.9. Edoxaban – LIXIANA (CAP) - EMEA/H/C/002629/MEA/006

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: PASS protocol for study DSE-EDO-04-14-EU: non-interventional study on edoxaban treatment in routine clinical practice for patients with non valvular atrial fibrillation
Action: For adoption of advice to CHMP

7.2.10. Edoxaban – LIXIANA (CAP) - EMEA/H/C/002629/MEA/007

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: PASS protocol for study DSE-EDO-05-14-EU: non-interventional study on edoxaban treatment in routine clinical practice in patients with venous thromboembolism in Europe
Action: For adoption of advice to CHMP

7.2.11. Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil – STRIBILD (CAP) - EMEA/H/C/002574/MEA/002.2

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: revised PASS protocol for study GS-EU-236-0141: non-interventional post-authorisation safety study to assess renal risk minimisation measures among Stribild-treated patients and factors associated with the risk of proximal renal tubulopathy, and its reversibility, including event rates
Action: For adoption of advice to CHMP

7.2.12. Estrogens conjugated, bazedoxifene – DUAVIVE (CAP) - EMEA/H/C/002314/MEA/002.1

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 002 [US PASS protocol, study no. B2311060] request for supplementary information (RSI) as adopted in May 2015
Action: For adoption of advice to CHMP

7.2.13. Estrogens conjugated, bazedoxifene – DUAVIVE (CAP) - EMEA/H/C/002314/MEA/003.1

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 003 [Final protocol for a drug utilisation study (DUS), study no. B2311061] request for supplementary information (RSI) as adopted in May 2015
Action: For adoption of advice to CHMP

7.2.14. Fingolimod – GILENYA (CAP) - EMEA/H/C/002202/ANX 011.7

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Isabelle Robine

Scope: MAH's responses to ANX 011.6 [protocol for a new prospective cohort study assessing the incidence of cardiovascular (CV) adverse events in patients starting Gilenya treatment] request for supplementary information (RSI) as adopted in March 2015
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.2.15. Golimumab – SIMPONI (CAP) - EMEA/H/C/000992/MEA/027.3

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: PASS protocol for a study of golimumab in ulcerative colitis (UC) using the Spanish ENEIDA Registry. This study seeks to evaluate whether the use of GLM is associated with risk of colectomy for intractable disease, advanced neoplasia (colorectal cancer (CRC) or high grade dysplasia (HGD)), and hepatosplenic T cell lymphoma (HSTCL) in patients with UC as compared with alternative therapies for similar severity of disease
Action: For adoption of advice to CHMP

7.2.16. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA/006.2

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's responses to MEA 006.1 [first annual report- observational prospective cohort study MI-MA194] request for supplementary information (RSI) as adopted in June 2015
Action: For adoption of advice to CHMP

7.2.17. Insulin lispro – LIPROLOG (CAP) - EMEA/H/C/000393/MEA/021.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 021 [US surveillance programme] request for supplementary information (RSI) as adopted in June 2015
Action: For adoption of advice to CHMP

7.2.18. Insulin lispro – HUMALOG (CAP) - EMEA/H/C/000088/MEA/028.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 028 [US surveillance programme] request for supplementary information (RSI) as adopted in June 2015
Action: For adoption of advice to CHMP

7.2.19. Ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP) - EMEA/H/C/003839/MEA/001.1

Applicant: AbbVie Ltd.

PRAC Rapporteur: Miguel-Angel Macia

Scope: MAH's responses to MEA 001 [observational. cohort study utilising the hepatitis C therapeutic registry & research network (HCV-TARGET)] request for supplementary information (RSI) as adopted in April 2015
Action: For adoption of advice to CHMP

7.2.20. Saxagliptin – ONGLYZA (CAP) - EMEA/H/C/001039/MEA/033.2 saxagliptin, metformin hydrochloride – KOMBOGLYZE (CAP) - EMEA/H/C/002059/MEA/010.2

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Revised protocol for PASS study CV181-099ST: comparison of risk of major cardiovascular events between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatments
Action: For adoption of advice to CHMP

7.2.21. Saxagliptin – ONGLYZA (CAP) - EMEA/H/C/001039/MEA/034.2 saxagliptin, metformin hydrochloride – KOMBOGLYZE (CAP) - EMEA/H/C/002059/MEA/011.2

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Revised protocol for PASS study CV181-100ST: comparison of risk of hospitalisation with acute liver failure between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatments
Action: For adoption of advice to CHMP

7.2.22. Saxagliptin – ONGLYZA (CAP) - EMEA/H/C/001039/MEA/035.2 saxagliptin, metformin hydrochloride – KOMBOGLYZE (CAP) - EMEA/H/C/002059/MEA/014.2

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Revised protocol for PASS study CV181-103ST: comparison of risk of hospitalisation for severe hypersensitivity (including severe cutaneous reactions) between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatments
Action: For adoption of advice to CHMP

7.2.23. Saxagliptin – ONGLYZA (CAP) - EMEA/H/C/001039/MEA/036.2 saxagliptin, metformin hydrochloride – KOMBOGLYZE (CAP) - EMEA/H/C/002059/MEA/012.2

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Revised protocol for PASS study CV181-101ST: comparison of risk of hospitalisation with infection between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatments
Action: For adoption of advice to CHMP

7.2.24. Saxagliptin – ONGLYZA (CAP) - EMEA/H/C/001039/MEA/037.2 Saxagliptin, metformin hydrochloride – KOMBOGLYZE (CAP) - EMEA/H/C/002059/MEA/013.2

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Revised protocol for PASS study CV181-157ST: comparison of risk of hospitalisation for acute kidney injury between patients with type 2 diabetes initiating saxagliptin and those initiating other oral anti-diabetic treatments
Action: For adoption of advice to CHMP

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

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

Applicant: Les Laboratories Servier

PRAC Rapporteur: To be appointed

Scope: Drug utilisation study, in five European countries, using cross sectional analysis, to assess the extent of prescriptions of trimetazidine for its withdrawn ophtalmological and/or ear, nose and throat (ENT) indications among general practitioners, ophtalmologists and ENT specialists
Action: For adoption of procedure timetable

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

7.4.1. 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 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

7.4.2. 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 of this study fulfils MEA 005. An updated RMP (version 3.0) is proposed accordingly.
Action: For adoption of PRAC Assessment Report

[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

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. Certolizumab pegol – CIMZIA (CAP) - EMEA/H/C/001037/MEA 005.2

Applicant: UCB Pharma SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of interim reports from ARTIS (RA0021), RABBIT (RA0020), US National Databank for Rheumatic Diseases (RA0005) and BSRBR (RA0022)
Action: For adoption of advice to CHMP

7.5.2. Filgrastim – FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 006; ZARZIO (CAP) - EMEA/H/C/000917/MEA 006

Applicant: Sandoz GmbH

PRAC Rapporteur: Julie Williams

Scope: Year 3 interim safety report on study EP006: safety follow-up of severe chronic neutropenia (SCN) patients included in phase IV study: safety data will be collected via cooperation with the Severe Chronic Neutropenia International Registry and reported annually
Action: For adoption of advice to CHMP

7.5.3. Golimumab – SIMPONI (CAP) - EMEA/H/C/000992/MEA 005.4

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth annual report on a German registry study RABBIT: long-term observational study of the safety of biologic treatments in rheumatoid arthritis
Action: For adoption of advice to CHMP

7.5.4. Golimumab – SIMPONI (CAP) - EMEA/H/C/000992/MEA 006.3

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourth annual report on a Swedish database registry: review and analysis of adverse events from the Swedish national registry system (CNTOART4003): evaluation of the long-term safety of golimumab across a number of indications, including rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis using Swedish national (whole population) medical and pharmaceutical datasets
Action: For adoption of advice to CHMP

7.5.5. Golimumab – SIMPONI (CAP) - EMEA/H/C/000992/MEA 007.1

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

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

Scope: Second report on a pregnancy research initiative to study the exposure to golimumab during pregnancy in patients with rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers (CNTO148ART4001)
Action: For adoption of advice to CHMP

7.5.6. Golimumab – SIMPONI (CAP) - EMEA/H/C/000992/MEA 008.2

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second annual report on an i3 drug safety epidemiology study (CNTO148ART4002): golimumab safety and surveillance program using the Optum research database
Action: For adoption of advice to CHMP

7.5.7. Indacaterol, glycopyrronium bromide – ULTIBRO BREEZHALER (CAP) - EMEA/H/C/002679/ANX/002.2; ULUNAR BREEZHALER (CAP) - EMEA/H/C/003875/ANX/003.1; XOTERNA BREEZHALER (CAP) - EMEA/H/C/003755/ANX/002.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: First interim report for PASS study CQVA149A2402: non-interventional study report multinational database cohort study to assess RMP specified safety outcomes in association with indacaterol/glycopyrronium bromide in Europe
Action: For adoption of advice to CHMP

7.5.8. Indacaterol, glycopyrronium bromide – ULTIBRO BREEZHALER (CAP) - EMEA/H/C/002679/MEA/003.2; ULUNAR BREEZHALER (CAP) - EMEA/H/C/003875/ MEA/004.1; XOTERNA BREEZHALER (CAP) - EMEA/H/C/003755/ MEA/003.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: First interim report for a drug utilisation study CQVA 149A2401: multinational, multi-database drug utilisation study of indacterol/ glycopyrronium bromide in Europe to determine the proportion of patients who do not meet the criteria specified in the product information and the proportion of patients who have missing information as per RMP or pre-defined high risk treatment conditions
Action: For adoption of advice to CHMP

7.5.9. Influenza vaccine (live attenuated, nasal) – FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA/004.3

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's responses to MEA 004.2 [PASS study D2560C00008, first summary safety report] request for supplementary information as adopted in June 2015
Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Umeclidinium bromide – INCRUSE (CAP) - EMEA/H/C/002809 /LEG/001.1 Umeclidinium bromide, vilanterol – ANORO (CAP) - EMEA/H/C/002751 /LEG/001.1; LAVENTAIR (CAP) - EMEA/H/C/003754 /LEG/001.1

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: MAH's responses to ANX-001 [PASS protocol study 201038: non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in COPD patients with UMEC/VI compared with tiotropium as adopted in March 2015: The MAH is requested to submit a copy of the electronic case report form (eCRF) that accurately represents the protocol of the study
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. Clofarabine – EVOLTRA (CAP) - EMEA/H/C/000613/S/0048 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Corinne Fechant

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

8.1.2. Galsulfase – NAGLAZYME (CAP) - EMEA/H/C/000640/S/0060 (without RMP)

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Rafe Suvarna

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

8.1.3. Lomitapide – LOJUXTA (CAP) - EMEA/H/C/002578/S/0020 (without RMP)

Applicant: Aegerion Pharmaceuticals Limited

PRAC Rapporteur: Menno van der Elst

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

8.1.4. Modified vaccinia Ankara virus – IMVANEX (CAP) - EMEA/H/C/0002596/S/0017 (without RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Rafe Suvarna

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

8.1.5. Nelarabine – ATRIANCE (CAP) - EMEA/H/C/000752/S/0031 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

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

8.2. Conditional renewals of the marketing authorisation

8.2.1. Ex vivo expanded autologous human corneal epithelial cells containing stem cells – HOLOCLAR (CAP) - EMEA/H/C/002450/R/00001 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.2.2. Vandetanib – CAPRELSA (CAP) - EMEA/H/C/0002315/R/0015 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Corinne Fechant

Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Fenofibrate, pravastatin – PRAVAFENIX (CAP) - EMEA/H/C/001243/R/0020 (with RMP)

Applicant: Laboratoires SMB S.A.

PRAC Rapporteur: Corinne Fechant

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. List of planned 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

10.1.1. Mycophenolate mofetil – CELLCEPT (CAP) – EMEA/H/C/000082/II/0121

Applicant: Roche Registration Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.4 and 4.6 of the SmPC in order to add a warning for pregnant women and update the safety information related to pregnancy
Action: For adoption of advice to CHMP

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

None

10.3. Other requests

10.3.1. Antiretroviral medicinal products:

Abacavir –ZIAGEN (CAP) - EMEA/H/C/000252/LEG 089.1; abacavir, lamivudine – KIVEXA (CAP) - EMEA/H/C/000581/LEG 045.1; abacavir, lamivudine, zidovudine – TRIZIVIR (CAP) - EMEA/H/C/000338/LEG 090.1; atazanavir– REYATAZ (CAP) - EMEA/H/C/000494/LEG 080.1; darunavir – PREZISTA (CAP) - EMEA/H/C/000707/LEG 070.1; efavirenz – STOCRIN (CAP) - EMEA/H/C/000250/LEG 071.1, SUSTIVA (CAP) - EMEA/H/C/000249/LEG 080.1; efavirenz, emtricitabine, tenofovir disoproxil – ATRIPLA (CAP) - EMEA/H/C/000797/LEG 040.1; elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil – STRIBILD (CAP) - EMEA/H/C/002574/LEG 014.1; emtricitabine – EMTRIVA (CAP) - EMEA/H/C/000533/LEG 049.2; emtricitabine, tenofovir disoproxil – TRUVADA (CAP) - EMEA/H/C/000594/LEG 043.1; emtricitabine, rilpivirine, tenofovir disoproxil – EVIPLERA (CAP) - EMEA/H/C/002312/LEG 031.1; etravirine – INTELENCE (CAP) - EMEA/H/C/000900/LEG 048.1; fosamprenavir – TELZIR (CAP) - EMEA/H/C/000534/LEG 076.1; indinavir – CRIXIVAN (CAP) - EMEA/H/C/000128/LEG 039.1; lamivudine – EPIVIR (CAP) - EMEA/H/C/000107/LEG 052.1, LAMIVUDINE VIIV (Art 58) - EMEA/H/W/000673/LEG 007.1; lamivudine, zidovudine – COMBIVIR (CAP) - EMEA/H/C/000190/LEG 038.1; lopinavir, ritonavir –ALUVIA (Art 58) - EMEA/H/W/000764/LEG 031.1, KALETRA (CAP) - EMEA/H/C/000368/LEG 118.1; nevirapine – VIRAMUNE (CAP) - EMEA/H/C/000183/LEG 061.1; rilpivirine – EDURANT (CAP) - EMEA/H/C/002264/LEG 026.1; ritonavir – NORVIR (CAP) - EMEA/H/C/000127/LEG 049.1; saquinavir – INVIRASE (CAP) - EMEA/H/C/000113/LEG 065.1; stavudine – ZERIT (CAP) - EMEA/H/C/000110/LEG

060.1; tenofovir disoproxil – VIREAD (CAP) - EMEA/H/C/000419/LEG 270.1; tipranavir - APTIVUS (CAP) - EMEA/H/C/000631/LEG 068.1

Applicant: AbbVie Ltd (Kaletra, Norvir), Boehringer Ingelheim International GmbH (Aptivus, Viramune), Bristol-Myers Squibb Pharma EEIG (Reyataz, Sustiva, Zerit), Bristol-Myers Squibb and Gilead Sciences Ltd.(Atripla), Gilead Sciences International Ltd.(Emtriva, Eviplera, Stribild, Truvada, Tybost, Viread), Janssen-Cilag International N.V.(Edurant, Intelence, Prezista), Merck Sharp & Dohme Ltd (Crixivan, Isentress, Stocrin), Roche Registration Ltd. (Invirase), ViiV Healthcare UK Limited (Celsentri, Combivir, Epivir, Lamivudine Viiv, Kivexa, Telzir, Trizivir, Ziagen)

PRAC Rapporteur (lead): Qun-Ying Yue; PRAC Co-Rapporteur: Isabelle Robine; Julie Williams

Scope: Review of class labelling on mitochondrial dysfunction, lactic acidosis and lipodystrophy
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

11.1.1. Hydroxyethyl starch (NAP) - DE/H/xxx/WS/266, SE/H/xxx/WS/268

Applicant: Fresenius Kabi Deutschland GmbH, B. BRAUN MELSUNGEN AG,

PRAC Rapporteur: Qun-Ying Yue, Martin Huber

Scope: PRAC consultation on two safety variations (DE/H/xxx/WS/266 and SE/H/xxx/WS/268) related to draft protocols for two Phase IV clinical studies on trauma and surgery patients imposed as the outcome of the article 107i referral
Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Antiretroviral medicinal products (NAP)

Applicant: Teva Pharma B.V., Mikle-Pharm GmBH

PRAC Rapporteur: Martin Huber

Scope: PRAC consultation on initial marketing authorisation applications for generic medicinal products and the need for the applicants to participate in the Antiretroviral Pregnancy Registry
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-v

12.2.1. Joint Paediatric Committee (PDCO)-PRAC Working Group - guideline on conduct of pharmacovigilance for medicines used by the paediatric population

Action: For discussion

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

None

12.4. Cooperation within the EU regulatory network

None

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

12.6.1. Consortium on progressive multifocal leukoencephalopathy (PML) - progress update

Action: For discussion

12.6.2. Innovative Medicines Initiative (IMI) project - ADAPT-SMART

Action: For discussion

12.6.3. Strategic review and learning meetings organised during the term of the European presidency: organisational aspects; clarification on responsibility for handling of declared interests and on involvement of external (non NCA) speakers

Action: For discussion

12.6.4. World Health Organization(WHO): Biological qualifier update

Action: For discussion

12.7. PRAC work plan

12.7.1. PRAC work plan 2016 - development

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. Granularity and Periodicity Advisory Group (GPAG)

None

12.10.3. Project and Maintenance Group (PMG) 2 - roadmap for PSUR issues

Action: For discussion

12.10.4. PSURs repository

None

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

Action: For adoption of the revised list

12.11. Signal management

12.11.1. Medical literature monitoring (MLM) update

Action: For discussion

12.11.2. 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 – EudraVigilance audit plan

Action: For information

12.13.2. EudraVigilance Access Policy

Action: For adoption

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 – imposed PASS

None

12.15.2. 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. Incident management

None

12.20. Others

None

13. Any other business

13.1. Good Pharmacovigilance Practice (GVP) Chapter P.II. on biologicals

Action: For discussion

13.2. Good Pharmacovigilance Practice (GVP) Module XII on safety-related actions on authorised medicinal products

Action: For discussion

13.3. Post-authorisation efficacy studies – first draft scientific guidance

Action: For adoption

13.4. Update on Pharmacovigilance systems and services

Action: For discussion

13.5. Good Pharmacovigilance Practice (GVP) Guideline on product or population specific considerations III: pregnancy and breastfeeding – concept paper

Action: For adoption

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/