11 April 2016
EMA/PRAC/262317/2016
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 11-14 April 2016

Chair: June Raine – Vice-Chair: Almath Spooner

11 April 2016, 13:00 – 19:00, room 3/A

12 April 2016, 08:30 – 19:00, room 3/A

13 April 2016, 08:30 – 19:00, room 3/A

14 April 2016, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

28 April 2016, 09:00 - 12:00, room 7/B, via Adobe Connect

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 11-14 April 2016. See April 2016 PRAC minutes (to be published post May 2016 PRAC meeting).

1.2. Agenda of the meeting of 11-14 April 2016

Action: For adoption

1.3. Minutes of the previous meeting on 14-17 March 2016

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

2.4. Planned public hearings

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

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 acute febrile neutrophilic dermatosis (Sweet's syndrome)
Action: For adoption of PRAC recommendation
EPITT 18630 – New signal
Lead Member State: SE

4.1.2. Agomelatine – THYMANAX (CAP), VALDOXAN (CAP)

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Signal of urinary retention
Action: For adoption of PRAC recommendation
EPITT 18637 – New signal
Lead Member State: NO

4.1.3. Agomelatine – THYMANAX (CAP), VALDOXAN (CAP)

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Signal of leukopenia
Action: For adoption of PRAC recommendation
EPITT 18638 – New signal
Lead Member State: NO

4.1.4. Cobicistat containing products: cobicistat – TYBOST (CAP), cobicistat, atazanavir sulfate– EVOTAZ (CAP),

[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

cobicistat, darunavir – REZOLSTA (CAP), cobicistat elvitegravir, emtricitabine, tenofovir alafenamide – GENVOYA (CAP), cobicistat elvitegravir, emtricitabine, tenofovir disoproxil fumarate – STRIBILD (CAP)

Applicant: Gilead Sciences International Ltd (Genvoya, Stribild, Tybost), Bristol-Myers Squibb Pharma EEIG (Evotaz), Janssen-Cilag International N.V. (Rezolsta)

PRAC Rapporteur: To be appointed

Scope: Signal of drug interaction with corticosteroids leading to adrenal suppression
Action: For adoption of PRAC recommendation
EPITT 18647 – New signal
Lead Member States: FR, IT, UK

4.1.5. Iomeprol (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of haemolysis
Action: For adoption of PRAC recommendation
EPITT 18625 – New signal
Lead Member State: NO

4.2. New signals detected from other sources

4.2.1. Canagliflozin – INVOKANA (CAP); canagliflozin, metformin – VOKANAMET (CAP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: To be appointed

Scope: Signal of potential increased risk of lower limb amputations
Action: For adoption of PRAC recommendation
EPITT 18650 – New signal
Lead Member States: DE, NL

4.2.2. Direct-acting antivirals (DAAV) indicated for the treatment of hepatitis C (interferon free): daclatasvir – DAKLINZA (CAP); dasabuvir – EXVIERA (CAP); ombitasvir, paritaprevir, ritonavir – VIEKIRAX (CAP); simeprevir - OLYSIO (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, ledipasvir – HARVONI (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG (Daklinza); AbbVie Ltd (Exviera, Viekirax); Janssen-Cilag International N.V. (Olysio); Gilead Sciences International Ltd (Harvoni, Sovaldi)

PRAC Rapporteur: To be appointed

Scope: Signal of unexpected early hepatocellular carcinoma recurrence
Action: For adoption of PRAC recommendation
EPITT 18653 – New signal
Lead Member States: ES, PT, UK

4.2.3. Fulvestrant – FASLODEX (CAP)

Applicant: AstraZeneca UK Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of interference with oestradiol assay leading to false oestradiol results
Action: For adoption of PRAC recommendation
EPITT 18636 – New signal
Lead Member State: SE

4.3. Signals follow-up and prioritisation

4.3.1. Olanzapine – ZYPADHERA (CAP), ZYPREXA (CAP), ZYPREXA VELOTAB (CAP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)
Action: For adoption of PRAC recommendation
EPITT 18534 – Follow-up to December 2015

4.3.2. Penicillins of the beta-lactamase resistant group: cloxacillin (NAP); dicloxacillin (NAP); flucloxacillin (NAP); nafcillin (NAP); oxacillin (NAP)

Applicant: various

PRAC Rapporteur: Margarida Guimarães

Scope: Signal of metabolic acidosis following administration of flucloxacillin in association with paracetamol
Action: For adoption of PRAC recommendation
EPITT 18514 – Follow-up to December 2015

4.3.3. Recombinant factor VIII: antihemophilic factor (recombinant) (NAP) moroctocog alfa – REFACTO AF (CAP) octocog alfa – ADVATE (CAP), HELIXATE NEXGEN (CAP), KOGENATE (CAP)

Applicant: Baxter AG (Advate, Recombinate), Bayer Pharma AG (Kogenate, Helixate NexGen), Pfizer Limited (ReFacto AF), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of inhibitor development in previously untreated patients (PUP)
Action: For adoption of PRAC recommendation
EPITT 18134 – Follow-up to March 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Bortezomib - EMEA/H/C/004207

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

5.1.2. Cediranib - EMEA/H/C/004003, Orphan

Applicant: AstraZeneca AB

Scope: Treatment of platinum sensitive relapsed (PSR) ovarian cancer
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.3. Enoxaparin sodium – EMEA/H/C/004264; EMEA/H/C/003795

Scope: Prophylaxis of thromboembolic disorders of venous origin
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.4. Methotrexate - EMEA/H/C/003983

Scope: Treatment of active rheumatoid arthritis, severe active juvenile idiopathic arthritis and severe recalcitrant disabling psoriasis
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.5. Opicapone - EMEA/H/C/002790

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

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

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

5.1.7. Parathyroid hormone - EMEA/H/C/003861, Orphan

Applicant: NPS Pharma Holdings Limited

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

5.1.8. Reslizumab - EMEA/H/C/003912

Scope: Treatment of asthma and elevated blood eosinophils in patients inadequately controlled on inhaled corticosteroids
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.9. 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

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

5.2.1. Dimethyl fumarate – TECFIDERA (CAP) - EMEA/H/C/002601/II/0026

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Submission of a revised RMP (version 7) in order to include the outcome of the evaluation from WS/689 (PML has been added as an important identified risk) and to implement the new template. The draft PASS protocol for category 3 study 109MS419(a retrospective, multicentre, observational study to assess the effect of Tecfidera delayed-release capsules on lymphocyte subsets in subjects with relapsing forms of multiple sclerosis) was also submitted. In addition, a discussion on the overall totality of the non-clinical and clinical work being undertaken to further understand the lymphopenia with Tecfidera treatment is included
Action: For adoption of PRAC AR

5.2.2. Pandemic influenza vaccine (H1N1)v (split virion, inactivated, adjuvanted) – PANDEMRIX[2] - 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 central nervous system (CNS) inflammation/damage following intramuscular administrations of Pandemrix, of non-adjuvanted H1N1 antigen and of AS03 adjuvant system
Action: For adoption of PRAC AR

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

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

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

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

Applicant: Shire Pharmaceuticals Ireland Ltd.

PRAC Rapporteur: Valerie Strassmann

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

[2] Marketing authorisation expired on 13 August 2015

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

5.3.1. Adalimumab – HUMIRA (CAP) - EMEA/H/C/000481/II/0146

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the treatment of non-infectious intermediate, posterior and panuveitis in adult patients taking adalimumab. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 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

5.3.2. Ataluren – TRANSLARNA (CAP) - EMEA/H/C/002720/II/0016/G

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Update of section 4.4 to remove precautions for use relating to the co-administration of ataluren with substrates or inducers of UGT1A9 and section 4.5 of the SmPC to remove statements relating to the potential effect of co-administration of ataluren with inducers or substrates of UGT1A9 and to add the results from studies PTC124-GD-026-HV and PTC124-GD-027-HV (MEA 011 and MEA 012). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes to the SmPC. Moreover, the RMP (version 4.2) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. Atazanavir – REYATAZ (CAP) - EMEA/H/C/000494/X/0094/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Isabelle Robine

Scope: Line extension for a new pharmaceutical form (oral powder), a new strength for the oral powder presentation (50 mg) and a new paediatric indication (patients from 3 months of age and weighing at least 5 kg) grouped with an update of the capsules presentation in light of new paediatric data. The RMP is also updated to include minor revisions with regard to nephrolithiasis folllowing PRAC's assesment of RMP version 7.3
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.4. Bevacizumab – AVASTIN (CAP) - EMEA/H/C/000582/II/0089

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of section 4.8 of the SmPC in order to update the safety information derived from phase III study GO25632. In addition, Annex II is updated to remove the investigation of suitable biomarkers to allow identification and selection of a more targeted population (ANX 068) from the list of conditions to the Marketing Authorisation (MA). Consequently, the RMP (version 24) is updated
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/0030/G

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

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

5.3.6. Carfilzomib – KYPROLIS (CAP) - EMEA/H/C/003790/II/0004/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marina Dimov Di Giusti

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add information on haemorrhage events and update of section 4.4 and 4.6 of the SmPC in order to add information on venous thrombolic events. The Package Leaflet and RMP are updated accordingly. In addition, the MAH took the opportunity to update the RMP with the request to better characterize infections in patients with relapsed/refractory multiple myeloma requested during the Marketing Authorisation Application (MAA) evaluation
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. Emtricitabine, tenofovir disoproxil – TRUVADA (CAP) - EMEA/H/C/000594/II/0126

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to add pre-exposure prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually acquired human immunodeficiency virus (HIV)-1 in adults at high risk. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8, 4.9, 5.1, 5.2 and 5.3 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

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

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

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

5.3.9. Human normal immunoglobulin – PRIVIGEN (CAP) - EMEA/H/C/000831/II/0100

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to add information on signs of haemolysis and transfusion-related acute lung injury (TRALI). The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to amend Annex II of the product information in line with the latest QRD template (version 9.1)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.10. Ibrutinib – IMBRUVICA (CAP) - EMEA/H/C/003791/II/0016

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to broaden the existing indication for chronic lymphocytic leukaemia (CLL) to include all previously untreated patients including those with 17p deletion or TP53 mutation based on the results from the final clinical study report (CSR) of study PCYC-1115-CA (MEA 021). As a consequence, sections 4.1, 4.6, 4.8, 5.1 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP (version 5.0) is updated accordingly
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

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

5.3.12. Insulin aspart – NOVORAPID (CAP) - EMEA/H/C/000258/II/0111

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of sections 1, 2, 4.2, 4.4, 6.3 and 6.6 of the SmPC to add the use of the YpsoPump insulin pump for the NovoRapid PumpCart presentation.The Package Leaflet and Labelling are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 9.1) and to implement minor corrections in the product information
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.13. Insulin degludec, insulin aspart – RYZODEG (CAP) - EMEA/H/C/002499/II/0017

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to include the paediatric population from 1 to 18 years of age for Ryzodeg. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 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

5.3.14. Lacosamide – VIMPAT (CAP) - EMEA/H/C/000863/II/0060/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to add monotherapy in the treatment of partial-onset seizures. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. Variation to the specification of the active substance and minor change to the test procedure for the active substance. Variation to the

specification of the finished product Vimpat 10mg/ml solution for infusion (EU/1/08/470/016-17). The change applies only to the parenteral presentations. In addition, the MAH took the opportunity to update the product information in line with the latest QRD template (version 9.1)
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

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

5.3.16. Meningococcal group a, c, w135 and y conjugate vaccine – NIMENRIX (CAP) - EMEA/H/C/002226/II/0049

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Extension of indication to include a wider paediatric population starting from 6 weeks of age. As a consequence, sections 4.1, 4.2, 4.5, 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

5.3.17. Meningococcal group a, c, w135 and y conjugate vaccine – NIMENRIX (CAP) - EMEA/H/C/002226/II/0053

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: Update of section 5.1 of the SmPC to include new booster and persistence data with a follow-up of up to 5 years after vaccination with MenACWY-TT. The RMP (version 7.0) is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.18. Obinutuzumab – GAZYVARO (CAP) - EMEA/H/C/002799/II/0007

Applicant: Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to add the treatment of patients with follicular lymphoma based on the results of the pivotal study GAO4753g. Consequently, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 of the SmPC, the Package Leaflet and RMP are updated accordingly. Furthermore, the MAH took the opportunity to make minor editorial changes to sections 4.4, 4.6, 5.3 and 6.6 of the SmPC
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.19. Pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/II/0007

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the second line treatment of non-small cell lung cancer (NSCLC). As a consequence, sections 4.1, 4.2 4.8, 5.1 and 5.2 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

5.3.20. Pioglitazone – ACTOS (CAP) - EMEA/H/C/000285/WS/0848; GLUSTIN (CAP) - EMEA/H/C/000286/WS/0848
pioglitazone, glimepiride – TANDEMACT (CAP) - EMEA/H/C/000680/WS/0848
pioglitazone, metformin – COMPETACT (CAP) - EMEA/H/C/000655/WS/0848; GLUBRAVA (CAP) - EMEA/H/C/000893/WS/0848

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: Update of the section 4.4 of the SmPC based on the results of two long term observational cohort studies assessing bladder cancer risk with pioglitazone. The RMP is updated accordingly. Furthermore, minor editorial changes were introduced in the product information. In addition, the MAH took the opportunity to update the details of local representatives in the Package Leaflet
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

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

5.3.22. Ustekinumab – STELARA (CAP) - EMEA/H/C/000958/X/0049/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Line extension to add a new pharmaceutical form (concentrate for solution for infusion), a new strength (130 mg) and a new route of administration (intravenous use) as well as an extension of indication to add as a new indication the treatment of Crohn's disease
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/10054/201509

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.2. Albiglutide – EPERZAN (CAP) - PSUSA/10175/201509

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Julie Williams

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

6.1.3. Alemtuzumab – LEMTRADA (CAP) - PSUSA/10055/201509

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

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

6.1.4. Aliskiren – RASILEZ (CAP); aliskiren, hydrochlorothiazide – RASILEZ HCT (CAP); aliskiren, amlodipine – RASILAMLO (CAP) - PSUSA/00089/201509

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

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

6.1.5. Apremilast – OTEZLA (CAP) - PSUSA/10338/201509

Applicant: Celgene Europe Limited

PRAC Rapporteur: Dolores Montero Corominas

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

6.1.6. Bazedoxifene, estrogens conjugated – DUAVIVE (CAP) - PSUSA/10321/201510

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

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

6.1.7. Bivalirudin – ANGIOX (CAP) - PSUSA/00421/201509

Applicant: The Medicines Company UK Ltd.

PRAC Rapporteur: Julie Williams

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

6.1.8. Bupropion, naltrexone – MYSIMBA (CAP) - PSUSA/10366/201509

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

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

6.1.9. Cabozantinib – COMETRIQ (CAP) - PSUSA/10180/201509

Applicant: TMC Pharma Services Ltd

PRAC Rapporteur: Sabine Straus

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

6.1.10. Canagliflozin – INVOKANA (CAP); canagliflozin, metformin – VOKANAMET (CAP) - PSUSA/10077/201509

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

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

6.1.11. Cangrelor – KENGREXAL (CAP) - PSUSA/10360/201509

Applicant: The Medicines Company UK Ltd

PRAC Rapporteur: Carmela Macchiarulo

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

6.1.12. Cholic acid – ORPHACOL (CAP) - PSUSA/10208/201509

Applicant: Laboratoires CTRS - Boulogne Billancourt

PRAC Rapporteur: Rafe Suvarna

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

6.1.13. Ciclosporin – IKERVIS (CAP) - PSUSA/10362/201509

Applicant: Santen Oy

PRAC Rapporteur: Julie Williams

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

6.1.14. Dabigatran – PRADAXA (CAP) - PSUSA/00918/201509

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

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

6.1.15. Dapagliflozin – FORXIGA (CAP) - PSUSA/10029/201510

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

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

6.1.16. Daptomycin – CUBICIN (CAP) - PSUSA/00931/201509

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

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

6.1.17. Denosumab – PROLIA (CAP) - PSUSA/00954/201509

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.18. Denosumab – XGEVA (CAP) - PSUSA/09119/201509

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.19. Dulaglutide – TRULICITY (CAP) - PSUSA/10311/201509

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

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

6.1.20. Eculizumab – SOLIRIS (CAP) - PSUSA/01198/201510

Applicant: Alexion Europe SAS

PRAC Rapporteur: Dolores Montero Corominas

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

6.1.21. Eltrombopag – REVOLADE (CAP) - PSUSA/01205/201509

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

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

6.1.22. Etravirine – INTELENCE (CAP) - PSUSA/01335/201509

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Isabelle Robine

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

6.1.23. Florbetapir (^{18}F) – AMYVID (CAP) - PSUSA/10032/201510

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Valerie Strassmann

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

6.1.24. Glycopyrronium bromide – ENUREV BREEZHALER (CAP); SEEBRI BREEZHALER (CAP); TOVANOR BREEZHALER (CAP) - PSUSA/10047/201509

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

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

6.1.25. Glycopyrronium bromide, indacaterol – ULTIBRO BREEZHALER (CAP); ULUNAR BREEZHALER (CAP); XOTERNA BREEZHALER (CAP) - PSUSA/10105/201509

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

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

6.1.26. Hepatitis A (inactivated) and hepatitis B (rDNA) vaccine (adsorbed) – AMBIRIX (CAP); TWINRIX ADULT (CAP); TWINRIX PAEDIATRIC (CAP) - PSUSA/01593/201509

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Rafe Suvarna

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

6.1.27. Insulin aspart – NOVOMIX (CAP); NOVORAPID (CAP) - PSUSA/01749/201509

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

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

6.1.28. Insulin degludec –TRESIBA (CAP); insulin degludec, insulin aspart - RYZODEG (CAP) - PSUSA/10036/201509

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

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

6.1.29. Insulin degludec, liraglutide – XULTOPHY (CAP) - PSUSA/10272/201509

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

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

6.1.30. Insulin human – INSUMAN (CAP) - PSUSA/10107/201509

Applicant: Sanofi-aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

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

6.1.31. Lacosamide – VIMPAT (CAP) - PSUSA/01816/201508

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Qun-Ying Yue

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

6.1.32. Naloxegol – MOVENTIG (CAP) - PSUSA/10317/201509

Applicant: AstraZeneca AB

PRAC Rapporteur: Almath Spooner

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

6.1.33. Oritavancin – ORBACTIV (CAP) - PSUSA/10368/201509

Applicant: The Medicines Company UK Ltd

PRAC Rapporteur: Adam Przybylkowski

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

6.1.34. Panitumumab – VECTIBIX (CAP) - PSUSA/02283/201509

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Julie Williams

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

6.1.35. Raltegravir - ISENTRESS (CAP); raltegravir, lamivudine – DUTREBIS (CAP) - PSUSA/10373/201509

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

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

6.1.36. Ranibizumab – LUCENTIS (CAP) - PSUSA/02609/201510

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

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

6.1.37. Retigabine – TROBALT (CAP) - PSUSA/02624/201509

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

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

6.1.38. Riociguat – ADEMPAS (CAP) - PSUSA/10174/201509

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

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

6.1.39. Rivaroxaban – XARELTO (CAP) - PSUSA/02653/201509

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

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

6.1.40. Sulesomab – LEUKOSCAN (CAP) - PSUSA/02803/201508

Applicant: Immunomedics GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.1.41. Tedizolid phosphate – SIVEXTRO (CAP) - PSUSA/10369/201509

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Miguel-Angel Macia

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

6.1.42. Telavancin – VIBATIV (CAP) - PSUSA/02879/201509

Applicant: Clinigen Healthcare Ltd

PRAC Rapporteur: Julie Williams

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

6.1.43. Teriparatide – FORSTEO (CAP) - PSUSA/02903/201509

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

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

6.1.44. Tobramycin – VANTOBRA (CAP) - PSUSA/10370/201509

Applicant: PARI Pharma GmbH

PRAC Rapporteur: Qun-Ying Yue

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

6.1.45. Trabectedin – YONDELIS (CAP) - PSUSA/03001/201509

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Torbjorn Callreus

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

6.1.46. Trastuzumab – HERCEPTIN (CAP) - PSUSA/03010/201509

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.1.47. Vinflunine – JAVLOR (CAP) - PSUSA/03123/201509

Applicant: Pierre Fabre Médicament

PRAC Rapporteur: Rafe Suvarna

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

6.1.48. Vortioxetine – BRINTELLIX (CAP) - PSUSA/10052/201509

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Veerle Verlinden

Scope: 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. Anagrelide – XAGRID (CAP), NAP - PSUSA/00208/201509

Applicant: Shire Pharmaceutical Contracts Ltd., various

PRAC Rapporteur: Isabelle Robine

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

6.2.2. Epoetin alfa – ABSEAMED (CAP); BINOCRIT (CAP); EPOETIN ALFA HEXAL (CAP), NAP - PSUSA/01237/201508

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

PRAC Rapporteur: Isabelle Robine

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

6.2.3. Irbesartan – APROVEL (CAP); IRBESARTAN ZENTIVA (CAP), NAP - PSUSA/01782/201508

Applicant: Sanofi Clir SNC (Aprovel), Sanofi-Aventis Groupe (Irbesartan Zentiva, Karvea), various

PRAC Rapporteur: Dolores Montero Corominas

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

6.2.4. Leflunomide – ARAVA (CAP); LEFLUNOMIDE MEDAC (CAP); LEFLUNOMIDE WINTHROP (CAP), NAP - PSUSA/01837/201509

Applicant: Sanofi-aventis Deutschland GmbH (Arava, Leflunomide Withrop), Medac Gesellschaft fur klinische Spezialpraparate GmbH (Leflunomide Medac), various

PRAC Rapporteur: Sabine Straus

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

6.2.5. Measles, mumps, rubella and varicella vaccine (live) – PROQUAD (CAP), NAP - PSUSA/01936/201509

Applicant: Sanofi Pasteur MSD SNC, various

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

6.2.6. Memantine – AXURA (CAP); EBIXA (CAP); MEMANTINE MERZ (CAP), NAP - PSUSA/01967/201509

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

PRAC Rapporteur: Dolores Montero Corominas

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

6.2.7. Zoledronic acid – ZOLEDRONIC ACID MEDAC (CAP), ZOMETA (CAP), NAP - PSUSA/03149/201508

Applicant: Medac Gesellschaft fur klinische Spezialpraparate GmbH (Zoledronic Acid Medac), Novartis Europharm Ltd (Zometa), various

PRAC Rapporteur: Doris Stenver

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

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

6.3.1. Almagate (NAP) - PSUSA/00000097/201505

Applicant: various

PRAC Lead: Dolores Montero Corominas

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

6.3.2. Asparaginase (NAP) - PSUSA/00003161/201508

Applicant: various

PRAC Lead: Roxana Stefania Stroe

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

6.3.3. Ciclesonide (NAP) - PSUSA/00000742/201508

Applicant: various

PRAC Lead: Julie Williams

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

6.3.4. Cilostazol (NAP) - PSUSA/00010209/201508

Applicant: various

PRAC Lead: Julie Williams

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

6.3.5. Dalteparin sodium (NAP) - PSUSA/00000922/201508

Applicant: various

PRAC Lead: Jolanta Gulbinovic

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

6.3.6. Erythromycin, isotretinoin (NAP) - PSUSA/00001796/201508

Applicant: various

PRAC Lead: Tatiana Magalova

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

6.3.7. Etonogestrel (NAP) - PSUSA/00001331/201509

Applicant: various

PRAC Lead: Menno van der Elst

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

6.3.8. Finasteride (NAP) - PSUSA/00001392/201508

Applicant: various

PRAC Lead: Ulla Wändel Liminga

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

6.3.9. Fluocinolone acetonide (intravitreal implant in applicator) (NAP) - PSUSA/00010224/201508

Applicant: various

PRAC Lead: Margarida Guimarães

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

6.3.10. Germanium (^{68}Ge) chloride, gallium (^{68}Ga) chloride (NAP) - PSUSA/00010364/201509

Applicant: various

PRAC Lead: Eva Jirsová

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

6.3.11. Hexoprenaline sulfate (NAP) - PSUSA/00003170/201508

Applicant: various

PRAC Lead: Roxana Stefania Stroe

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

6.3.12. Influenza vaccine (split virion, inactivated) (NAP) - PSUSA/00010298/201508

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

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

6.3.13. Influenza vaccine (split virion, inactivated, prepared in cell cultures) (NAP) - PSUSA/00010299/201508

Applicant: various

PRAC Lead: Brigitte Keller-Stanislawski

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

6.3.14. Influenza vaccine (surface antigen, inactivated) (NAP) - PSUSA/00001744/201508

Applicant: various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Influenza vaccine (surface antigen, inactivated, adjuvanted) (NAP) - PSUSA/00010300/201508

Applicant: various

PRAC Lead: Carmela Macchiarulo

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

6.3.16. Influenza vaccine (surface antigen, inactivated, virosome) (NAP) - PSUSA/00001746/201508

Applicant: various

PRAC Lead: Carmela Macchiarulo

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

6.3.17. Meropenem (NAP) - PSUSA/00001989/201508

Applicant: various

PRAC Lead: Jan Neuhauser

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

6.3.18. Nifedipine (NAP) - PSUSA/00002156/201508

Applicant: various

PRAC Lead: Menno van der Elst

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

6.3.19. Olodaterol (NAP) - PSUSA/00010245/201509

Applicant: various

PRAC Lead: Sabine Straus

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

6.3.20. Rilmenidine (NAP) - PSUSA/00002643/201508

Applicant: various

PRAC Lead: Julia Pallos

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

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Bortezomib – VELCADE (CAP) - EMEA/H/C/000539/LEG 053

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a cumulative review of cases reporting progressive multifocal leukoencephalopathy (PML) with the use of bortezomib submitted by the MAH following the recommendation of the PSUSA/00000424/201504 procedure adopted in November 2015
Action: For adoption of advice to CHMP

6.4.2. Diphtheria (D), tetanus (T), pertussis (acellular, component) (Pa), hepatitis B (rDNA) (HBV), poliomyelitis (inactivated) (IPV) and haemophilus influenzae type b (Hib) conjugate vaccine (adsorbed) – INFANRIX HEXA (CAP) - EMEA/H/C/000296/LEG 116.1

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of MAH's responses to LEG 116 [evaluation of additional information on the recently observed increase in the reported cases of regression of psychomotor development and a cumulative review of cases in relation with lack of reconstitution following the recommendation of the PSUSA/00001122/201410 procedure] as per request for supplementary information adopted in November 2015
Action: For adoption of advice to CHMP

6.4.3. Everolimus – AFINITOR (CAP) - EMEA/H/C/001038/LEG 028

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a cumulative review of cases of ejection fraction decrease submitted by the MAH following the recommendation of the PSUSA/00010268/201503 procedure adopted in November 2015
Action: For adoption of advice to CHMP

6.4.4. Piperaquine tetraphosphate, dihydroartemisinin – EURARTESIM (CAP) - EMEA/H/C/001199/LEG 015

Applicant: Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a re-analysis of the data in the effectiveness survey distributed to physicians submitted by the MAH following the recommendation of the PSUSA/00001069/201504 procedure adopted in September 2015
Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

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

7.1.1. Afamelanotide – SCENESSE (CAP) - EMEA/H/C/PSP/0033.1

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a revised protocol for a retrospective chart review study comparing long term safety data and outcome endpoints in patients receiving and not receiving Scenesse, or having discontinued the use of Scenesse. The second primary objective of the study should be the assessment of the compliance with risk minimisation recommendations and the controlled access programme for patients receiving Scenesse
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.2. Blinatumomab – BLINCYTO (CAP) - EMEA/H/C/PSP/0041

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Mladá

Scope: Evaluation of a protocol for study 20150136: an observational study measuring the safety and effectiveness of blinatumomab as well as utilisation and treatment practices
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.3. Idebenone – RAXONE (CAP) - EMEA/H/C/PSP/0034.1

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a revised PASS protocol for a non-interventional study of clinical experience in patients prescribed Raxone for the treatment of Leber's hereditary optic neuropathy (LHON)
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.4. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSP/0020.2

Applicant: Celgene Europe Limited

PRAC Rapporteur: Isabelle Robine

Scope: Evaluation of a revised PASS protocol for study CC-5013-MM-034: a 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

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

7.2.1. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/003718/MEA/006

Applicant: Genzyme Therapeutics Ltd

[3] In accordance with Article 107n of Directive 2001/83/EC
[4] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

PRAC Rapporteur: Torbjorn Callreus

Scope: Draft protocol for pregnancy registry study OBS13436: an international Lemtrada pregnancy exposure cohort in multiple sclerosis
Action: For adoption of advice to CHMP

7.2.2. Dulaglutide – TRULICITY (CAP) - EMEA/H/C/002825/MEA/001.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: MAH's responses to MEA 001.1 [revised PASS protocol regarding the utilisation of dulaglutide in European countries: a cross-sectional, multi-country and multi-source drug utilisation study using electronic health record databases] as per request for supplementary information adopted in December 2015
Action: For adoption of advice to CHMP

7.2.3. Dulaglutide – TRULICITY (CAP) - EMEA/H/C/002825/MEA/002.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: MAH's responses to MEA 002.1 [revised PASS protocol on the utilisation and safety of dulaglutide in European countries: a modified prescription-event monitoring and network database study (multi-database collaborative research programme of observational studies)] as per request for supplementary information adopted in December 2015
Action: For adoption of advice to CHMP

7.2.4. Fenofibrate, pravastatin – PRAVAFENIX (CAP) - EMEA/H/C/001243/MEA/007.5

Applicant: Laboratoires SMB s.a.

PRAC Rapporteur: Isabelle Robine

Scope: Revised PASS protocol for a European, observational, three-year cohort comparative study on the safety of the fixeddose combination pravastatin 40 mg/fenofibrate 160 mg (Pravafenix) versus statin alone in real clinical practice (FENOPRA-IV-14-1)
Action: For adoption of advice to CHMP

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

7.3.1. Cyproterone, ethinylestradiol (NAP) - EMEA/H/N/PSR/J/0003

Applicant: Bayer Pharma AG, various

PRAC Rapporteur: To be appointed

Scope: Final study results for an imposed joint PASS: drug utilisation study (DUS) (database) for cyproterone/ethinylstradiol 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 procedure timetable

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

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

7.4.1. Aliskiren – RASILEZ (CAP) - EMEA/H/C/000780/WS/0890 aliskiren, hydrochlorothiazide – RASILEZ HCT (CAP) - EMEA/H/C/000964/WS/0890

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Submission of final results of study SPP100A2417: a multi-database cohort study to assess the incidence rates of colorectal hyperplasia among hypertensive patients
Action: For adoption of PRAC Assessment Report

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

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

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

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

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Martin Huber

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

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

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

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

[6] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

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

7.5.1. Exenatide – BYDUREON (CAP) - EMEA/H/C/002020/MEA/010.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Interim results of study H8O-MC-B016: a modified prescription event monitoring to identify possible cases of pancreatitis to be conducted in the UK, enrolling primary care patients with type 2 diabetes mellitus who receive prescription for exenatide once weekly
Action: For adoption of advice to CHMP

7.5.2. Influenza vaccine (split virion, inactivated) – IDFLU (CAP) - EMEA/H/C/000966/MEA/032.3; INTANZA (CAP) - EMEA/H/C/000957/MEA/032.3

Applicant: Sanofi Pasteur, Sanofi Pasteur MSD SNC

PRAC Rapporteur: Miguel-Angel Macia

Scope: Interim results of the enhanced passive safety surveillance for 2015-2016 campaign (study FLU07E)
Action: For adoption of advice to CHMP

7.5.3. Insulin detemir – LEVEMIR (CAP) - EMEA/H/C/000528/MEA/045.4

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

Scope: Second annual progress report (01 Nov 2014 to 31 Oct 2015) for a diabetes pregnancy registry (study NN304-4016): an international non-interventional prospective cohort study to evaluate the safety of treatment with Levemir (insulin detemir) in pregnant women with diabetes mellitus
Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Panitumumab – VECTIBIX (CAP) - EMEA/H/C/000741/LEG 032.3

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Julie Williams

Scope: Annual update on the European Society of Pathology - (ESP) External Quality Assurance (EQA) programme in relation to KRAS testing
Action: For adoption of advice to CHMP

7.7. New Scientific Advice

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

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

7.8. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/S/0013 (without RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

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. Ataluren – TRANSLARNA (CAP) - EMEA/H/C/002720/R/0022 (without RMP)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

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

8.3. Renewals of the marketing authorisation

8.3.1. Levetiracetam – LEVETIRACETAM ACCORD (CAP) - EMEA/H/C/002290/R/0012 (with RMP)

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Veerle Verlinden

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

8.3.2. Levetiracetam – MATEVER (CAP) - EMEA/H/C/002024/R/0023 (without RMP)

Applicant: Pharmathen S.A.

PRAC Rapporteur: Veerle Verlinden

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

8.3.3. Pramipexole – PRAMIPEXOLE ACCORD (CAP) - EMEA/H/C/002291/R/0010 (without RMP)

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Doris Stenver

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

8.3.4. Telmisartan – TELMISARTAN TEVA PHARMA (CAP) - EMEA/H/C/002511/R/0014 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Carmela Macchiarulo

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

8.3.5. Varenicline – CHAMPIX (CAP) - EMEA/H/C/000699/R/0061 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Doris Stenver

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

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

Disclosure of information on results of pharmacovigilance inspections could undermine the protection of the purpose of these inspections, investigations and audits. Therefore such information is not reported in the agenda.

9.3. Others

10. Other safety issues for discussion requested by the CHMP or the EMA

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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. Ondansetron (NAP)

Applicant: Novartis, Bristol Laboratories Limited

PRAC Rapporteur: Milena Radoha Bergoč

Scope: PRAC consultation on the assessment of additional data submitted following the finalisation of PSUSA/00002217/201502 regarding the risk of congenital cardiac septal defect in off-label use during pregnancy
Action: For adoption of advice to Member States

11.2.2. Serotonin–noradrenaline reuptake inhibitors (SNRIs) (NAP, CAP); Selective serotonin reuptake inhibitors (SSRIs) (NAP)

Applicant: various

PRAC Rapporteur: Julie Williams

Scope: PRAC consultation on the assessment of a systematic review and meta-analysis published in the BMJ on suicidality, aggression and akathisia during antidepressant treatment
Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh

None

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

12.3.1. Guideline on safety and efficacy follow-up – Risk management plan of advanced therapy medicinal products (ATMP) - revision

PRAC lead: Julie Williams, Brigitte Keller-Stanislawski
Action: For discussion

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators - predictions

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance audits

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance systems and their quality systems

None

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

12.10.1. Granularity and Periodicity Advisory Group (GPAG)

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

12.10.2. Periodic safety update reports

None

12.10.3. PSUR action group – roadmap for PSUR issues: Joint PRAC/CMDh recommendation paper on common understanding - finalisation

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

12.10.4. PSURs repository - Transition to mandatory use

Action: For discussion

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. Good Pharmacovigilance Practice (GVP) module IX on Signal management – revision 1 and addendum

PRAC lead: Sabine Straus
Action: For discussion

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

PRAC lead: Sabine Straus
Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Additional monitoring

None

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

Action: For adoption of the list

12.12.3. Management and reporting of adverse reactions to medicinal products

None

12.13. EudraVigilance database

12.13.1. EudraVigilance activities related to the confirmation of full functionality

None

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. Good Pharmacovigilance Practices (GVP) module VIII on PASS - revision 2 and addendum

Action: For adoption

12.15.2. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public hearings – Rules of procedure

Action: For adoption

12.18.2. Public hearings - Plan for a 'mock-up' public hearing

Action: For discussion

12.18.3. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Delegated Regulation[8] on safety features appearing on the packaging of medicinal products for human use

Action: For discussion

12.20.2. EMA guidance on management of confidentiality and declarations of interests for observers participating in EMA scientific meetings

Action: For information

12.20.3. EMA hosted industry platform on the operation of the EU pharmacovigilance legislation - Report from quarterly meeting

Action: For discussion

12.20.4. EU Pharmacovigilance systems – quarterly updates to industry

Action: For discussion

12.20.5. EMA Procedure Management department - update

Action: For discussion

12.20.6. Good Pharmacovigilance Practices (GVP) – revised PRAC process for review and adoption of revised GVP modules in 2015-16

Action: For discussion

13. Any other business

[8] Delegated Regulation No 2016/161

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/