04 July 2016
EMA/PRAC/463028/2016
Procedure Management and Committees Support Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 04-08 July 2016

Chair: June Raine – Vice-Chair: Almath Spooner

04 July 2016, 13:00 – 19:30, room 3/A

05 July 2016, 08:30 – 19:30, room 3/A

06 July 2016, 08:30 – 19:30, room 3/A

07 July 2016, 08:30 –19:30, room 3/A

08 July 2016, 08:30 – 12:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

21 July 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 04-08 July 2016. See July 2016 PRAC minutes (to be published post September 2016 PRAC meeting).

1.2. Agenda of the meeting of 04-08 July 2016

Action: For adoption

1.3. Minutes of the previous meeting on 06-09 June 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

3.1.1. Paracetamol (NAP) (modified release formulation)

Applicant: GlaxoSmithKline Consumer Healthcare AB (Alvedon 665), various

PRAC Rapporteur: To be appointed; PRAC Co-rapporteur: To be appointed

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

Action: For adoption of a list of questions

3.1.2. Retinoids: acitretin (NAP); adapalene (NAP); alitretinoin - PANRETIN (CAP); isotretinoin (NAP); tretinoin (NAP)

Applicant: Eisai Ltd (Panretin), various

PRAC Rapporteur: To be appointed; PRAC Co-rapporteur: To be appointed

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

Action: For adoption of a list of questions

3.2. Ongoing procedures

3.2.1. Canagliflozin – INVOKANA (CAP); canagliflozin, metformin – VOKANAMET (CAP) - EMEA/H/A-20/1442

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann; PRAC Co-rapporteur: Menno van der Elst

Scope: Review of the benefit-risk balance of canagliflozin following notification by 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 outstanding issues (LoOI)

3.2.2. 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) - EMEA/H/A-20/1438

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: Margarida Guimarães; PRAC Co-rapporteur: Dolores Montero Corominas

Scope: Review of the benefit-risk balance of DAAV 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 outstanding issues (LoOI)

3.2.3. Gadolinium-containing contrast agents (GdCA): gadobenic acid (NAP); gadobutrol (NAP); gadodiamide (NAP); gadopentetic acid (NAP); gadoteric acid (NAP); gadoteridol (NAP); gadoxetic acid (NAP); gadoversetamide – OPTIMARK (CAP) - EMEA/H/A-31/1437

Applicant: Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Doris Stenver

Scope: Review of the benefit-risk balance following notification by the European

Commission of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a list of experts for the ad-hoc expert group meeting

3.3. Procedures for finalisation

3.3.1. Idelalisib – ZYDELIG (CAP) - EMEA/H/A-20/1439

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna; PRAC Co-rapporteur: Ulla Wändel Liminga

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

Action: For adoption of a recommendation to CHMP

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

None

3.5. Others

None

4. Signals assessment and prioritisation[1]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Acenocoumarol (NAP), fluindione (NAP), phenindione (NAP), phenprocoumon (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of calciphylaxis

Action: For adoption of PRAC recommendation

EPITT 18710 – New signal

Lead Member States: DE, BG

4.1.2. Aripiprazole – ABILIFY (CAP), ABILIFY MAINTENA (CAP)

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: To be appointed

[1] Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

Scope: Signal of compulsive shopping

Action: For adoption of PRAC recommendation

EPITT 18683 – New signal

Lead Member States: PT, SE

4.1.3. Ceftriaxone (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

Action: For adoption of PRAC recommendation

EPITT 18715 – New signal

Lead Member State: LV

4.1.4. Ipilimumab – YERVOY (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Signal of type 1 diabetes mellitus

Action: For adoption of PRAC recommendation

EPITT 18674 – New signal

Lead Member State: NL

4.1.5. Loperamide (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of serious cardiac events with high doses of loperamide from abuse and misuse

Action: For adoption of PRAC recommendation

EPITT 18339 – New signal

Lead Member State: CY, EE, PL

4.1.6. Vildagliptin – GALVUS (CAP), JALRA (CAP), XILIARX (CAP); vildagliptin, metformin – EUCREAS (CAP), ICANDRA (CAP), ZOMARIST (CAP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of pemphigoid

Action: For adoption of PRAC recommendation

EPITT 18692 – New signal

Lead Member State: SE

4.2. New signals detected from other sources

4.2.1. Exenatide – BYETTA (CAP), BYDUREON (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of incorrect use of device associated with (serious) adverse reactions including hyperglycaemia and hypoglycaemia

Action: For adoption of PRAC recommendation

EPITT 18688 – New signal

Lead Member State: SE

4.2.2. Fluoroquinolones (systemic use): 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: To be appointed

Scope: Signal of uveitis

Action: For adoption of PRAC recommendation

EPITT 18686 – New signal

Lead Member State: DE

4.2.3. Human coagulation(plasma-derived) factor VIII: Human coagulation factor VIII (antihemophilic factor A) (NAP); human coagulation factor VIII (inhibitor bypassing fraction) (NAP); human coagulation factor VIII, human von Willebrand factor - VONCENTO (CAP) Recombinant factor VIII: antihemophilic factor (recombinant) (NAP); moroctocog alfa – REFACTO AF (CAP) octocog alfa – ADVATE (CAP), HELIXATE NEXGEN (CAP), IBLIAS (CAP), KOGENATE (CAP), KOVALTRY; simoctocog alfa – NUWIQ (CAP); turoctocog alfa – NOVOEIGHT (CAP)

Applicant: Baxter AG (Advate), Bayer Pharma AG (Helixate NexGen, Iblias, Kogenate, Kovaltry), CSL Behring GmbH (Voncento), Novo Nordisk A/S (NovoEight), Octapharma AB (Nuwiq), Pfizer Limited (ReFacto AF), various

PRAC Rapporteur: To be appointed

Scope: Signal of inhibitor development in previously untreated patients (PUPs) with haemophilia A treated with plasma-derived *vs* recombinant coagulation factor VIII concentrates

Action: For adoption of PRAC recommendation

EPITT 18701 – New signal

Lead Member State: DE

4.2.4. Methylphenidate (NAP)

Applicant: various

PRAC Rapporteur: Julie Williams

Scope: Signal of priapism

Action: For adoption of PRAC recommendation

EPITT 18719 – New signal

Lead Member State: UK

4.3. Signals follow-up and prioritisation

4.3.1. Ferrous sulfate (NAP)

Applicant: various

PRAC Rapporteur: Leonor Chambel

Scope: Signal of mouth ulceration

Action: For adoption of PRAC recommendation

EPITT 18623 – Follow-up to March 2016

4.3.2. Human albumin solutions (NAP)

Applicant: various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of increased risk of mortality in patients with severe traumatic brain injury and in patients with burns

Action: For adoption of PRAC recommendation

EPITT 13948 – Follow-up to November 2012

4.3.3. Proton pump inhibitors (PPIs): Esomeprazole – NEXIUM CONTROL (CAP), NAP; lansoprazole (NAP); omeprazole (NAP); pantoprazole – CONTROLOC CONTROL (CAP) - EMEA/H/C/001097/SDA/015, PANTECTA CONTROL (CAP) - EMEA/H/C/001099/SDA/015, PANTOLOC CONTROL (CAP) - EMEA/H/C/001100/SDA/014, PANTOZOL CONTROL (CAP) - EMEA/H/C/001013/SDA/015, SOMAC CONTROL (CAP) - EMEA/H/C/001098/SDA/020, NAP; rabeprazole (NAP)

Applicant: various

PRAC Rapporteur: Rafe Suvarna

Scope: Signal of elevated circulating levels of chromogranin A

Action: For adoption of PRAC recommendation

EPITT 18614 – Follow-up to March 2016

4.3.4. Tramadol, paracetamol (NAP)

Applicant: various

PRAC Rapporteur: Julie Williams

Scope: Signal of hyponatraemia and syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Action: For adoption of PRAC recommendation

EPITT 18471 – Follow-up to March 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Bezlotoxumab – EMEA/H/C/004136

Scope: Prevention of *Clostridium difficile* infection (CDI) recurrence

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

5.1.2. Dasabuvir, ombitasvir, paritaprevir, ritonavir – EMEA/H/C/004235

Scope: Treatment of hepatitis C

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

5.1.3. Edotreotide – EMEA/H/C/004140, Orphan

Applicant: Advanced Accelerator Applications

Scope: Diagnosis of gastro-entero-pancreatic neuroendocrine tumours

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

5.1.4. 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

5.1.5. Expanded human allogeneic mesenchymal adult stem cells extracted from adipose tissue – EMEA/H/C/004258, Orphan

Applicant: Tigenix, S.A.U.; ATMP[2]

Scope: Treatment of complex perianal fistula(s)

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

5.1.6. Follitropin delta – EMEA/H/C/003994

Scope: Controlled ovarian stimulation

[2] Advanced-therapy medicinal product

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

5.1.7. Human immunoglobulin (Ig)G1 monoclonal antibody specific for human interleukin-1 alpha – EMEA/H/C/004388

Scope (accelerated assessment): Treatment of metastatic colorectal cancer

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

5.1.8. Ivabradine – EMEA/H/C/004117

Scope: Treatment of angina pectoris

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

5.1.9. Obeticholic acid – EMEA/H/C/004093, Orphan

Applicant: Intercept Italia s.r.l

Scope: Treatment of primary biliary cirrhosis

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

5.1.10. 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

5.1.11. Pegfilgrastim – EMEA/H/C/004342

Scope: Treatment of neutropenia

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

5.1.12. Pegfilgrastim – EMEA/H/C/004023

Scope: Treatment of neutropenia

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

5.1.13. Sildenafil – EMEA/H/C/004186

Scope: Treatment of pulmonary arterial hypertension

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

5.1.14. Venetoclax – EMEA/H/C/004106, Orphan

Applicant: AbbVie Ltd.

Scope: Treatment of adult patients with chronic lymphocytic leukaemia (CLL)

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. Abacavir - ZIAGEN(CAP) - EMEA/H/C/000252/WS0956/0097/G; abacavir, lamivudine - KIVEXA(CAP) - EMEA/H/C/000581/WS0956/0070/G; abacavir, lamivudine, zidovudine - TRIZIVIR(CAP) - EMEA/H/C/000338/WS0956/0102/G;

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Claire Ferard

Scope: Update of the RMPs for abacavir (ABC)-containing products (Ziagen RMP (version 14); Kivexa RMP (version 6); Trizivir RMP (version 3)), specifically the educational material (slide set) has been streamlined to ensure key messages are clear and that the information is consistent with recent updates to the ABC hypersensitivity reactions language in the SmPC made as part of WS/0733. Annex IID of the product information has been updated accordingly. In addition, the MAH took the opportunity to update the RMP with the recently approved 'class label' variations on lipodystrophy, lactic acidosis and latest mitochondria information

Action: For adoption of PRAC Assessment Report

5.2.2. 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 added as an important identified risk). 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 lymphopenia associated with Tecfidera treatment is included

Action: For adoption of PRAC Assessment Report

5.2.3. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/II/0026/G

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Update of Annex IID and of the RMP in order to update the educational material (slide set) and website. Furthermore, the MAH took the opportunity to align the information of the RMP with the recently approved changes to the product information concerning information on lactic acidosis and lipodystrophy

Action: For adoption of PRAC Assessment Report

5.2.4. Human fibrinogen, human thrombin - EVICEL (CAP) - EMEA/H/C/000898/II/0039

Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of a revised RMP (version 14) including updates on data exposure, medication error cases and effectiveness of risk minimisations measures related to the potential risk of air/gas embolism associated with spray application

Action: For adoption of PRAC Assessment Report

5.2.5. Ibandronic acid – BONDRONAT (CAP) - EMEA/H/C/000101/WS0942/0074; BONVIVA (CAP) - EMEA/H/C/000501/WS0942/0056

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Submission of a revised RMP to implement the patient reminder card as an additional risk minimisation measure following the PRAC recommendation provided in PSUSA/001702/201506

Action: For adoption of PRAC Assessment Report

5.2.6. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/II/0103

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of an updated RMP (version 9.0) in order to add hepatitis B reactivation as a new important identified risk

Action: For adoption of PRAC Assessment Report

5.2.7. Naltrexone, bupropion - MYSIMBA (CAP) - EMEA/H/C/003687/II/0005/G

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of amended study designs for both the renal impairment study (effect of renal impairment on the pharmacokinetics of naltrexone PR/ bupropion PR tablet (category 3 study)) and the hepatic impairment study (effect of hepatic impairment on the pharmacokinetics of naltrexone PR /bupropion PR tablet (category 3 study)) as outlined in the currently approved RMP (version 8)

Action: For adoption of PRAC Assessment Report

5.2.8. Nilotinib - TASIGNA (CAP) - EMEA/H/C/000798/II/0083

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Submission of a revised RMP (version 15) in order to add hepatitis B reactivation as a new important identified risk

Action: For adoption of PRAC Assessment Report

5.2.9. Retigabine - TROBALT (CAP) - EMEA/H/C/001245/II/0044

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Doris Stenver

Scope: Submission of a revised RMP (version 17) in order to delete category 3 post-authorisation study (PASS) WEUKSTV4551 exploring the risk of urinary retention (UR) among patients treated with retigabine and other antiepileptic drugs (AEDs)

Action: For adoption of PRAC Assessment Report

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

5.3.1. 5-aminolevulinic acid – AMELUZ (CAP) - EMEA/H/C/002204/II/0020

Applicant: Biofrontera Bioscience GmbH

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the treatment of actinic keratosis of mild to moderate severity on the face and scalp (Olsen grade 1 to 2) and of field cancerisation based on the phase III clinical study ALA-AK-CT007. 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

5.3.2. Abacavir – ZIAGEN (CAP) - EMEA/H/C/000252/WS0948/0096; abacavir, lamivudine – KIVEXA (CAP) - EMEA/H/C/000581/WS0948/0069; abacavir, dolutegravir, lamivudine – TRIUMEQ (CAP) - EMEA/H/C/002754/WS0948/0027;

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Claire Ferard

Scope: Update of sections 4.4 and 4.5 of the SmPC to remove the current information regarding a potential interaction between abacavir and ribavirin. The Package Leaflet has been updated accordingly. In addition, the RMPs (Ziagen RMP (version 13); Kivexa RMP (version 5); Triumeq RMP (version 10)) were updated accordingly

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

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Extension of indication in combination with methotrexate (MTX) in the treatment of adults with rheumatoid arthritis (RA) who have highly active disease with poor prognostic factors not previously treated with MTX. As a consequence, sections 4.1 and 5.1 of the SmPC are updated based on results from the AVERT study (IM101226). The Package Leaflet and the RMP (version 20) are updated accordingly

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

5.3.4. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0006/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.5 of the SmPC based on the final results of the clinical pharmacology study CLDK378A2113 and results of a sub-group evaluating the impact of gastric pH-elevating agents on the steady-state pharmacokinetic (PK), efficacy, and safety of ceritinib in anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) patients. The final clinical study report for study CLDK378A2113 is submitted to fulfil MEA 003. In addition, the MAH is proposing a change to the due date for the provision of the final study report for study CLDK378A2110 (MEA 001). The RMP is updated (version 3.0) accordingly

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

5.3.5. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0039

Applicant: Pfizer Limited

PRAC Rapporteur: Claire Ferard

Scope: Extension of indication to include the treatment of adults with ROS1-positive advanced non-small cell lung cancer (NSCLC) based on the results of study A8081001 (a multinational, multicentre, open-label, single-arm study of the safety, pharmacokinetics, pharmacodynamics, and antitumor activity of crizotinib in patients with advanced cancer). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC, the Package Leaflet and RMP (version 7.0) are updated accordingly

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

5.3.6. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0012

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information to reflect findings from a recently completed phase 3b study (study H9X-MC-GBDG (GBDG)) concerning the use of dulaglutide in combination with sulphonylurea alone. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10)

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

5.3.7. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0013

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of sections 4.2, 4.7, 4.8 and 5.1 of the SmPC for Trulicity following completion of a phase 3b study (study H9X-MCGBDI (GBDI)) to reflect the study's findings concerning the use of dulaglutide in combination with basal insulin. The Package Leaflet is updated accordingly

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

5.3.8. Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0032

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the SmPC section 4.4 and 4.8 with new information on the drug-induced liver injury. Consequently, the section of the Annex II on 'key elements to be included in the educational material' has been updated. The RMP (version 39) is updated accordingly

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

5.3.9. Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0035/G

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the clinical study report (CSR) for study TRC112765 exploring the safety of eltrombopag in subjects with solid tumours receiving gemcitabine monotherapy or gemcitabine plus cisplatin or carboplatin. The RMP (version 40) is updated accordingly. In addition, the MAH took the opportunity to revise due dates for submission of final reports for two studies in the pharmacovigilance plan

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/WS0926/0017; empagliflozin, metformin - SYNJARDY(CAP) - EMEA/H/C/003770/WS0926/0016

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to include data from study 1275.9. In addition, the MAH took the opportunity to remove the optional sentence on 'medicinal product subject to medical prescription' from Annex IIIA. Moreover, the RMPs (version 8.0 for Jardiance; version 6.0 for Synjardy) are updated accordingly

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

5.3.11. 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

5.3.12. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/X/0029

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Line extension to add new pharmaceutical form and strengths (film-coated tablets 40 mg and 80 mg) to the currently approved presentations for Xtandi

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

5.3.13. Eslicarbazepine acetate - ZEBINIX (CAP) - EMEA/H/C/000988/II/0053

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include the use of Zebinix as monotherapy in adults, in addition to the previously authorised indication as adjunctive therapy. 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 and RMP (version 15.0) are updated accordingly

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

5.3.14. Eslicarbazepine acetate - ZEBINIX (CAP) - EMEA/H/C/000988/X/0050/G

Applicant: Bial - Portela & Cª, S.A.

PRAC Rapporteur: Martin Huber

Scope: Grouping of a line extension application to add a new pharmaceutical form (50 mg/ml oral suspension) and a type II variation (new indication) to add the treatment of children aged 2 years and older. Consequently, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC, the Package Leaflet and the RMP (version 14.0) are updated accordingly

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

5.3.15. Fosaprepitant - IVEMEND (CAP) - EMEA/H/C/000743/II/0031

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to include data from the clinical study P031. In addition, the MAH took the opportunity to bring the product information in line with the QRD template (version 9.1). Furthermore, the MAH took the opportunity to align section 4.4 of the SmPC (and Package leaflet respectively) for fosaprepitant (Ivemend) with the changes approved through procedure EMEA/H/C/000527/X/0049/G for aprepitant (Emend). Moreover, the RMP (version 4.0) is updated accordingly

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

5.3.16. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0024

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Update of sections 4.4 and 4.8 of the SmPC to add an appropriate warning relating to interstitial lung disease (ILD) as well as ILD as a post-marketing adverse drug reaction. In addition, the MAH took the opportunity to bring the product information in line with the revised QRD template. The RMP is updated accordingly

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

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

Applicant: Bayer Pharma AG

PRAC Rapporteur: Claire Ferard

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

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

5.3.18. 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

5.3.19. Oseltamivir - TAMIFLU (CAP) - EMEA/H/C/000402/II/0122

Applicant: Roche Registration Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Update of section 5.1 of the SmPC and RMP to reflect the results of the IRIS study (study NV20237): a prospective, multicentre, information-gathering study, comprising virological surveillance and assessment of clinical outcomes, which enrolled patients over a 7-year period. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template version

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

5.3.20. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0027

Applicant: Ariad Pharma Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to include recommendations for dose modifications in case of hepatic toxicity during the treatment, and to include a reduced starting dose of 30 mg for patients with hepatic impairment. The Package Leaflet is updated accordingly

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

5.3.21. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0032/G

Applicant: Ariad Pharma Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 of the SmPC based on data from ongoing study AP24534-07-101 with a median duration of follow-up of approximately 48 months for the CP-chronic myeloid leukaemia (CML) patients and 3.6 months for the advanced phase Ph+ leukemia patients, as well as 48-month follow-up data from the ongoing study AP24534-10-201 (PACE). The Package Leaflet and the RMP (version 14) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes in the SmPC and to align the annexes with the latest QRD template (version 10)

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

5.3.22. Radium (^{223}Ra) - XOFIGO (CAP) - EMEA/H/C/002653/II/0014/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Rafe Suvarna

Scope: 1) Submission of clinical study report for study BC1-06, 'a double-blind, randomized, multiple dose, phase III, multicentre study of alpharadin in the treatment of patients with symptomatic hormone refractory prostate cancer with skeletal metastases' (MEA 001) 2) Submission of clinical study report for study 15995 'Radium-223 dichloride in castration-resistant (hormone-refractory) prostate cancer patients with bone metastases', an early access clinical trial in the USA. (MEA 002) 3) Submission of a clinical study report (based on primary completion) for study 16216 'Radium-223 dichloride in castration-resistant (hormone-refractory) prostate cancer patients with bone metastases' an early access clinical trial outside USA. (MEA 003) 4) The RMP (version 2.0) is updated with regard to the clinical study reports submitted, the due dates in part III section 4, and additionally to reflect the change in SmPC based on the recent reassessment of the primary reference standard for radium-223 (issued by the National Institute of Standards and Technology (NIST)), the active moiety of Xofigo (recently approved EMEA/H/C/2653/II/011)

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

5.3.23. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/II/0011

Applicant: Bayer Pharma AG

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to include pulmonary arterial hypertension associated with congenital heart disease (PAH-CHD). As a consequence, sections 4.4 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct information regarding one of the cytochrome P450 (CYP) isoforms involved in the metabolism of riociguat in sections 4.5 and 5.2. 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

5.3.24. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/II/0042/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 5.1 of the SmPC following the submission of a prospective, single-arm, non-interventional, open-label cohort study conducted to investigate the safety and effectiveness in a real-world setting, study XANTUS (SN 15914) in order to fulfil MEA 025. In addition, update of section 5.1 of the SmPC following the submission of a prospective, non-interventional, open-label cohort study that was conducted in patients with acute deep vein thrombosis (DVT) to investigate the safety and effectiveness in a real-world setting, study XALIA (SN 15915) in order to fulfil MEA 027. The RMP (version 9.0) is updated accordingly. Additionally the final clinical study reports for studies X-TRA (SN 16320, phase IIIb) and VENTURE-AF (SN 15694, phase IIIb) were also included in the RMP. Finally, the MAH took the opportunity to introduce a minor editorial change in the list of representatives in the package leaflets of all strengths

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

5.3.25. Tedizolid phosphate - SIVEXTRO (CAP) - EMEA/H/C/002846/II/0009

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of sections 4.4, 4.5 and 5.2 of the SmPC based on the completed drug-drug interaction study MK-1986-004. The Package Leaflet is updated accordingly. In addition the MAH took the opportunity to implement editorial changes in the annexes and to update the annexes in line with the latest QRD template (version 10). The RMP (version 2.0) is updated by removing the missing information for potential risks for drug-drug interactions mediated by CYP3A4, as well as addressing the identified risk for drug-drug interactions mediated via inhibition of breast cancer resistance protein (BCRP), adding updates made to timelines for ongoing and planned studies for long term safety and Asian population experience

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

5.3.26. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0061

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final clinical study report (CSR) for study WA29049 (single blind

phase IV pharmacodynamic study to evaluate neutrophil distribution kinetics and function following single-dose tocilizumab treatment in healthy subjects) as requested in MEA 30.5. The RMP (version 19.0) is updated accordingly

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

5.3.27. 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. Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/201512

Applicant: Clinuvel (UK) Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Amifampridine - FIRDAPSE (CAP) - PSUSA/00000141/201512

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Bimatoprost, timolol - GANFORT (CAP) - PSUSA/00002961/201511 (with RMP)

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Torbjorn Callreus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Canakinumab - ILARIS (CAP) - PSUSA/00000526/201512

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Clofarabine - EVOLTRA (CAP) - PSUSA/00000805/201512 (with RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - PSUSA/00010028/201512

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Dasabuvir - EXVIERA (CAP) - PSUSA/00010363/201512

Applicant: AbbVie Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Edoxaban - LIXIANA (CAP) - PSUSA/00010387/201512

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Fondaparinux - ARIXTRA (CAP) - PSUSA/00001467/201512

Applicant: Aspen Pharma Trading Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Human fibrinogen, human thrombin - EVARREST (CAP); EVICEL (CAP); RAPLIXA (CAP); TACHOSIL (CAP) - PSUSA/00010297/201512

Applicant: Omrix Biopharmaceuticals N. V. (Evicel and Evarrest), ProFibrix BV (Mallinckrodt) (Raplixa), Takeda Austria GmbH (TachoSil)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Human papillomavirus 9-valent vaccine (recombinant, adsorbed) - GARDASIL 9 (CAP) - PSUSA/00010389/201512

Applicant: Sanofi Pasteur MSD

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Influenza vaccine (intranasal, live attenuated) - FLUENZ TETRA (CAP) - PSUSA/00001742/201512

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Lenalidomide - REVLIMID (CAP) - PSUSA/00001838/201512

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Liraglutide - SAXENDA (CAP); VICTOZA (CAP) - PSUSA/00001892/201512

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Lutetium (^{177}Lu) - LUMARK (CAP) - PSUSA/00010391/201512

Applicant: I.D.B. Radiopharmacy B.V.

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Matrix-applied characterised autologous cultured chondrocytes - MACI (CAP) - PSUSA/00010116/201512

Applicant: Aastrom Biosciences DK ApS

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Mirabegron - BETMIGA (CAP) - PSUSA/00010031/201512

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Nonacog gamma - RIXUBIS (CAP) - PSUSA/00010320/201512

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Olaparib - LYNPARZA (CAP) - PSUSA/00010322/201512

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Omalizumab - XOLAIR (CAP) - PSUSA/00002214/201512

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - PSUSA/00010367/201512

Applicant: AbbVie Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Pertuzumab - PERJETA (CAP) - PSUSA/00010125/201512

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - 10 valent - SYNFLORIX (CAP) - PSUSA/00009262/201512

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Ponatinib - ICLUSIG (CAP) - PSUSA/00010128/201512

Applicant: Ariad Pharma Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Saquinavir - INVIRASE (CAP) - PSUSA/00002684/201512 (with RMP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Marianne Lunzer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Secukinumab - COSENTYX (CAP) - PSUSA/00010341/201512

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Sofosbuvir - SOVALDI (CAP) - PSUSA/00010134/201512

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/201512

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Thyrotropin alfa - THYROGEN (CAP) - PSUSA/00002940/201511

Applicant: Genzyme Europe BV

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Ticagrelor - BRILIQUE (CAP) - PSUSA/00002948/201512

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Umeclidinium bromide, vilanterol - ANORO (CAP); LAVENTAIR (CAP) - PSUSA/00010264/201512

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Ustekinumab - STELARA (CAP) - PSUSA/00003085/201512

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Verteporfin - VISUDYNE (CAP) - PSUSA/00003110/201512

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Ziconotide - PRIALT (CAP) - PSUSA/00003142/201512

Applicant: Eisai Ltd

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Bosentan - STAYVEER (CAP); TRACLEER (CAP); NAP - PSUSA/00000425/201511

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

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Doxorubicin - CAELYX (CAP); MYOCET (CAP); NAP - PSUSA/00001172/201511

Applicant: Janssen-Cilag International N.V. (Caelyx), Teva B.V. (Myocet), various

PRAC Rapporteur: Rafe Suvarna

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Human hepatitis B immunoglobulin - ZUTECTRA (CAP); NAP - PSUSA/00001631/201511

Applicant: Biotest Pharma GmbH (Zutectra), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Alendronate, alfacalcidol (NAP) - PSUSA/00010308/201512

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Apomorphine (NAP) - PSUSA/00000227/201511

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Atomoxetine (NAP) - PSUSA/00000262/201511

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Benazepril (NAP) - PSUSA/00000313/201511

Applicant: various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Benzydamine (NAP) - PSUSA/00000375/201510

Applicant: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Clevidipine (NAP) - PSUSA/00010288/201511

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Dexketoprofen (NAP) - PSUSA/00000997/201510

Applicant: various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Dextromethorphan (NAP) - PSUSA/00001009/201511

Applicant: various

PRAC Lead: Veerle Verlinden

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Diacerein (NAP) - PSUSA/00001026/201512

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Furosemide, spironolactone (NAP) - PSUSA/00001493/201512

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Indapamide (NAP) - PSUSA/00001731/201511

Applicant: various

PRAC Lead: Valerie Strassmann

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Minoxidil (non-topical formulations) - PSUSA/00002066/201510

Applicant: various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Minoxidil (topical formulation) (NAP) - PSUSA/00002067/201510

Applicant: various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Mycophenolic acid (apart from mycophenolate mofetil) (NAP) - PSUSA/00010243/201510

Applicant: various

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Naltrexone (NAP) - PSUSA/00002117/201511

Applicant: various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Rimexolone (NAP) - PSUSA/00002647/201510

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Salmeterol (NAP) - PSUSA/00002681/201510

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Sultamicillin (NAP) - PSUSA/00002829/201511

Applicant: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Technetium (^{99m}Tc) mebrofenin (NAP) - PSUSA/00002861/201511

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Terazosin (NAP) - PSUSA/00002895/201511

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Treprostinil (NAP) - PSUSA/00003013/201511

Applicant: various

PRAC Lead: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Aripiprazole - ABILIFY (CAP) - EMEA/H/C/000471/LEG 075

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Leonor Chambel

Scope: Following the recommendation of PSUSA/00000234/201507, the MAH was requested to provide a review and an analysis regarding the serious adverse events under the system organ class (SOC) 'eye disorder'; a cumulative review and analysis of all events of pulmonary embolism, and review the reported cases of interaction between aripiprazole and other antipsychotics, including a discussion on this potential pharmacodynamic interaction and the possibility to submit a study to assess this interaction

Action: For adoption of advice to CHMP

6.4.2. Aripiprazole - ABILIFY MAINTENA (CAP) - EMEA/H/C/002755/LEG 007

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Following the recommendation of PSUSA/00000234/201507, submission of a review and an analysis regarding the serious adverse events under the system organ class (SOC) 'eye disorder'; a cumulative review and analysis of all events of pulmonary embolism, and review the reported cases of interaction between aripiprazole and other antipsychotics, including a discussion on this potential pharmacodynamic interaction and the possibility to submit a study to assess this interaction

Action: For adoption of advice to CHMP

6.4.3. Colesevelam - CHOLESTAGEL (CAP) - EMEA/H/C/000512/LEG 031

Applicant: Genzyme Europe BV

PRAC Rapporteur: Menno van der Elst

Scope: Following the recommendation of PSUSA/00000864/201503, submission of a review on whether the ease of administration can be increased by introducing e.g. a score line or by changing the size and/or shape of the tablets, with the aim to prevent that patients split or crush tablets

Action: For adoption of advice to CHMP

6.4.4. Ingenol mebutate - PICATO (CAP) - EMEA/H/C/002275/LEG 008

Applicant: Leo Pharma A/S

PRAC Rapporteur: Julie Williams

Scope: Following PSUSA/00010035/201507, submission of a review relating to study LP0105-1020 (efficacy and safety of ingenol mebutate gel 0.06% when applied once daily for 2, 3 or 4 consecutive days to a treatment area of approximately 250 cm^2 on trunk and extremities in subjects with actinic keratosis)

Action: For adoption of advice to CHMP

6.4.5. Insulin degludec - TRESIBA (CAP) - EMEA/H/C/002498/LEG 010

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Following PSUSA/00010036/201409, submission of an updated review of all post-marketing cases (using the standard MedDRA query (SMQ) 'drug-related hepatic disorders'), including narratives

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. Dinutuximab - UNITUXIN (CAP) - EMEA/H/C/PSP/0035.1

Applicant: United Therapeutics Europe Ltd

PRAC Rapporteur: Sabine Straus

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

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.2. Eliglustat - CERDELGA (CAP) - EMEA/H/C/PSP/0047

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

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

Scope: PASS protocol for registry study OBS14099: a prospective, multicentre, observational post authorisation safety sub-registry to characterize the long-term safety profile of eliglustat of adult patients with Gaucher disease

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.3. Glycerol phenylbutyrate - RAVICTI (CAP) - EMEA/H/C/PSP/0048

Applicant: Horizon Pharma Ireland Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: PASS protocol for a multicentre prospective non-interventional registry in patients with urea cycle disorders on treatment with glycerol phenylbutyrate to characterise patients` demographics, and to document long-term safety and clinical outcomes

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.4. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/PSP/0049

Applicant: Raptor Pharmaceuticals Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: PASS protocol for a an open-label, observational safety study of Quinsair (nebulised levofloxacin hemihydrate) in patients with cystic fibrosis and chronic *Pseudomonas Aeruginosa* infection, using data collected through European cystic fibrosis registries

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.5. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSP/044.1

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Revised protocol for a prospective non-interventional post-authorisation safety study (study CC-5013-MDS-010), designed as myelodysplastic syndromes (MDS) disease registry of patients with transfusion dependent international prognostic scoring system (IPSS) low or intermediate-1-MDS and isolated deletion (5q)

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. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 019

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for a drug utilisation study (DUS) of alirocumab in Europe to assess the effectiveness of the dosing recommendation to avoid very low low-density lipoprotein (LDL)-C levels (study OBS14697)

[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

Action: For adoption of advice to CHMP

7.2.2. Apixaban – ELIQUIS (CAP) - EMEA/H/C/002148/MEA/012.5

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: PASS protocol for study B0661073: a drug utilisation study (DUS) in Denmark to monitor potential off-label use with apixaban

Action: For adoption of advice to CHMP

7.2.3. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/MEA 006.2

Applicant: Celgene Europe Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's responses to MEA 006.1 [revised PASS protocol for CPRD (UK) data analysis for PsA and psoriasis] as per the request for supplementary information (RSI) adopted in February 2016

Action: For adoption of advice to CHMP

7.2.4. Cobicistat - TYBOST (CAP) - EMEA/H/C/002572/MEA 012.3

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: MAH's responses to MEA 012.2 [drug utilisation study for COBI, DUS-GS-EU-216-1230: a prospective, observational drug utilisation study of cobicistat in adults with human immunodeficiency virus (HIV)-1 infection due to feasibility related issues] as per request for supplementary information (RSI) adopted by PRAC in January 2016

Action: For adoption of advice to CHMP

7.2.5. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/MEA 167

Applicant: Pfizer Limited

PRAC Rapporteur: Rafe Suvarna

Scope: PASS protocol for study B1801396 investigating the relationship between etanercept exposure and major birth defects in an observational study using data from Sweden, Finland and Denmark, as per the conclusions of variation II/184

Action: For adoption of advice to CHMP

7.2.6. Hydrocortisone - PLENADREN (CAP) - EMEA/H/C/002185/MEA 005.3

Applicant: Shire Services BVBA

PRAC Rapporteur: Qun-Ying Yue

Scope: MAH's responses to MEA 005.2 [revised PASS protocol for study SWE-DUS, study 10918 -404 (SHP617-404): a Swedish, retrospective, study progress reports to be provided

on a yearly basis evaluating the pattern of Plenadren use from as part of the PSURs Swedish quality registries] as per the request for supplementary information (RSI) adopted by PRAC in February 2016

Action: For adoption of advice to CHMP

7.2.7. Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/MEA 001.1

Applicant: ThromboGenics NV

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA001 [revised protocol for a drug utilisation study TG-MV-017 on the use of intravitreal Jetrea in clinical practice as adopted in July 2013] as per request for supplementary information (RSI) adopted by PRAC in July 2013

Action: For adoption of advice to CHMP

7.2.8. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/MEA 011.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: MAH's responses to MEA 011.2 [revised protocol for a PASS to collect and/or retrieve prospective data from sizeable patient cohorts with ovarian cancer] as per request for supplementary information (RSI) adopted by PRAC in February 2016

Action: For adoption of advice to CHMP

7.2.9. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/MEA 023.3

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Revised protocol for study SN 16167, a survey regarding educational materials for prescriber and patients receiving rivaroxaban for stroke prevention or deep vein thrombosis treatment post-launch

Action: For adoption of advice to CHMP

7.2.10. Sonidegib - ODOMZO (CAP) - EMEA/H/C/002839/MEA 021.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 021 [revised protocol for study CLDE225A2404: a non-interventional, multi-national, multi-centre PASS to assess the long-term safety and tolerability of Odomzo (sonidegib) administered in patients with locally advanced basal cell carcinoma (laBCC)] as per request for supplementary information (RSI) adopted by PRAC in February 2016

Action: For adoption of advice to CHMP

7.2.11. Vernakalant - BRINAVESS (CAP) - EMEA/H/C/001215/MEA 026.2

Applicant: Cardiome UK Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 026.1 [revised PASS protocol for vernakalant intravenous (IV) sterile concentrate prospective safety registry study: a prospective observational registry study to characterise normal conditions of use, dosing and safety following administration of vernakalant intravenous (IV) sterile concentrate (study 6621 049-00)] as per request for supplementary information (RSI) adopted by PRAC in March 2016

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/005

Applicant: Bayer Pharma AG, various

PRAC Rapporteur: Menno van der Elst

Scope: Final study results for an imposed joint PASS: drug utilisation study (DUS) (survey) 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

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

7.4.1. Aliskiren – RASILEZ (CAP) - EMEA/H/C/000780/WS0890/0107; aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS0890/0077

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Submission of the 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. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0050

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Claire Ferard

Scope: Submission of the final clinical study report for study CICL670A2301 (category 3 study in the RMP), an international sentinel surveillance of patients with transfusional hemosideroris treated with Exjade in actual practice setting. This submission also served to comply with Article 46 of Regulation (EC) No 1901/2006

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

Action: For adoption of PRAC Assessment Report

7.4.3. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/II/0040

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Claire Ferard

Scope: Submission of the final clinical study report for PASS study Instanyl-5001 to evaluate the effectiveness of risk minimisation measures: a survey among health care professionals to assess their knowledge and attitudes on prescribing conditions of Instanyl in France and the Netherlands

Action: For adoption of PRAC Assessment Report

7.4.4. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/II/0055

Applicant: MedImmune LLC

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final clinical study report (CSR) for PASS study MA-VA-MEDI3250-1115: a post-marketing cohort study of the safety of Fluenz Tetra in subjects from 2 to 49 years of age

Action: For adoption of PRAC Assessment Report

7.4.5. Nepafenac - NEVANAC (CAP) - EMEA/H/C/000818/II/0033

Applicant: Alcon Laboratories (UK) Ltd

PRAC Rapporteur: Dolores Montero Corominas

Scope: Submission of the final study report for the drug utilisation study, 'Evaluation of the use of Nepafenac in selected European populations' (category 3 study) to quantify and describe off-label use of nepafenac in order to fulfil MEA 012

Action: For adoption of PRAC Assessment Report

7.4.6. Tacrolimus - PROTOPIC (CAP) - EMEA/H/C/000374/II/0063

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Almath Spooner

Scope: Submission of the final clinical study report of the non-interventional, registry PASS study JOELLE (JOint European Longitudinal Lymphoma and skin cancer Evaluation) final results. The RMP was updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Interim report for a long-term observational study of ataluren safety and effectiveness in usual care

Action: For adoption of advice to CHMP

7.5.2. Bazedoxifene - CONBRIZA (CAP) - EMEA/H/C/000913/MEA 012.7

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Interim report for PASS study B1781044: a cohort study of venous thromboembolism and other clinical endpoints among osteoporotic women prescribed bazedoxifene, bisphosphonates or raloxifene in Europe

Action: For adoption of advice to CHMP

7.5.3. Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - EMEA/H/C/002574/MEA 002.3

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Rafe Suvarna

Scope: Interim report for PASS study GS-EU-236-0141: a non-interventional PASS 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

7.5.4. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - OPTAFLU (CAP) - EMEA/H/C/000758/MEA 050.3

Applicant: Novartis Influenza Vaccines Marburg GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 050.2 [interim results of the enhanced passive safety surveillance of the seasonal cell culture trivalent influenza vaccine (Optaflu) for the 2015-16 influenza season in England in the pharmacies setting (study V58_41OB)] as per request for supplementary information (RSI) adopted by the PRAC in March 2016

Action: For adoption of advice to CHMP

7.5.5. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[7]) - EMEA/H/W/002300/MEA 001.1

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's responses to MEA 001 [first annual report for study Malaria-076, an open extension to study Malaria-055 to evaluate long-term efficacy, safety and immunogenicity of Mosquirix against malaria disease caused by *Plasmodium falciparum* in infants and children in Africa, describing the incidence of severe malaria in the long-term over a 3-year period (from January 2014 to December 2016) of follow-up pooled across transmission settings, in both age categories: infants 6-12 weeks and children aged 5 to 17 months] as per request for supplementary information adopted by the PRAC in March 2016

Action: For adoption of advice to CHMP

7.5.6. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/MEA 256.7

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Claire Ferard

Scope: MAH's responses to MEA 0256.6 [first interim results fora drug utilisation study (DUS) GS-EU-104-0433 in paediatric patients with human immunodeficiency virus (HIV-1) infection, to describe the characteristics of HIV-1 infected patients up to 18 years of age treated with Viread within the EU in order to determine if they are being managed in accordance with the European SmPC] as per request for supplementary information (RSI) as adopted by the PRAC in March 2016

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 005.7

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Fourth interim report of the canagliflozin independent data monitoring committee (IDMC) for the DIA3008 CANVAS study as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.6.2. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 006.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Second interim report of the canagliflozin independent data monitoring committee (IDMC) for the NE-3001 CREDENCE study as requested in the RMP additional

[7] Article 58 of Regulation (EC) No 726/2004 allows the Agency's Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO), on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

pharmacovigilance activity

Action: For adoption of advice to CHMP

7.6.3. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 006.4

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Valerie Strassmann

Scope: Third interim report of the canagliflozin independent data monitoring committee (IDMC) for the NE-3001 CREDENCE study as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.6.4. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 004.7

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Fourth interim report of the canagliflozin independent data monitoring committee (IDMC) for the DIA3008 CANVAS study as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.6.5. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 005.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Second interim report of the canagliflozin independent data monitoring committee (IDMC) for the NE-3001 CREDENCE study as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.6.6. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 005.4

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Menno van der Elst

Scope: Third interim report of the canagliflozin independent data monitoring committee (IDMC) for the NE-3001 CREDENCE study as requested in the RMP additional pharmacovigilance activity

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0064 (without RMP)

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Rafe Suvarna

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/R/0004 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Mladá

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/R/0035 (without RMP)

Applicant: Takeda Pharma A/S

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. Alendronic acid, colecalciferol - ADROVANCE (CAP) - EMEA/H/C/000759/R/0036 (without RMP)

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Azilsartan medoxomil - EDARBI (CAP) - EMEA/H/C/002293/R/0018 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Colistimethate sodium - COLOBREATHE (CAP) - EMEA/H/C/001225/R/0024 (without RMP)

Applicant: Forest Laboratories UK Limited

PRAC Rapporteur: Rafe Suvarna

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Desloratadine - DESLORATADINE ACTAVIS (CAP) - EMEA/H/C/002435/R/0008 (without RMP)

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Efavirenz - EFAVIRENZ TEVA (CAP) - EMEA/H/C/002352/R/0018 (without RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Margarida Guimarães

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/R/0065 (without RMP)

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Rafe Suvarna

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Levetiracetam - LEVETIRACETAM ACTAVIS (CAP) - EMEA/H/C/002355/R/0013 (without RMP)

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Veerle Verlinden

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Levetiracetam - LEVETIRACETAM SUN (CAP) - EMEA/H/C/002051/R/0013 (without RMP)

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Veerle Verlinden

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Pioglitazone, glimepiride - TANDEMACT (CAP) - EMEA/H/C/000680/R/0049 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Piperaquine tetraphosphate, artenimol - EURARTESIM (CAP) - EMEA/H/C/001199/R/0023 (without RMP)

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

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Repaglinide - REPAGLINIDE ACCORD (CAP) - EMEA/H/C/002318/R/0005 (without RMP)

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Sunitinib - SUTENT (CAP) - EMEA/H/C/000687/R/0062 (with RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Vemurafenib - ZELBORAF (CAP) - EMEA/H/C/002409/R/0034 (without RMP)

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

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

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

10.3.1. Dapagliflozin – EDISTRIDE (CAP) - EMEA/H/C/004161/LEG 001.1; FORXIGA (CAP) - EMEA/H/C/002322/LEG 019.1 dapagliflozin, metformin – EBYMECT (CAP) - EMEA/H/C/004162/LEG 001.1; XIGDUO (CAP) - EMEA/H/C/002672/LEG 005.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: PRAC consultation on the assessment of the risk of toe amputation with dapagliflozin-containing medicinal products in the context of the ongoing article 20 of Regulation (EC) No 726/2004 for canagliflozin-containing medicinal products

Action: For adoption of advice to CHMP

10.3.2. Empagliflozin – JARDIANCE (CAP) - EMEA/H/C/002677/LEG 006 empagliflozin, metformin – SYNJARDY (CAP) - EMEA/H/C/003770/LEG 004

Applicant: Boehringer Ingelheim GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: PRAC consultation on the assessment of the risk of toe amputation with empagliflozin-containing medicinal products in the context of the ongoing article 20 of Regulation (EC) No 726/2004 for canagliflozin-containing medicinal products

Action: For adoption of advice to CHMP

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. Valproate and related substances: sodium valproate, valproic acid, valproate semisodium, valpromide (NAP)

Applicant: Sanofi, various

PRAC Lead: Sabine Straus

Scope: PRAC consultation on the need for boxed warning and patient alert card in addition to risk minimisation measures adopted as an outcome of the completed referral procedure under Article 31 referral of Directive 2001/83/EC

Action: For adoption of advice to CHMP

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. CHMP guideline on influenza guideline

Action: For adoption

12.3.2. Guideline on safety and efficacy follow-up – risk management plan of ATMPs

Action: For discussion

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

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE)

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. 2016 PRAC work plan – status update

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - PRAC work tracking including quarterly workload measures and performance indicators for the last three months - predictions

Action: For discussion

12.8.2. Marketing Authorisation Applications - planned for the remainder of 2016

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Margarida Guimarães

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Sabine Straus

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. 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. 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 hearings - Dry-run

Action: For discussion

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.19.2. Withdrawn products - Update on the handling of notifications

Action: For discussion

12.20. Others

12.20.1. Effects tables in selected important benefit/risk reviews - Pilot phase

PRAC lead: Rafe Suvarna

Action: For discussion

12.20.2. EMA hosted industry platform on the operation of the EU pharmacovigilance legislation - Report from quarterly meeting on 01 July 2016

Action: For discussion

12.20.3. Strategy on measuring the impact of pharmacovigilance - draft reflection paper on PRAC criteria to prioritise collaborative impact research

PRAC lead: Marieke De Bruin

Action: For discussion

12.20.4. Type II variations - procedural timetables

Action: For discussion

13. Any other business

None

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/