2 May 2017
EMA/PRAC/280563/2017

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 2-5 May 2017

Chair: June Raine – Vice-Chair: Almath Spooner

2 May 2017, 13:00 – 19:30, room 3/A

3 May 2017, 08:30 – 19:30, room 3/A

4 May 2017, 08:30 – 19:30, room 3/A

5 May 2017, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

18 May 2017, 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 scope 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 2-5 May 2017. See May 2017 PRAC minutes (to be published post June 2017 PRAC meeting).

1.2. Agenda of the meeting on 2-5 May 2017

Action: For adoption

1.3. Minutes of the previous meeting on 3-6 April 2017

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

3.2.1. 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(s): Mallinckrodt Deutschland GmbH (Optimark); various

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Valerie Strassmann

Scope: Re-examination of the review of the benefit-risk balance following notification by the European Commission of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Action: For discussion

3.2.2. Retinoids: acitretin (NAP); adapalene (NAP); alitretinoin - PANRETIN (CAP); bexarotene – TARGRETIN (CAP); isotretinoin (NAP); tazarotene (NAP); tretinoin (NAP) - EMEA/H/A-31/1446

Applicant(s): Eisai Ltd (Panretin, Targretin), various

PRAC Rapporteur: Ana Sofia Diniz Martins; PRAC Co-rapporteur: Julie Williams

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 outstanding issues (LoOI)

3.3. Procedures for finalisation

3.3.1. 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 (CAP) - EMEA/H/A-31/1448

Applicant(s): Baxter AG (Advate), Bayer Pharma AG (Helixate Nexgen, Iblias, Kogenate, Kovaltry), CSL Behring GmbH (Voncento), Pfizer Limited (Refacto AF), various

PRAC Rapporteur: Julie Williams; PRAC Co-rapporteur: Brigitte Keller-Stanislawski

Scope: Review of the benefit-risk balance of factor VIII following notification by Germany of a referral under Article 31 of Directive 2001/83/EC, 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. Acetazolamide (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of acute generalized erythematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 18892 - New signal

Lead Member State(s): SE

4.1.2. Azithromycin (NAP), clarithromycin (NAP), erythromycin (NAP), roxithromycin (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 18891 - New signal

Lead Member State(s): IE, IT, FI

4.1.3. Cladribine – LITAK (CAP); NAP

Applicant(s): Lipomed GmbH, various

PRAC Rapporteur: To be appointed

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

Action: For adoption of PRAC recommendation

[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

EPITT 18875 – New signal

Lead Member State(s): UK

4.2. New signals detected from other sources

4.2.1. Insulin[2]: insulin aspart – NOVOMIX (CAP), NOVORAPID (CAP); insulin bovine (NAP); insulin degludec – TRESIBA (CAP); insulin degludec, insulin aspart – RYZODEG (CAP), insulin degludec, liraglutide – XULTHOPY (CAP); insulin detemir – LEVEMIR (CAP); insulin glargine – ABASAGLAR (CAP), LANTUS (CAP), LUSDUNA (CAP), TOUJEO (CAP); insulin glulisine – APIDRA (CAP); insulin human (rDNA) – ACTRAPHANE (CAP), ACTRAPID (CAP), INSULATARD (CAP), INSULIN HUMAN WINTHROP (CAP), INSUMAN (CAP), MIXTARD (CAP), PROTAPHANE (CAP); insulin human, insulin isophane (NAP); insulin lispro – HUMALOG (CAP), LIPROLOG (CAP); insulin porcine (NAP)

Applicant(s): Eli Lilly Regional Operations GmbH (Abasaglar); Eli Lilly Nederland B.V. (Humalog, Liprolog); Novo Nordisk A/S (Actraphane, Actrapid, Insulatard, Levemir, Mixtard, NovoMix, NovoRapid, Protaphane, Ryzodeg, Tresiba, Xulthopy); Merck Sharp & Dohme Limited (Lusduna); Sanofi-aventis Deutschland GmbH (Apidra, Lantus, Toujeo, Insulin Human Winthrop, Insuman); various

PRAC Rapporteur: To be appointed

Scope: Signal of potential increased risk of medication error associated with pre-filled pens and cartridges presentations, leading to inadequate diabetes control

Action: For adoption of PRAC recommendation

EPITT 18893 – New signal

Lead Member State(s): BE, DK, IT, NL, SE, UK

4.3. Signals follow-up and prioritisation

4.3.1. Amoxicillin (NAP)

Applicant(s): various

PRAC Rapporteur: Jan Neuhauser

Scope: Signal of drug rash eosinophilia systemic symptoms (DRESS) syndrome

Action: For adoption of PRAC recommendation

EPITT 18802 – Follow-up to January 2017

4.3.2. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/SDA/027

Applicant(s): Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

[2] Pre-filled pens and cartridges

Scope: Signal of cytomegalovirus (CMV) reactivation

Action: For adoption of PRAC recommendation

EPITT 18789 – Follow-up to December 2016

4.3.3. Pirfenidone - ESBRIET (CAP) - EMEA/H/C/002154/SDA/014

Applicant(s): Roche Registration Limited

PRAC Rapporteur: Julie Williams

Scope: Signal of colitis

Action: For adoption of PRAC recommendation

EPITT 18793 – Follow-up to December 2016

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Beclometasone dipropionate anhydrous, formoterol fumarate dihydrate, glycopyrronium bromide - EMEA/H/C/004257

Scope: Treatment and reduction of exacerbations in adult patients with chronic obstructive pulmonary disease (COPD) with airflow limitation and who are at risk of exacerbations

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

5.1.2. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - EMEA/H/C/004391

Scope: Treatment of human immunodeficiency virus type 1 (HIV-1) infection

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

5.1.3. Efavirenz, emtricitabine, tenofovir disoproxil – EMEA/H/C/004240

Scope: Treatment of human immunodeficiency virus type 1 (HIV-1) infection

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

5.1.4. Entecavir - EMEA/H/C/004377

Scope: Treatment of chronic hepatitis B virus (HBV) infection

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

5.1.5. Lutetium (^{177}Lu) dotatate - EMEA/H/C/004123, Orphan

Applicant: Advanced Accelerator Applications

Scope: Treatment of gastro-entero-pancreatic neuroendocrine tumours

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

5.1.6. Paclitaxel - EMEA/H/C/004154, Orphan

Applicant: Oasmia Pharmaceutical AB

Scope: Treatment of ovarian cancer

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

5.1.7. Rituximab - EMEA/H/C/004723

Scope: Treatment of non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukaemia (CLL)

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

5.1.8. Rituximab - EMEA/H/C/004724

Scope: Treatment of non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukaemia (CLL) and rheumatoid arthritis (RA)

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

5.1.9. Rituximab - EMEA/H/C/004725

Scope: Treatment of non-Hodgkin's lymphoma (NHL), Granulomatosis with polyangiitis and microscopic polyangiitis

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

5.1.10. Trastuzumab - EMEA/H/C/004346

Scope: Treatment of metastatic and early breast cancer and metastatic gastric cancer (MGC)

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. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0049

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 23) in order to amend the clinical study report (CSR) timelines, patient number and the primary and secondary endpoints listed in the EU RMP for study HGS1006-C1121/BEL114054: an ongoing phase 3, multicentre, multinational, randomized, double-blind, placebo-controlled 104-week treatment study to evaluate the

efficacy and safety of intravenous (IV) belimumab 10 mg/kg plus standard of care (SOC) compared to placebo plus SOC in adult subjects with active lupus nephritis (LN)

Action: For adoption of PRAC Assessment Report

5.2.2. Bevacizumab - AVASTIN (CAP) - EMEA/H/C/000582/II/0095

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Update of the RMP (version 28.0) in order to remove the post-authorisation measure (PAM) relating to the submission of an extension protocol to obtain additional long-term follow-up (LTFU) information from the paediatric population after patients complete a minimum of 5.5 year follow-up period as defined in the protocol of study BO20924 (BERNIE): an open-label, multicentre, randomized study of the safety and effect on event-free survival of bevacizumab in combination with standard chemotherapy in childhood and adolescent patients with metastatic rhabdomyosarcoma and non-rhabdomyosarcoma soft tissue sarcoma, as well as to amend the submission date of its final report (addendum clinical study report (CSR))

Action: For adoption of PRAC Assessment Report

5.2.3. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS1169/0028; Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/WS1169/0032

Applicant: AbbVie Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of the RMPs for Exviera (version 3.0) and Viekirax (version 3.0) following the CHMP opinion dated 15 December 2016 (EMA/CHMP/847450/2016) on the procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free) in order to implement 'hepatitis B reactivation' as an important identified risk, 'emergence of hepatocellular carcinoma' and 'recurrence of hepatocellular carcinoma' as important potential risks, 'patients with previous hepatocellular carcinoma (HCC)' as missing information. The requested studies have also been reflected in the RMPs accordingly

Action: For adoption of PRAC Assessment Report

5.2.4. Everolimus - AFINITOR (CAP) - EMEA/H/C/001038/WS1160/0053; VOTUBIA (CAP) - EMEA/H/C/002311/WS1160/0043

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Martin Huber

Scope: Update of Annex II and the RMPs (version 13) to extend the due date for study CRAD001Y2201 (a phase 2 study of everolimus in combination with exemestane versus everolimus alone versus capecitabine in the treatment of postmenopausal women with oestrogen receptor positive (ER+) locally advanced, recurrent, or metastatic breast cancer after recurrence or progression on prior letrozole or anastrozole) in the oncology setting

(Afinitor) from 3Q 2017 to Q1 2018 and for study CRAD001MIC03 (an international disease registry collecting data on manifestations, interventions, and outcomes in patients with tuberous sclerosis complex – TOSCA) in the tuberous sclerosis complex (TSC) setting (Votubia) from December 2017 to Q2 2018. Furthermore, the MAH took the opportunity to introduce some administrative changes to the RMP

Action: For adoption of PRAC Assessment Report

5.2.5. Fidaxomicin - DIFICLIR (CAP) - EMEA/H/C/002087/II/0028

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP (version 7) in order to remove the post-authorisation measure (PAM) MEA003 regarding clinical study 2819-CL-2001: an open-label, prospective, interventional study in adult patients who received a second treatment course of fidaxomicin to treat a recurrent *Clostridium difficile* infection (CDI) that developed within 3 months after completion of an initially successful treatment of a primary CDI with fidaxomicin, due to the non-feasibility of the study

Action: For adoption of PRAC Assessment Report

5.2.6. Hydrocortisone - PLENADREN (CAP) - EMEA/H/C/002185/II/0024, Orphan

Applicant: Shire Services BVBA

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of the RMP (version 3.1) in order to submit protocol amendments of SHP617-400 (EU-AIR) study: a European multicentre, multi-country, post-authorisation, observation study (registry) of patients with chronic adrenal insufficiency (category 3). In addition, the MAH took the opportunity to implement a change agreed by the PRAC/CHMP as part of the assessment of MEA 005.3 dated July 2016 to remove from the RMP reference to study SHP617-404 (SWE-DUS): a category 3 study to monitor off-label use of Plenadren to evaluate physician prescribing patterns

Action: For adoption of PRAC Assessment Report

5.2.7. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/WS1163/0051; Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS1163/0041

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of the RMPs for Harvoni (version 6.0) and Sovaldi (version 6.0) following the CHMP opinion dated 15 December 2016 (EMA/CHMP/847450/2016) on the procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAs) indicated for the treatment of hepatitis C (interferon free) in order to implement 'hepatitis B reactivation' as an important identified risk, 'emergence of hepatocellular carcinoma' and 'recurrence of hepatocellular carcinoma' as important potential risks, 'patients with previous hepatocellular carcinoma (HCC)' as missing information. The requested studies have also been reflected in the RMPs accordingly

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0107

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information following the MAH's initiative to update its clinical trials safety database to include all currently completed clinical trials for both the intravenous (IV) and subcutaneous (SC) formulations. The adverse reactions' table in section 4.8 as well as the description of selected adverse reactions of special interest is amended. As a consequence, section 4.4 is brought in line with the amended section 4.8. The Package Leaflet and the RMP (version 22) are updated accordingly

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

5.3.2. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0043, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to add data from study C25007: a single-arm study of brentuximab vedotin in patients with relapsed or refractory Hodgkin lymphoma who are not suitable for stem cell transplantation or multi-agent chemotherapy. The submission of the clinical study report fulfils SOB 011 of the conditional marketing authorisation for Adcetris. The RMP (version 8.0) is updated accordingly

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

5.3.3. Ceritinib - ZYKADIA (CAP) - EMEA/H/C/003819/II/0010

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect the safety and efficacy findings of study A2303 (a phase III, multicentre, randomized, open label, study of oral *vs* standard chemotherapy in adult patients with anaplastic lymphoma kinase (ALK)-rearranged (ALK-positive) advanced non-small cell lung cancer (NSCLC) who have been treated previously with chemotherapy (platinum doublet) and crizotinib) to further confirm the efficacy of ceritinib in the treatment of patients previously treated with crizotinib. Annex II, the Package Leaflet, Labelling and the RMP (version 5) 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/0012

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include Zykadia as first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated to update the information based primarily on the supporting study CLDK378A2301 (ASCEND-4: a phase III multicentre, randomized study of oral ceritinib versus standard chemotherapy in previously untreated adult patients with ALK rearranged (ALK-positive), stage IIIB or IV, non-squamous NSCLC). The Package Leaflet and the RMP (version 6.0) are updated accordingly

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

5.3.5. Cobicistat - TYBOST (CAP) - EMEA/H/C/002572/WS1086/0034 Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - EMEA/H/C/002574/WS1086/0077

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Patrick Batty

Scope: Submission of the final report for study GS-US-236-0140: a phase IV, randomized, open-label study evaluating the renal effect of elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate (DF) or other tenofovir DF-containing regimens (ritonavir-boosted atazanavir plus emtricitabine/tenofovir DF or efavirenz/emtricitabine/tenofovir DF) compared to ritonavir-boosted atazanavir plus abacavir/lamivudine in antiretroviral treatment-naïve human immunodeficiency virus (HIV)-1 infected adults with an estimated glomerular filtration rate (eGFR)≥70 mL/min. The RMP (version 2.0) is updated accordingly

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

5.3.6. Daclizumab - ZINBRYTA (CAP) - EMEA/H/C/003862/II/0007

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add 'autoimmune haemolytic anaemia' with a frequency uncommon and to include a warning concerning symptoms of this adverse drug reaction. The Package Leaflet and the RMP (version 5.0) are updated accordingly. In addition, the MAH took the opportunity to implement minor editorial amendments throughout the Product Information

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

5.3.7. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0035

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to include 'liver function abnormalities' as an adverse event observed in the post-marketing setting and to clarify events not observed in placebo-controlled studies. The Package Leaflet and the RMP (version 8) are updated accordingly. The MAH has also taken the opportunity to make minor administrative changes

in the Package Leaflet

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

5.3.8. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0036/G

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Grouped variation including: 1) submission of a clinical study report (CSR) for study 109HV321: a randomized, double-blind, phase 3b study to evaluate the safety and tolerability of BG00012 (dimethyl fumarate) when administered as 240 mg BID (twice daily) dose regimen with and without aspirin compared to placebo or following a slow titration (category 3); 2) submission of a CSR for study 109MS406 (ASSURE): a phase 4, randomized, double-blind study with a safety extension period to evaluate the effect of aspirin on flushing events in subjects with relapsing-remitting multiple sclerosis treated with Tecfidera (dimethyl fumarate) delayed-release capsules (category 4). The RMP (version 9.0) is updated accordingly

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

5.3.9. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0037

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: Submission of a clinical study report (CSR) for study 109MS307: an open-label study to assess the immune response to vaccination in Tecfidera-treated versus interferon-treated subjects with relapsing forms of multiple sclerosis (category 3). As a consequence, section 4.5 of the SmPC is updated. The Package Leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.10. Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - EMEA/H/C/002574/II/0079

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to include the treatment of human immunodeficiency virus type 1 (HIV-1) infected adolescents, with nucleoside reverse transcriptase inhibitors (NRTI) resistance or toxicities precluding the use of first line agents, aged 12 to < 18 years and weighing ≥ 35 kg. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated based on results from study GS-US-236-0112 (a phase 2/3, open-label study of the pharmacokinetics, safety, and antiviral activity through 48 weeks of treatment with elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate single tablet regimen (STR) in HIV-1 infected antiretroviral treatment-naive adolescents). The Package Leaflet and the RMP (version 12) are updated accordingly. In addition, the MAH took the opportunity to introduce minor linguistic amendments to the Product Information

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/0135

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to include pre-exposure prophylaxis of human immunodeficiency virus (HIV) infection in adolescents aged 12 to < 18 years at high risk. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated based on extrapolation of data for emtricitabine, tenofovir disoproxil fumarate, and Truvada in HIV-infected and uninfected subjects. The Package Leaflet and the RMP (version 15) are updated accordingly. In addition, the MAH took the opportunity to introduce minor linguistic amendments to the Product Information

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

5.3.12. Follitropin delta - REKOVELLE (CAP) - EMEA/H/C/003994/II/0003/G

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations including: 1) introduction of a pre-filled cartridge as a new presentation for Rekovelle strength 12 µg/0.36mL; 2) addition of a new pack size for the strength 36 µg/1.08mL and addition of a new pack size for the strength 72 µg/2.16mL. As a consequence, sections 2, 4.2, 6.3, 6.5, 6.6 and 8 of the SmPC are updated. The Package Leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.13. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - EMEA/H/C/000721/II/0085

Applicant: GSK Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of study EPI-HPV-069: a meta-analysis assessing the risk of three autoimmune diseases following vaccination with Cervarix: autoimmune thyroiditis (AIT), Guillain-Barre syndrome (GBS) and inflammatory bowel disease (IBD). The RMP (version 18) is updated accordingly and includes minor updates related to other studies

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

5.3.14. Icatibant - FIRAZYR (CAP) - EMEA/H/C/000899/II/0034/G, Orphan

Applicant: Shire Orphan Therapies GmbH

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variation including: 1) extension of indication to include adolescents and children over 2 years old for the use of Firazyr for symptomatic treatment of acute attacks of hereditary angioedema. As a consequence, section 4.1, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 5.3

and 6.6. of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to reflect the results of a juvenile toxicity study in SmPC section 5.3; 2) update section 5.2 of the SmPC to reflect the effect of age (elderly), gender and race on pharmacokinetics of icatibant. The Package Leaflet and the RMP (version 6.0) are updated accordingly. All relevant pharmacokinetics studies have been previously assessed, as part of prior submissions

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

5.3.15. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/II/0003, Orphan

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Extension of indication to include treatment of patients with Duchenne muscular dystrophy in whom respiratory function has started to decline and who are currently not taking concomitant glucocorticoids. The RMP (version 2.0) is updated accordingly

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

5.3.16. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/II/0032/G

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Patrick Batty

Scope: Grouped variation including: 1) extension of indication of the approved chronic lymphocytic leukaemia (CLL) indication for Zydelig to include its use in combination with bendamustine and rituximab based on the results of the primary analysis of pivotal study GS-US-312-0115 (a phase 3, randomized, double-blind, controlled study evaluating the efficacy and safety of idelalisib (GS-1101) in combination with bendamustine and rituximab for previously treated chronic lymphocytic leukaemia). As a consequence, sections 4.1, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and the RMP (version 2.2) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet; 2) submission of the final clinical study report (CSR) for study 101-08 (a phase 2, single-arm study evaluated idelalisib monotherapy and in combination with rituximab in elderly subjects with previously untreated CLL or small lymphocytic lymphoma. Inclusion of this report provides additional safety data to support the evaluation of the use of idelalisib in patients with CLL) and fulfilment of PAM008; 3) submission of the final clinical study report (CSR) for study GS-US-312-0123 (a phase 3 randomized study evaluated idelalisib in combination with bendamustine and rituximab in subjects with previously untreated CLL)

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

5.3.17. Insulin degludec, liraglutide - XULTOPHY (CAP) - EMEA/H/C/002647/II/0017

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope Update of section 4.2 of the SmPC in order to update the information on use of Xultophy in patients with hepatic impairment based on clinical trial NN2211-1328 (a single-

centre, open-label trial investigating the pharmacokinetics and the safety profile after a single dose of liraglutide in subjects with hepatic impairment and in subjects with normal hepatic function), the LEAD 1-6 meta-analysis as well as other liraglutide trials. In addition, 'fatigue' has been added to the tabulated list of adverse reactions in section 4.8 of the SmPC. The Package Leaflet and the RMP (version 6.0) are updated accordingly. 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

5.3.18. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/WS1158/0154/G; LIPROLOG (CAP) - EMEA/H/C/000393/WS1158/0117/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Grouped variation including: 1) addition of a pre-filled pen: Humalog and Liprolog 100 U/mL Junior KwikPen to administer insulin in half unit increments and containing insulin lispro 3mL cartridge already approved for use; 2) addition of a new pack size of 10 (2x5) pre-filled pens (multipack) for Humalog and Liprolog 100 U/ml Junior KwikPen, including insulin lispro 3mL cartridge already approved for use.; 3) update of sections 4.2 and 4.4 of the SmPC of the already authorised 100 U/mL Humalog and Liprolog presentations to include the paediatric population. The Package Leaflet and the RMP (version 8.0) are updated accordingly

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

5.3.19. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0042

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC to reflect the final results of study CA184-169: a randomized double-blind phase III study of ipilimumab administered at 3 mg/kg versus at 10 mg/kg in subjects previously treated or untreated with unresectable or metastatic melanoma, in order to fulfil ANX 014.1. The MAH also provided with this variation application efficacy and safety data from study CA184-169 in two subgroups: female ≥ 50 years of age and with brain metastases in order to fulfil MEA 015.1. Annex II.D and the RMP (version 14.0) are updated accordingly. In addition the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to include some editorial changes and correct some typos throughout the product information, and 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

5.3.20. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/II/0002, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect the final overall survival

analysis of C16010 China continuation study, a phase 3 study comparing ixazomib plus lenalidomide and dexamethasone versus placebo plus lenalidomide in patients with relapsed and/or refractory multiple myeloma, in order to fulfil specific obligation (SOB) 002. Annex II.E and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to make a small correction in sections 4.7 and 9 of the SmPC and to the German translations

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

5.3.21. Lacosamide - VIMPAT (CAP) - EMEA/H/C/000863/II/0065/G

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations including an extension of indication to include monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in children from 4 to less than 16 years old with epilepsy. For the treatment initiation pack, it is proposed to extend only the adjunctive treatment to adolescents weighting more than 50 kg (not suitable for monotherapy and children and adolescents weighting less than 50 kg). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 12) are updated accordingly. In addition, the MAH took the opportunity to bring Annex IIIA in line with the latest QRD template (version 10) and to introduce combined SmPC for film coated tablets. Furthermore, sections 6.3 and 6.5 of the SmPC for the syrup presentation only are updated due to the extension of shelf life of the finished product after first opening from 4 weeks to 6 months and addition of a 10 mL dosing syringe for syrup, as an additional dosing device to use in the paediatric population

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

5.3.22. Liraglutide - VICTOZA (CAP) - EMEA/H/C/001026/II/0042

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the prevention of major adverse cardiovascular events (MACE) in adults with type 2 diabetes mellitus (T2DM) at high cardiovascular risk and as an adjunct to standard of care therapy in section 4.1 of the SmPC implementing the clinical study results of the LEADER study (EX2211-3748): liraglutide effect on and action in diabetes, evaluation of cardiovascular outcome results (category 3 study: to specifically address the important potential risk of cardiovascular disorders in patients with T2DM). As a consequence, sections 4.2, 4.4, 4.7, 4.8, 5.1 and 6.5 of the SmPC, the Package Leaflet, Labelling and RMP (version 27) are updated accordingly

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

5.3.23. Lopinavir, ritonavir - KALETRA (CAP) - EMEA/H/C/000368/II/0161/G

Applicant: AbbVie Ltd.

PRAC Rapporteur: Caroline Laborde

Scope: Grouped variation including: 1) extension of indication to include children aged 14 days and older in the treatment of human immunodeficiency virus (HIV)-1. As a consequence, sections 4.1, 4.2, 4.3, 4.8, 5.1 and 5.2 of the SmPC are updated. The studies provided in support of the paediatric indication are part of the agreed PIP decision P/0144/2012. In addition, the MAH further updated section 4.4 to add information regarding the use of Kaletra oral solution with feeding tubes. The Package Leaflet, Labelling and RMP (version 8) are updated accordingly; 2) addition of a new pack size of 120 mL in (2 x 60ml bottles) for Kaletra 80mg/ml and 20 mg/ml oral solution (EU/1/01/172/003); 3) addition of a new 2 ml oral dose syringe for the 120 mL presentation

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

5.3.24. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/II/0017

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Almath Spooner

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to reflect the long-term safety and efficacy data from study VX12 809 105: a phase 3, rollover study to evaluate the safety and efficacy of long term treatment with lumacaftor/ivacaftor in subjects aged 12 years and older with cystic fibrosis, homozygous or heterozygous for the F508del cystic fibrosis transmembrane conductance regulator (CFTR) mutation (MEA 001). The RMP (version 2.7) is updated accordingly. 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

5.3.25. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0032

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to add administration guidance and update the safety information based on final results from imposed PAES CA209067: an interventional, randomized, double-blind study in subjects treated with nivolumab monotherapy, ipilimumab monotherapy and nivolumab combined with ipilimumab. Annex II, the Package Leaflet and the RMP (version 5.8) are updated accordingly. This submission fulfils ANX 016. In addition, the MAH took the opportunity to introduce minor editorial and formatting revisions in the Product Information

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

5.3.26. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0016, Orphan

Applicant: Roche Registration Limited

PRAC Rapporteur: Patrick Batty

Scope: Extension of indication to include an indication in combination with chemotherapy, followed by obinutuzumab maintenance therapy in patients achieving a response for the treatment of patients with previously untreated advanced follicular lymphoma. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The

Package Leaflet and the RMP (version 3.0) are updated accordingly. In addition, the due date for provision of the final clinical study report for study BO21223/GALLIUM, a multicentre, phase 3, open-label, randomized study in previously untreated patients with advanced indolent non-Hodgkin's lymphoma evaluating the benefit of obinutuzumab plus chemotherapy compared to rituximab plus chemotherapy followed by obinutuzumab or rituximab maintenance therapy in responders, listed in the RMP as a category 3 is updated. Furthermore, the Product Information is brought in line with the missing information of QRD template (version 9.1). The MAH took the opportunity to introduce some clarification/editorial changes to the SmPC for accuracy and clarity

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

5.3.27. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0023/G

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Sabine Straus

Scope: Grouped variation including: 1) extension of indication to add the treatment of urothelial carcinoma in patients previously treated with chemotherapy based on the results from study KEYNOTE-045, a phase 3, randomized, active-controlled, multi-site, open-label trial evaluating pembrolizumab administered at 200 mg Q3W versus investigators' choice of paclitaxel, docetaxel, or vinflunine in patients previously treated with chemotherapy; 2) extension of indication to add the treatment of urothelial carcinoma in patients ineligible for cisplatin (not previously treated) based on the results from study KEYNOTE-52, a phase 2, single-arm, multisite, open-label trial of pembrolizumab at 200 mg Q3W in the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC have been updated. Furthermore, the MAH is proposing a change to section 4.3 of the SmPC to add that only patients with severe hypersensitivity should be excluded from therapy, and a change to section 4.4 of the SmPC adding possible hypersensitivity and anaphylaxis as part of infusion reactions. The Package Leaflet and the RMP (version 7.0) are updated accordingly

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

5.3.28. Raltegravir - ISENTRESS (CAP) - EMEA/H/C/000860/X/0059

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Line extension to add a new strength of 600mg film-coated tablets. The RMP (version 11.0) is updated accordingly

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

5.3.29. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/II/0020

Applicant: Bayer Pharma AG

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of adult patients with hepatocellular

carcinoma (HCC) who have been previously treated with one systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and RMP (version 5.0) are updated accordingly. Furthermore, the Product Information is brought in line with the latest QRD template (version 10.0)

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

5.3.30. Rituximab - TRUXIMA (CAP) - EMEA/H/C/004112/II/0002/G

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Doris Stenver

Scope: Grouped variations consisting of: 1) change in pack size of the finished product: change in the fill weight/fill volume of sterile multidose (or single-dose, partial use) parenteral medicinal product, including biological/immunological medicinal products. The RMP (version 6) is updated accordingly; 2) change in the manufacturing process of the finished product, including an intermediate used in the manufacture of the finished product. The RMP (version 6) is also updated to harmonise the safety concerns sections with the latest RMP for the reference product

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

5.3.31. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/II/0052/G

Applicant: Bayer Pharma AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Grouped variations consisting of: 1) addition to the authorised indications: treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults, to Xarelto 10 mg. The RMP (version 10) is updated. 2) change in pack sizes of the finished product: change in the number of units in a pack. 3) change in immediate packaging of the finished product: change in type of container or addition of a new container- solid, emi-solid and non-sterile liquid pharmaceutical forms; 4) addition of information on interactions with selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs) in section 4.5 and a related warning in section 4.4 of the SmPC .In addition, MedDRA terminology is updated in the adverse drug reactions; 5) deletion of 'patients undergoing major orthopaedic surgery other than elective hip or knee replacement surgery' and 'remedial pro-coagulant therapy for excessive haemorrhage' from the summary of safety concerns

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

5.3.32. Sevelamer carbonate - RENVELA (CAP) - EMEA/H/C/000993/WS0965/0035; Sevelamer - SEVELAMER CARBONATE ZENTIVA (CAP) - EMEA/H/C/003971/WS0965/0007

Applicant: Genzyme Europe BV

PRAC Rapporteur: Laurence de Fays

Scope: Extension of indication to include the control of hyperphosphataemia in paediatric patients (>6 years of age and a body surface area (BSA) of >0.75 m^2) with chronic kidney

disease. As a consequence, section 4.2 of the SmPC is updated to detail the posology in the paediatric patients. The Package Leaflet and the RMP (version 8.0) are updated accordingly

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

5.3.33. Simeprevir - OLYSIO (CAP) - EMEA/H/C/002777/II/0031

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Update of section 5.1 of the SmPC in order to update the efficacy information following results from study HPC3002, a prospective 3-year follow-up study in subjects previously treated in a phase IIb or phase III study with a TMC435-containing regimen for the treatment of hepatitis C virus (HCV) infection listed as a category 3 study in the RMP and in fulfilment of MEA005. The RMP (version 4.0) is updated accordingly and includes updates of changes already agreed in procedures II/0021, II/0027 and EMEA/H/A-20/1438/C/2777/0019

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

5.3.34. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/II/0036

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to add the treatment of chronic hepatitis C in adolescents aged 12 to <18 years. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add information on posology, warnings, safety, efficacy and pharmacokinetics. The Package Leaflet and the RMP (version 5.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the Product Information is brought in line with the latest QRD template (version 10)

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

5.3.35. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/II/0006

Applicant: Otsuka Pharmaceutical Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Update of section 5.1 of the SmPC based on final results from study 156-08-271 (TEMPO 4:4) listed as a PAES in Annex II. This study is a multicentre, open-label, extension study (extension of trial 156-04-251) to evaluate the long-term efficacy and safety of oral tolvaptan tablet regimens in patients with autosomal dominant polycystic kidney disease (ADPKD) over 5 years. Annex II and the RMP (version 13.1) are updated accordingly to reflect the completion of 156-08-271 study. In addition, the MAH took the opportunity to add the current anatomical therapeutic chemical (ATC) code applicable for tolvaptan as assigned by WHO[3]

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

[3] World Health Organization

6. Periodic safety update reports (PSURs)

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

6.1.1. Alglucosidase alfa - MYOZYME (CAP) - PSUSA/00000086/201609

Applicant: Genzyme Europe BV

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Alipogene tiparvovec - GLYBERA (CAP) - PSUSA/00010056/201610

Applicant: uniQure biopharma B.V., ATMP[4]

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.3. Aliskiren - RASILEZ (CAP); aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - PSUSA/00000089/201609

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Bazedoxifene - CONBRIZA (CAP) - PSUSA/00000302/201610

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Buprenorphine, naloxone - SUBOXONE (CAP) - PSUSA/00002113/201609

Applicant: Indivior UK Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

[4] Advanced Therapy Medicinal Product

Action: For adoption of recommendation to CHMP

6.1.6. Choriogonadotropin alpha - OVITRELLE (CAP) - PSUSA/00000736/201609

Applicant: Merck Serono Europe Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/201610 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Defibrotide - DEFITELIO (CAP) - PSUSA/00010086/201610

Applicant: Gentium S.r.l.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Delamanid - DELTYBA (CAP) - PSUSA/00010213/201610

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Eculizumab - SOLIRIS (CAP) - PSUSA/00001198/201610

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Edoxaban - LIXIANA (CAP) - PSUSA/00010387/201610

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Eltrombopag - REVOLADE (CAP) - PSUSA/00001205/201609

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Empagliflozin – JARDIANCE (CAP); empagliflozin, metformin - SYNJARDY (CAP) - PSUSA/00010388/201610

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - PSUSA/00010515/201610 (with RMP)

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Granisetron[5] - SANCUSO (CAP) - PSUSA/00010101/201610

Applicant: Kyowa Kirin Limited

PRAC Rapporteur: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Idarucizumab - PRAXBIND (CAP) - PSUSA/00010435/201610

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[5] Transdermal patch only

6.1.17. Insulin aspart - NOVOMIX (CAP); NOVORAPID (CAP) - PSUSA/00001749/201609

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Insulin degludec, liraglutide - XULTOPHY (CAP) - PSUSA/00010272/201609 (with RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Insulin degludec - TRESIBA (CAP); insulin degludec, insulin aspart - RYZODEG (CAP) - PSUSA/00010036/201609

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Insulin glargine - ABASAGLAR (CAP); LANTUS (CAP); TOUJEO (CAP) - PSUSA/00001751/201610

Applicant: Eli Lilly Regional Operations GmbH (Abasaglar), Sanofi-aventis Deutschland GmbH (Lantus, Toujeo)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Lurasidone - LATUDA (CAP) - PSUSA/00010114/201610

Applicant: Sunovion Pharmaceuticals Europe Ltd

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Macitentan - OPSUMIT (CAP) - PSUSA/00010115/201610

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Meningococcal group A, C, W135, Y conjugate vaccine (conjugated to tetanus toxoid carrier protein) - NIMENRIX (CAP) - PSUSA/00010044/201610

Applicant: Pfizer Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Micafungin - MYCAMINE (CAP) - PSUSA/00002051/201610

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Miglustat - ZAVESCA (CAP) - PSUSA/00002062/201610

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Netupitant, palonosetron - AKYNZEO (CAP) - PSUSA/00010393/201610

Applicant: Helsinn Birex Pharmaceuticals Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Nintedanib[6] - OFEV (CAP) - PSUSA/00010319/201610

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[6] Respiratory indication only

6.1.28. Ocriplasmin - JETREA (CAP) - PSUSA/00010122/201610

Applicant: ThromboGenics NV

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Ofatumumab - ARZERRA (CAP) - PSUSA/00002202/201610

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) – FOCLIVIA (CAP); prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - PSUSA/00010008/201610

Applicant: Seqirus S.r.l

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Panitumumab - VECTIBIX (CAP) - PSUSA/00002283/201609

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Para-aminosalicyic acid[7] - GRANUPAS (CAP) - PSUSA/00010171/201610

Applicant: Lucane Pharma

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Pasireotide - SIGNIFOR (CAP) - PSUSA/00009253/201610

Applicant: Novartis Europharm Ltd

[7] Centrally authorised product

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Pazopanib - VOTRIENT (CAP) - PSUSA/00002321/201610

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Pitolisant - WAKIX (CAP) - PSUSA/00010490/201609

Applicant: BIOPROJET PHARMA

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Posaconazole - NOXAFIL (CAP) - PSUSA/00002480/201610

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Prucalopride - RESOLOR (CAP) - PSUSA/00002568/201610

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Ramucirumab - CYRAMZA (CAP) - PSUSA/00010323/201610

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ranibizumab - LUCENTIS (CAP) - PSUSA/00002609/201610

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Siltuximab - SYLVANT (CAP) - PSUSA/00010254/201610

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Sofosbuvir, ledipasvir - HARVONI (CAP) - PSUSA/00010306/201610

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/201610

Applicant: Amgen Europe B.V., ATMP[8]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.43. Thalidomide - THALIDOMIDE CELGENE (CAP) - PSUSA/00002919/201610

Applicant: Celgene Europe Limited

PRAC Rapporteur: Claire Ferard

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Tocilizumab - ROACTEMRA (CAP) - PSUSA/00002980/201610

Applicant: Roche Registration Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

[8] Advanced Therapy Medicinal Product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Trifluridine, tipiracil - LONSURF (CAP) - PSUSA/00010517/201610

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Umeclidinium bromide - INCRUSE (CAP) - PSUSA/00010263/201610

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Vortioxetine - BRINTELLIX (CAP) - PSUSA/00010052/201609

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Laurence de Fays

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. Brinzolamide - AZOPT (CAP); NAP - PSUSA/00000432/201608

Applicant: Alcon Laboratories (UK) Ltd (Azopt), various

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Mercaptopurine - XALUPRINE (CAP); NAP - PSUSA/00001988/201609

Applicant: Nova Laboratories Limited (Xaluprine), various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Octocog alfa - ADVATE (CAP); HELIXATE NEXGEN (CAP); IBLIAS (CAP); KOGENATE BAYER (CAP); KOVALTRY (CAP); NAP - PSUSA/00002200/201608

Applicant: Baxter AG (Advate), Bayer Pharma AG (Helixate NexGen, Iblias, KOGENATE Bayer, Kovaltry), 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. Biperiden (NAP) - PSUSA/00000415/201608

Applicant: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Cetirizine, pseudoephedrine (NAP) - PSUSA/00000629/201608

Applicant: various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Chlorquinaldol[9], promestriene (NAP) - PSUSA/00009272/201609

Applicant: various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Drospirenone, ethinylestradiol (NAP) - PSUSA/00010217/201609

Applicant: various

PRAC Lead: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[9] Vaginal tablet only

6.3.5. Esketamine (NAP) - PSUSA/00001266/201608

Applicant: various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Estradiol[10] (NAP) - PSUSA/00010440/201608

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Germanium (^{68}Ge) chloride, gallium (^{68}Ga) chloride (NAP) - PSUSA/00010364/201609

Applicant: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Ketoprofen[11] (NAP) - PSUSA/00009205/201609

Applicant: various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Latanoprost[12] (NAP) - PSUSA/00001834/201610

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Oxcarbazepine (NAP) - PSUSA/00002235/201608

Applicant: various

[10] Except cream, balm, emulsion for application in female genital area
[11] Topical use only
[12] Paediatric indications only

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Penciclovir (NAP) - PSUSA/00002333/201608

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Pilocarpine[13] (NAP) - PSUSA/00002410/201608

Applicant: various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Tolterodine (NAP) - PSUSA/00002993/201609

Applicant: various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Tuberculin purified protein derivative (NAP) - PSUSA/00003063/201609

Applicant: various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/LEG 029.1

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 029 [submission of a safety assessment of all haemorrhagic

[13] Ophthalmic formulation only

events for cinacalcet events in all controlled clinical studies with cinacalcet, irrespective of indication as requested in the conclusions of EMEA/H/C/PSUSA/00000756/201602 adopted by the PRAC on 29 September 2016] as per the request for supplementary information (RSI) adopted in January 2017

Action: For adoption of advice to CHMP

6.4.2. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/LEG 030

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a detailed review of drug-related hepatic disorders as requested in the conclusions of EMEA/H/C/PSUSA/00000756/201602 adopted by the PRAC on 29 September 2016

Action: For adoption of advice to CHMP

6.4.3. Ranibizumab - LUCENTIS (CAP) - EMEA/H/C/000715/LEG 071.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 071 [submission of a detailed review on vascular death, all-cause mortality, and main vascular events observed in RIDE (a phase III randomized study of ranibizumab injection in subjects with clinically significant macular edema (ME) with center involvement secondary to diabetes mellitus) and RISE (a phase III randomized study of ranibizumab injection in subjects with clinically significant ME with center involvement secondary to diabetes mellitus) as requested in the conclusions of PSUSA/00002609/201510 adopted by PRAC in April 2016] as per the request for supplementary information (RSI) adopted in November 2016

Action: For adoption of advice to CHMP

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[14]

7.1.1. Brentuximab vedotin – ADCETRIS (CAP) - EMEA/H/C/PSA/S/0009.1

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Submission of a revised PASS protocol following substantial amendments for study MA25101: an observational cohort study of the safety of brentuximab vedotin in the treatment of relapsed or refractory CD30+ Hodgkin lymphoma and relapsed or refractory systemic anaplastic large cell lymphoma (sALCL) as per the request for supplementary

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

information (RSI) adopted in December 2016

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

7.1.2. Hydroxyethyl starch (NAP) - EMEA/H/N/PSA/S/0011.1

Applicant: B. Braun Melsungen AG

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of a revised PASS protocol for a retrospective drug utilisation study (DUS) (ENCEPP/SDDP/12540) to investigate the routine use of hydroxyethyl starch (HES)-containing infusion solutions of B.Braun in hospitals settings as per the request for supplementary information (RSI) adopted in January 2017

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

7.1.3. Teicoplanin (NAP) - EMEA/H/N/PSA/S/0013.1

Applicant: Sanofi-aventis (Targocid)

PRAC Rapporteur: Valerie Strassmann

Scope: Revised protocol following substantial amendments for a PASS study: a prospective, observational cohort, evaluating the incidence of nephrotoxicity and other adverse events of interest in patients treated with the higher recommended teicoplanin loading dose (12mg/kg twice a day), and comparison with external historical comparator data as per the request for supplementary information (RSI) adopted in February 2017

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[15]

7.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.2

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of a revised PASS protocol for study OBS13434: a prospective, multicentre, observational, PASS to evaluate the long term safety profile of alemtuzumab treatment in patients with relapsing forms of multiple sclerosis (RMS) as per the request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.2. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 008.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

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

Scope: MAH's responses to MEA 008 [assessment of a retrospective, observational cohort study protocol, using four administrative claims databases, to assess the incidence of diabetic ketoacidosis among patients with type 2 diabetes mellitus (T2DM) treated with canagliflozin-containing medicines or other antihyperglycemic agents], as per request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.3. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 007.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: MAH's responses to MEA 007 [assessment of a retrospective, observational cohort study protocol, using four administrative claims databases, to assess the incidence of diabetic ketoacidosis among patients with type 2 diabetes mellitus (T2DM) treated with canagliflozin-containing medicines or other antihyperglycemic agents], as per request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.4. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/MEA 001.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: MAH's response to MEA-001 [submission of an updated protocol for PASS L01XC24: a survey measuring the effectiveness of the educational materials regarding the minimisation of risk of interference for blood typing with daratumumab] as per request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.5. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/MEA 045.1

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 045 [PASS protocol for study GS-EU-276-4027, a drug utilisation study (DUS) to characterize: 1) prescribers' level of knowledge about the key risks of Truvada for a pre-exposure prophylaxis (PrEP) indication and assess the effectiveness of risk minimisation measures; 2) prescribing practices in routine clinical practice of Truvada for PrEP by describing the demographics of human immunodeficiency virus (HIV)-1 uninfected individuals who were prescribed Truvada for PrEP, and the prescribed dosing schedule for Truvada for PrEP as reported by the prescriber, as a result of variation II/0126 finalised at CHMP/PRAC in July 2016 to extend the indication to PrEP] as per request for supplementary information (RSI) adopted in January 2017

Action: For adoption of advice to CHMP

7.2.6. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 033

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study MK-8259-050: an observational PASS of golimumab in treatment of poly-articular juvenile idiopathic arthritis (pJIA) using the German Biologics JIA registry (BiKeR) as requested in the conclusions of variation procedure II/63

Action: For adoption of advice to CHMP

7.2.7. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/MEA 047.3

Applicant: Sanofi-aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 047.2: MAH's responses to MEA 047.2 [PASS protocol and statistical analysis plan for study HUBIN-C-06380: a prospective cohort study organised as exposure registry], as per request for supplementary information (RSI) adopted in June 2016

Action: For adoption of advice to CHMP

7.2.8. Lipegfilgrastim - LONQUEX (CAP) - EMEA/H/C/002556/MEA 004.2

Applicant: Sicor Biotech UAB

PRAC Rapporteur: Patrick Batty

Scope: Updated PASS protocol for study XM22-ONC-50002: a multi-country, multicentre, retrospective observational study to describe the pattern of lipegfilgrastim use, and specifically to quantify the extent of lipegfilgrastim off-label use in routine clinical practice in several countries in the European Union (EU) to reflect a revised list of countries

Action: For adoption of advice to CHMP

7.2.9. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.2

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 003.1 [PASS protocol for study NB-451: a multinational, multicentre, prospective, non-interventional, PASS of prolonged-release naltrexone hydrochloride/bupropion hydrochloride for weight loss in the European Union (EU)] as per request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.2.10. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 004.2

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 004.1 [revised PASS protocol for study NB-452: a survey to evaluate the effectiveness of the physician prescribing checklist (PPC) among physicians in the European Union] as per request for supplementary information (RSI) adopted in September 2016

Action: For adoption of advice to CHMP

7.2.11. Olaratumab - LARTRUVO (CAP) - EMEA/H/C/004216/MEA 001

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sabine Straus

Scope: Submission of a protocol for study I5B-MC-B001: an observational PASS to evaluate the safety and effectiveness of olaratumab in combination with doxorubicin in patients with advanced soft tissue sarcoma (STS) including rare subtypes (as requested in the conclusions of the initial MAA)

Action: For adoption of advice to CHMP

7.2.12. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 005

Applicant: Teva Pharmaceuticals Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of a protocol for study C38072-AS-50027: a long-term non-interventional study comparing the risk of malignancy in severe asthma patients treated with reslizumab and patients not treated with reslizumab (RMP category 3)

Action: For adoption of advice to CHMP

7.2.13. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 003.1

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Julie Williams

Scope: MAH's response to MEA 003 [PASS protocol for study AC-065A403 to evaluate risk minimisation measures for mEDication errors with Uptravi during the titration phase in patients with pulmonary arterial hypertension (PAH) in Clinical prAcTicE (EDUCATE)], as per request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.14. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/MEA 025.1

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Valerie Strassmann

Scope: MAH's responses to MEA 025 [PASS protocol: to evaluate the effectiveness of risk minimisation measures: a survey among healthcare professionals and patient/caregivers to assess their knowledge and attitudes on prescribing and home administration conditions of

velaglucerase alfa in six European countries], as per request for supplementary information (RSI) adopted in December 2016

Action: For adoption of advice to CHMP

7.2.15. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002

Applicant: AbbVie Ltd.

PRAC Rapporteur: Patrick Batty

Scope: Submission of a protocol for a prospective observational study to assess the long term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[16]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[17]

7.4.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0108/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Scope: Grouped variations including 1) submission of the final clinical study report from epidemiological IM101045A study: safety of non-biologic disease-modifying antirheumatic drugs (DMARDs) and biologic treatment for rheumatoid arthritis (RMP category 3 study); 2) submission of the final clinical study report from epidemiological IM101045B study: safety and outcomes in patients treated with abatacept and other anti-rheumatic therapies (RMP category 3 study). IM101045A and IM101045B are both observational studies, sharing overlapping safety objectives (assessment of the risk of infections, infusion-related reactions, autoimmune disorders, injection reactions and combination use). The RMP (version 22) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0159

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final clinical study report (CSR) for study P06-134: a long-term non-interventional registry to assess safety and effectiveness of Humira in subjects with moderately to severely active Crohn's disease in fulfilment of MEA 056.9

[16] In accordance with Article 107p-q of Directive 2001/83/EC
[17] 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. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0162

Applicant: AbbVie Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final national report for the biologics registry: Anti-Rheumatic Treatment in Sweden (ARTIS) after ending AbbVie's support by end 2015 in fulfilment of MEA 066.5

Action: For adoption of PRAC Assessment Report

7.4.4. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/II/0100

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: Submission of the final report for study 1160.144 evaluating the potential off-label use of dabigatran etexilate in Europe: a drug utilisation study (DUS) in Cegedim France, Denmark, and UK in Clinical Practice Research Datalink (CPRD)

Action: For adoption of PRAC Assessment Report

7.4.5. Human rotavirus, live attenuated - ROTARIX (CAP) - EMEA/H/C/000639/II/0094

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final study report for EPI-ROTA-007 VS US DB: a phase 4, open, observational study of the safety of Rotarix, administered to a birth cohort in US States health insurance plans. The RMP (version 17) is updated in order to amend information in relation to EPI-ROTA-007 VS US DB study, EPI-ROTA-052 BOD EU SUPP (an observational community-based strain surveillance study) as agreed in the conclusions of variation II/86. In addition, the MAH took this opportunity to further update the RMP with the new due date for submission of the final study report for ROTA-085 PMS (a special drug use investigation for Rotarix (investigation of incidence of intussusception after vaccination for rotavirus gastroenteritis) conducted with the objective to determine the incidence of intussusception after vaccination with Rotarix in Japan)

Action: For adoption of PRAC Assessment Report

7.4.6. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/II/0064

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final study report for study MI-MA194: a post-marketing observational evaluation of the safety of Fluenz in children and adolescents with high-risk conditions

Action: For adoption of PRAC Assessment Report

7.4.7. Peginterferon alfa-2a - PEGASYS (CAP) - EMEA/H/C/000395/II/0092

Applicant: Roche Registration Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final report from a systematic review and individual patient data meta-analysis of peginterferon alfa-2a (PEG-IFN) studies to identify optimal stopping rules in order to provide the final outcome related to the assessment of a response guided therapy (RGT) for Pegasys in hepatitis B virus (HBV)-infected patients

Action: For adoption of PRAC Assessment Report

7.4.8. Rufinamide - INOVELON (CAP) - EMEA/H/C/000660/II/0041, Orphan

Applicant: Eisai Ltd

PRAC Rapporteur: Claire Ferard

Scope: Submission of the final clinical study report (CSR) for study E2080-E044-401, a European registry of anti-epileptic drug use in patients with Lennox-Gastaut syndrome (LGS), listed as a category 3 study in the RMP, in fulfilment of MEA 002.1. E2080-E044-401 is a non-interventional EU registry study entering patients (aged ≥4 years) with LGS who required a modification in anti-epileptic therapy (either the addition of another anti-epileptic drugs (AED) or the change of one drug to another) in order to evaluate the long-term safety of rufinamide

Action: For adoption of PRAC Assessment Report

7.4.9. Saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/WS0960/0040/G saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/WS0960/0033/G

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Group of variations consisting of final epidemiological study results for studies D1680R00011 (a cohort study comparing risk of major cardiovascular (CV) events between patients with type 2 diabetes mellitus (T2DM) who are new initiators of saxagliptin and those who are new initiators of oral antidiabetic drug (OAD) treatments in classes other than DPP-4 inhibitors), D1680R00012 (a cohort study comparing risk of hospitalization with acute liver failure between patients with T2DM exposed to saxagliptin and those exposed to other OAD treatments), D1680R00013 (a cohort study comparing risk of hospitalization with infections between patients with T2DM exposed to saxagliptin and those exposed to other OAD treatments), D1680R00014 (a cohort study comparing risk of hospitalization for severe hypersensitivity (including severe cutaneous reactions) between patients with T2DM exposed to saxagliptin and those exposed to other OAD treatments) and D1680R00015 (a cohort study comparing risk of hospitalization for acute kidney injury between patients with T2DM initiating saxagliptin and those initiating other OAD treatments), and consequent update of the RMP. As a consequence, the RMP (version 11) is updated accordingly. In

addition, routine changes are made in parts III (pharmacovigilance plan, overview of planned pharmacovigilance actions) and IV. A safety review based on the literature is also included to investigate acute kidney injury associated with saxagliptin, saxagliptin and metformin at requested by PRAC

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. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.3

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: Second annual progress report for PASS OBS13434: a prospective, multicentre, observational, PASS to evaluate the long term safety profile of alemtuzumab treatment in patients with relapsing forms of multiple sclerosis (MS) with the aim to better characterize the long-term safety profile of alemtuzumab in relapsing MS patients and to determine the incidence of adverse events of special interest (AESIs)

Action: For adoption of advice to CHMP

7.5.2. Bazedoxifene - CONBRIZA (CAP) - EMEA/H/C/000913/MEA 012.9

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Fourth annual interim report for the period October 2015 to October 2016 of EU PASS 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. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.17

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for study BEL115467/HGS1006-C1113: a randomized, double-blind placebo-controlled large safety study evaluating the incidence of all-cause mortality and adverse events of special interest (including serious infections, malignancies, serious infusion and hypersensitivity reactions and serious psychiatric events) in patients with systemic lupus erythematosus

Action: For adoption of advice to CHMP

7.5.4. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 006

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study MB 102-103 ST/D1690R00008 - (EUPAS12113): a pharmacoepidemiology observational study assessing the risk of severe complications of urinary tract infections (UTI) between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.5. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 007

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study MB102-110 ST/D1690R00004 - (EUPAS11684): a pharmacoepidemiology observational study assessing the risk of acute renal failure/kidney injury between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.6. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 008

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study MB102-104 ST/D1690R00005 - (EUPAS12110): a pharmacoepidemiology observational study assessing the risk of acute hepatic failure/acute liver injury between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.7. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/MEA 009

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study MB 102-118ST/D1690R00007 - (EUPAS12116): a pharmacoepidemiology observational study assessing the risk of cancer between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.8. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 001.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study MB 102-103 ST/D1690R00008 - (EUPAS12113): a pharmacoepidemiology observational study assessing the risk of severe complications of urinary tract infections (UTI) between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.9. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 002.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study MB102-110 ST/D1690R00004 - (EUPAS11684): a pharmacoepidemiology observational study assessing the risk of acute renal failure/kidney injury between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.10. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 003.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study MB102-104 ST/D1690R00005 - (EUPAS12110): a pharmacoepidemiology observational study assessing the risk of acute hepatic failure/acute liver injury between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.11. Dapagliflozin - FORXIGA (CAP) - EMEA/H/C/002322/MEA 004.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: First interim report for study MB 102-118ST/D1690R00007 - (EUPAS12116): a pharmacoepidemiology observational study assessing the risk of cancer between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.12. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/MEA 005

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First interim report for study MB 102-103 ST/D1690R00008 - (EUPAS12113): a pharmacoepidemiology observational study assessing the risk of severe complications of

urinary tract infections (UTI) between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.13. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/MEA 006

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First interim report for study MB102-110 ST/D1690R00004 - (EUPAS11684): a pharmacoepidemiology observational study assessing the risk of acute renal failure/kidney injury between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.14. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/MEA 007

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First interim report for study MB102-104 ST/D1690R00005 - (EUPAS12110): a pharmacoepidemiology observational study assessing the risk of acute hepatic failure/acute liver injury between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.15. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/MEA 008

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First interim report for study MB 102-118ST/D1690R00007 - (EUPAS12116): a pharmacoepidemiology observational study assessing the risk of cancer between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.16. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 008

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First interim report for study MB 102-103 ST/D1690R00008 - (EUPAS12113): a pharmacoepidemiology observational study assessing the risk of severe complications of urinary tract infections (UTI) between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.17. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 009

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First interim report for study MB102-110 ST/D1690R00004 - (EUPAS11684): a pharmacoepidemiology observational study assessing the risk of acute renal failure/kidney injury between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.18. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 010

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First interim report for study MB102-104 ST/D1690R00005 - (EUPAS12110): a pharmacoepidemiology observational study assessing the risk of acute hepatic failure/acute liver injury between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.19. Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/MEA 011

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: First interim report for study MB 102-118ST/D1690R00007 - (EUPAS12116): a pharmacoepidemiology observational study assessing the risk of cancer between patients with type 2 diabetes mellitus (T2DM) exposed to dapagliflozin and those exposed to other antidiabetic treatments

Action: For adoption of advice to CHMP

7.5.20. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/MEA 001.1

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Second interim annual report for EuroSIDA PASS study 201177: a prospective observational cohort study in patients receiving dolutegravir (category 3) to investigate the risk of hypersensitivity reactions (HSR), hepatotoxicity and serious rash (division of acquired immune deficiency syndrome (DAIDS) grading scale category 3 or 4)

Action: For adoption of advice to CHMP

7.5.21. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/MEA 007.1

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Second interim report for EuroSIDA PASS study 201177DTG: a prospective observational cohort study to monitor the occurrence of hypersensitivity reaction and hepatotoxicity in patients receiving dolutegravir (category 3) to investigate the risk of hypersensitivity reactions (HSR), hepatotoxicity and serious rash (division of acquired immune deficiency syndrome (DAIDS) grading scale category 3 or 4)

Action: For adoption of advice to CHMP

7.5.22. Insulin human - INSUMAN (CAP) - EMEA/H/C/000201/MEA 041

Applicant: Sanofi-aventis Deutschland GmbH

PRAC Rapporteur: Jean-Michel Dogné

Scope: First annual interim study report of the Insuman implantable registry HUBIN-C-06380: a European observational cohort of patients with type 1 diabetes treated via intraperitoneal route with Insuman implantable 400 IU/mL in Medtronic MiniMed implantable pump

Action: For adoption of advice to CHMP

7.5.23. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/ANX 003.2

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: First biennial interim results for study TED-R-13-002: an international Short bowel syndrome registry: a prospective, long-term observational cohort study of patients with short bowel syndrome

Action: For adoption of advice to CHMP

7.5.24. Turoctocog alfa - NOVOEIGHT (CAP) - EMEA/H/C/002719/MEA 004.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 004.1 [Submission of an interim report for the post-authorisation safety study NN7008-3553, a multicentre non-interventional study of safety and efficacy of turoctocog alfa (recombinant factor VIII (rFVIII)) during long-term treatment of severe and moderately severe haemophilia A (FVIII ≤2%)] as per request for supplementary information (RSI) adopted in January 2017:

Action: For adoption of advice to CHMP

7.5.25. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.12

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Annual report for PSOLAR (PSOriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry program designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics

Action: For adoption of advice to CHMP

7.6. Others

None

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

None

8.2. Conditional renewals of the marketing authorisation

8.2.1. Allogeneic T cells genetically modified with a retroviral vector encoding for a truncated form of the human low affinity nerve growth factor receptor (ΔLNGFR) and the herpes simplex I virus thymidine kinase (HSV-TK Mut2) - ZALMOXIS (CAP) - EMEA/H/C/002801/R/0003 (without RMP)

Applicant: MolMed SpA, ATMP[18]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

[18] Advanced therapy medicinal product

Action: For adoption of advice to CAT and CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/R/0033 (with RMP)

Applicant: Bayer Pharma AG

PRAC Rapporteur: Claire Ferard

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Copper (^{64}Cu) chloride - CUPRYMINA (CAP) - EMEA/H/C/002136/R/0014 (with RMP)

Applicant: Sparkle S.r.l.

PRAC Rapporteur: Patrick Batty

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Glycopyrronium bromide - SEEBRI BREEZHALER (CAP) - EMEA/H/C/002430/R/0020 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Glycopyrronium bromide- TOVANOR BREEZHALER (CAP) - EMEA/H/C/002690/R/0022 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Glycopyrronium bromide - ENUREV BREEZHALER (CAP) - EMEA/H/C/002691/R/0020 (without RMP)

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Ibandronic acid - IBANDRONIC ACID ACCORD (CAP) - EMEA/H/C/002638/R/0013 (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

8.3.7. Ingenol mebutate - PICATO (CAP) - EMEA/H/C/002275/R/0023 (with RMP)

Applicant: LEO Laboratories Ltd

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/R/0032 (without RMP)

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Valerie Strassmann

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Memantine hydrochloride - MEMANTINE MERZ (CAP) - EMEA/H/C/002711/R/0012 (without RMP)

Applicant: Merz Pharmaceuticals GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Mirabegron - BETMIGA (CAP) - EMEA/H/C/002388/R/0026 (with RMP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Dolores Montero Corominas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Temsirolimus - TORISEL (CAP) - EMEA/H/C/000799/R/0065 (without RMP)

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

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

10.1.1. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0007

Applicant: Actelion Registration Ltd.

PRAC Rapporteur: Julie Williams; PRAC Co-rapporteur: Martin Huber

Scope: PRAC consultation on a type II variation on an update of sections 4.4 and 4.5 of the SmPC in order to add information on pharmacokinetic (PK) interactions with gemfibrozil and rifampicin in healthy subjects, based on the final clinical study report of the completed clinical pharmacology drug-drug interaction study AC-065-113. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update information on the hydrolysis of selexipag based on data from the previously submitted absolute bioavailability study AC-065-110 including minor amendments to sections 5.1 and 5.2 of the SmPC and to bring the Product Information (PI) in line with the latest QRD template (version 10)

Action: For adoption of advice to CHMP

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

None

10.3. Other requests

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. Metformin (NAP)

Applicant: Merck (Glucophage, Stagid), various

PRAC Lead: Caroline Laborde

Scope: PRAC consultation on the assessment of the detailed review on the safety of metformin during pregnancy submitted to Member States following the request in the conclusion of PSUSA/00002001/201504 adopted by the PRAC in December 2015

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

12.2.1. EMA Scientific Co-ordination Board (SciCoBo) - update

PRAC lead: June Raine

Action: For discussion

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

12.3.1. Healthcare Professionals' Working Party (HCPWP) – recommendation on additional risk minimisation measures (aRMMs)

PRAC lead: Almath Spooner, Sabine Straus

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. PRAC strategic review and learning meeting, 16-18 October 2017

PRAC lead: Maia Uusküla

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

12.6.1. EMA framework of collaboration with academia

Action: For discussion

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

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

12.11.2. Signal management – handling of MAHs' signals after the go-live of the new EudraVigilance system

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 – experience analysis

Action: For discussion

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- EudraVigilance auditable requirement project – recommendation on the independent final audit report

Action: For adoption

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

None

13. Any other business

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/