29 August 2017
EMA/PRAC/568796/2017

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 29 August-1 September 2017

Chair: June Raine – Vice-Chair: Almath Spooner

29 August 2017, 13:00 – 19:30, room 3/A

30 August 2017, 08:30 – 19:30, room 3/A

31 August 2017, 08:30 – 19:30, room 3/A

01 September 2017, 08:30 – 16:00, room 3/A

Organisational, regulatory and methodological matters (ORGAM)

14 September 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 29 August-1 September 2017. See (current) September 2017 PRAC minutes (to be published post October 2017 PRAC meeting).

1.2. Agenda of the meeting of 29 August-1 September 2017

Action: For adoption

1.3. Minutes of the previous meeting of 3-6 July 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

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Daclizumab - ZINBRYTA (CAP) – EMEA/H/A-20/1456

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia; PRAC Co-rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

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

Action: For adoption of a list of outstanding issues (LoOI)

3.2.2. Paracetamol[1] (NAP); paracetamol, tramadol[1] (NAP) - EMEA/H/A-31/1445

Applicant(s): GlaxoSmithKline Consumer Healthcare AB (Alvedon 665 mg modified-release tablet), various

PRAC Rapporteur: Laurence de Fays; PRAC Co-rapporteur: Ulla Wändel Liminga

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

Action: For adoption of a list of outstanding issues (LoOI) (or a recommendation to CMDh)

3.2.3. Valproate and related substances: sodium valproate, valproic acid, valproate semisodium, valpromide (NAP) - EMEA/H/A-31/1454

Applicant(s): Sanofi-Aventis, various

PRAC Rapporteur: Sabine Straus; PRAC Co-rapporteur: Jean-Michel Dogné

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

Action: For adoption of a list of participants and agenda for the public hearing and adoption of a list of questions for the ad-hoc expert group

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

3.4.1. Human coagulation (plasma-derived) factor VIII: human coagulation factor VIII (antihaemophilic factor A) (NAP); human coagulation factor VIII (inhibitor bypassing fraction) (NAP); human coagulation factor VIII, human von Willebrand

[1] Modified release formulations only
[2] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

factor - VONCENTO (CAP)
Recombinant factor VIII: antihaemophilic factor (recombinant) (NAP); efmoroctocog alfa – ELOCTA (CAP); moroctocog alfa – REFACTO AF (CAP) octocog alfa – ADVATE (CAP), HELIXATE NEXGEN (CAP), IBLIAS (CAP), KOGENATE (CAP), KOVALTRY (CAP); turoctocog alfa – NOVOEIGHT (CAP); simoctocog alfa – NUWIQ (CAP); susoctocog alfa – OBIZUR (CAP) - EMEA/H/A-31/1448

Applicant(s): Baxter AG (Advate), Bayer Pharma AG (Helixate Nexgen, Iblias, Kogenate, Kovaltry), CSL Behring GmbH (Voncento), Novo Nordisk A/S (NovoEight), Octapharma AB (Nuwiq), Pfizer Limited (Refacto AF), Swedish Orphan Biovitrum AB (publ) (Elocta), Baxalta Innovations GmbH (Obizur), various

PRAC Rapporteur: Jan Neuhauser; PRAC Co-rapporteur: Ghania Chamouni

Scope: Re-examination procedure under Article 32 of Directive 2001/83/EC of the 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

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Amlodipine (NAP); rifampicin (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of drug interaction between amlodipine and rifampicin leading to reduced antihypertensive effect of amlodipine

Action: For adoption of PRAC recommendation

EPITT 18933 – New signal

Lead Member State(s): BG, DK

4.1.2. Cefalexin[4] (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

[3] 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

[4] First-generation cephalosporin

Scope: Signal of acute generalised exanthematous pustulosis (AGEP)

Action: For adoption of PRAC recommendation

EPITT 18911 – New signal

Lead Member State(s): ES

4.1.3. Dexmedetomidine – DEXDOR (CAP)

Applicant(s): Orion Corporation

PRAC Rapporteur: Julie Williams

Scope: Signal of polyuria

Action: For adoption of PRAC recommendation

EPITT 18926 – New signal

Lead Member State(s): UK

4.1.4. Dulaglutide – TRULICITY (CAP)

Applicant(s): Eli Lilly Nederland B.V.

PRAC Rapporteur: Carmela Macchiarulo

Scope: Signal of gastrointestinal stenosis and obstruction

Action: For adoption of PRAC recommendation

EPITT 18931– New signal

Lead Member State(s): IT

4.1.5. Hydroxycarbamide – SIKLOS (CAP), NAP

Applicant(s): Addmedica, various

PRAC Rapporteur: Laurence de Fays

Scope: Signal of cutaneous lupus erythematosus

Action: For adoption of PRAC recommendation

EPITT 18939 – New signal

Lead Member State(s): BE

4.1.6. Ipilimumab – YERVOY (CAP)

Applicant(s): Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Signal of histiocytosis haematophagic

Action: For adoption of PRAC recommendation

EPITT 18929 – New signal

Lead Member State(s): NL

4.1.7. Filgrastim - ACCOFIL (CAP), FILGRASTIM HEXAL (CAP), GRASTOFIL (CAP), NIVESTIM (CAP), RATIOGRASTIM (CAP), TEVAGRASTIM (CAP), ZARZIO (CAP), NAP; lenograstim (NAP); lipegfilgrastim – LONQUEX (CAP); pegfilgrastim – NEULASTA (CAP), RISTEMPA (CAP)

Applicant(s): Accord Healthcare Limited (Accofil), Amgen Europe B.V. (Neulasta, Ristempa), Hexal AG (Filgrastim Hexal), Apotex Europe BV (Grastofil), Hospira UK Limited (Nivestim), Ratiopharm GmbH (Ratiograstim), Sicor Biotech UAB (Lonquex), Teva GmbH, Sandoz GmbH (Tevagrastim), various

PRAC Rapporteur: To be appointed

Scope: Signal of aortitis

Action: For adoption of PRAC recommendation

EPITT 18940 – New signal

Lead Member State(s): FI, FR, UK

4.1.8. Pemetrexed – ALIMTA (CAP)

Applicant(s): Eli Lilly Nederland B.V.

PRAC Rapporteur: Ghania Chamouni

Scope: Signal of nephrogenic diabetes insipidus

Action: For adoption of PRAC recommendation

EPITT 18930 – New signal

Lead Member State(s): FR

4.1.9. Rivaroxaban – XARELTO (CAP); Azithromycin (NAP); clarithromycin (NAP); dirithromycin (NAP); erythromycin (NAP); flurithromycin (NAP); josamycin (NAP); midecamycin (NAP); miocamycin (NAP); oleandomycin (NAP); rokitamycin (NAP); roxithromycin (NAP); solithromycin (NAP); spiramycin (NAP); telithromycin – KETEK (CAP); troleandomycin (NAP)

Applicant(s): Aventis Pharma S.A. (Ketek), Bayer AG (Xarelto), various

PRAC Rapporteur: To be appointed

Scope: Signal of increased risk of bleeding following drug interaction between rivaroxaban and macrolide antibiotics

Action: For adoption of PRAC recommendation

EPITT 18934 – New signal

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

4.2. New signals detected from other sources

4.2.1. Azithromycin (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of increased rate of relapses of haematological malignancies and mortality in hematopoietic stem cell transplantation (HSCT) patients with azithromycin

Action: For adoption of PRAC recommendation

EPITT 18907 – New signal

Lead Member State(s): FI

4.2.2. Doxycycline (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of doxycycline induced Jarisch-Herxheimer reaction

Action: For adoption of PRAC recommendation

EPITT 18937 – New signal

Lead Member State(s): DE, UK

4.2.3. Megestrol (NAP); Vitamin K antagonists: acenocoumarol (NAP); fluindione (NAP); phenindione (NAP); phenprocoumon (NAP); warfarin (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of drug interaction leading to elevated international normalised ratio (INR)/haemorrhage with megestrol and vitamin K antagonists

Action: For adoption of PRAC recommendation

EPITT 18910 – New signal

Lead Member State(s): BG, IE

4.3. Signals follow-up and prioritisation

4.3.1. Azithromycin (NAP); tobramycin[5] – TOBI PODHALER (CAP) - EMEA/H/C/002155/SDA/032, VANTOBRA (CAP) - EMEA/H/C/002633/SDA/002; NAP

Applicant(s): Novartis Europharm Ltd (Tobi Podhaler), Pari Pharma GmbH (Vantobra); various

[5] For inhalation use only

PRAC Rapporteur: Menno van der Elst

Scope: Signal of possible interaction between tobramycin and azithromycin leading to lower effectiveness of tobramycin

Action: For adoption of PRAC recommendation

EPITT 18855 – Follow-up to April 2017

4.3.2. Meningococcal group B vaccine (rDNA, component, adsorbed) - BEXSERO (CAP) - EMEA/H/C/002333/SDA/025

Applicant(s): GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: Signal of arthritis and synovitis

Action: For adoption of PRAC recommendation

EPITT 18764 – Follow-up to April 2017

4.3.3. Mesalazine (NAP)

Applicant(s): various

PRAC Rapporteur: Patrick Batty

Scope: Signal of risk of photosensitivity reactions

Action: For adoption of PRAC recommendation

EPITT 18869 – Follow-up to April 2017

4.3.4. Methotrexate - JYLAMVO (CAP), NORDIMET (CAP) - EMEA/H/C/003983/SDA/002; NAP

Applicant(s): Nordic Group B.V. (Nordimet); Therakind Limited (Jylamvo); various

PRAC Rapporteur: Martin Huber

Scope: Signal of pulmonary alveolar haemorrhage

Action: For adoption of PRAC recommendation

EPITT 18850 – Follow-up to April 2017

4.3.5. Pramipexole – MIRAPEXIN (CAP) - EMEA/H/C/000134/SDA/040, SIFROL (CAP) - EMEA/H/C/000133/SDA/042, OPRYMEA (CAP) - EMEA/H/C/000941/SDA/017, PRAMIPEXOLE TEVA (CAP) - EMEA/H/C/000940/SDA/010, PRAMIPEXOLE ACCORD (CAP) - EMEA/H/C/002291/SDA/008; NAP

Applicant(s): Boehringer Ingelheim International GmbH (Mirapexin, Sifrol), Krka, d.d., Novo mesto (Oprymea), Teva B.V. (Pramipexole Teva), Accord Healthcare Ltd (Pramipexole Accord); various

PRAC Rapporteur: Doris Stenver

Scope: Signal of dystonia

Action: For adoption of PRAC recommendation

EPITT 18866 – Follow-up to April 2017

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Anagrelide - EMEA/H/C/004585

Scope: Treatment and reduction of elevated platelet counts in patients at essential thrombocythaemia risk

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

5.1.2. Benralizumab – EMEA/H/C/004433

Scope: Treatment of severe asthma with an eosinophilic phenotype

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

5.1.3. Bevacizumab - EMEA/H/C/004360

Scope: Treatment of breast cancer, non-small cell lung cancer, renal cell cancer, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer, platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer

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

5.1.4. Bevacizumab - EMEA/H/C/004728

Scope: Treatment of metastatic breast cancer, unresectable advanced, metastatic or recurrent non-small cell lung cancer, unresectable advanced metastatic or recurrent non-squamous non-small cell lung cancer, advanced and/or metastatic renal cell cancer, advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer, platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer

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

5.1.5. Budesonide - EMEA/H/C/004655, Orphan

Applicant: Dr. Falk Pharma GmbH

Scope: Treatment of eosinophilic esophagitis (EoE)

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

5.1.6. Ciclosporin - EMEA/H/C/004229

Scope: Treatment of moderate dry eye disease in adults

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

5.1.7. D-biotin - EMEA/H/C/004153

Scope: Treatment of progressive multiple sclerosis (primary or secondary)

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

5.1.8. Darunavir - EMEA/H/C/004273

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

5.1.9. Fulvestrant - EMEA/H/C/004649

Scope: Treatment of breast cancer

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

5.1.10. Human fibrinogen, human thrombin - EMEA/H/C/004446

Scope: Treatment of haemostasis

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

5.1.11. Imatinib - EMEA/H/C/004748

Scope: Treatment of newly diagnosed and chronic Philadelphia chromosome (bcr-abl) positive (Ph+) chronic myeloid leukaemia (CML), gastrointestinal stromal tumours (GIST), unresectable dermatofibrosarcoma protuberans (DFSP) and recurrent and/or metastatic DFSP

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

5.1.12. Padeliporfin - EMEA/H/C/004182

Scope: Treatment of prostate cancer

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

5.1.13. Plitidepsin - EMEA/H/C/004354, Orphan

Applicant: Pharma Mar, S.A.

Scope: Treatment of multiple myeloma

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

5.1.14. Rucaparib - EMEA/H/C/004272, Orphan

Applicant: Clovis Oncology UK Ltd

Scope: Treatment of ovarian cancer

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

5.1.15. Semaglutide - EMEA/H/C/004174

Scope: Treatment to improve glycaemic control in adults with type 2 diabetes mellitus (T2DM) and to prevent cardiovascular events

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

5.1.16. Shingles herpes zoster vaccine, live - EMEA/H/C/004336

Scope: Treatment and prevention of herpes zoster (HZ) and HZ-related complications

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

5.1.17. Velmanase alfa - EMEA/H/C/003922, Orphan

Applicant: Chiesi Farmaceutici S.p.A.

Scope: Treatment for long-term enzyme replacement therapy in patients with alpha-mannosidosis

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

5.1.18. Viable T-cells - EMEA/H/C/002397, Orphan

Applicant: Kiadis Pharma Netherlands B.V., ATMP[6]

Scope: Adjunctive treatment in haematopoietic stem cell transplantation (HSCT) for a malignant disease

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. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0030

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: Update of the RMP (version 7.0) in order to reflect changes requested in the conclusion of the PSUSA procedure (PSUSA/00010077/201603) finalised in November 2016

[6] Advanced therapy medicinal product

and LEG reviewing cases of pancreatitis as well as the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442). In addition, the RMP is updated to reflect labelling changes resulting from a variation procedure to add information on fatal diabetic ketoacidosis (DKA) cases to the existing DKA warning and following the referral procedure under Article 31 of Directive 2001/83/EC reviewing metformin-containing medicines completed in October 2016 (EMEA/H/A-31/1432)

Action: For adoption of PRAC Assessment Report

5.2.2. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/II/0031

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: Update of the RMP (version 7.0) in order to reflect changes requested in the outcome of the PSUSA procedure (PSUSA/00010077/201603) finalised in November 2016 and LEG reviewing cases of pancreatitis as well as the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442). In addition, the RMP is updated to reflect labelling changes resulting from a variation procedure to add information on fatal diabetic ketoacidosis (DKA) cases to the existing DKA warning and following the referral procedure under Article 31 of Directive 2001/83/EC reviewing metformin-containing medicines completed in October 2016 (EMEA/H/A-31/1432)

Action: For adoption of PRAC Assessment Report

5.2.3. Denosumab - XGEVA (CAP) - EMEA/H/C/002173/II/0054

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of the RMP (version 25) in order to reflect that cataract is no longer considered as a potential risk associated with denosumab therapy, following the recent completion of study 20080560 (a phase 3, randomized, double-blind, placebo-controlled study to evaluate new or worsening lens opacifications in subjects with non-metastatic prostate cancer receiving denosumab for bone loss due to androgen deprivation therapy) where results showed no difference between the risk of developing cataracts in the denosumab and placebo groups

Action: For adoption of PRAC Assessment Report

5.2.4. 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

5.2.5. Insulin human - ACTRAPHANE (CAP) - EMEA/H/C/000427/WS1197/0072; ACTRAPID (CAP) - EMEA/H/C/000424/WS1197/0066; INSULATARD (CAP) - EMEA/H/C/000441/WS1197/0069; MIXTARD (CAP) - EMEA/H/C/000428/WS1197/0073; PROTAPHANE (CAP) - EMEA/H/C/000442/WS1197/0068

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Doris Stenver

Scope: Update of the RMP (version 2.1) in line with the Guidance on format of the RMP in the EU (revision 2). Moreover, significant changes to the safety specification are proposed with this RMP update as some risks are now considered fully characterised and appropriately managed: 1) removal of the following important identified risks: hypoglycaemia, anaphylactic reactions, peripheral neuropathy, refraction disorders, lipodystrophy, urticaria, rash, oedema and diabetic retinopathy; 2) removal of the following important potential risks: immunogenicity, allergic reactions and lack of efficacy related to the new NN729 manufacturing process; and 3) Removal of the following missing information: special patient groups

Action: For adoption of PRAC Assessment Report

5.2.6. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0049

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Update of the RMP (version 17) in order to amend the study objectives and milestones for two studies: 1) study CA184332 (a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab (Yervoy) as first line therapy in a community setting, a category 3 study in the RMP (MEA 029): to submit the final study report with 2-years of follow-up); 2) study CA184338 (a multi-site retrospective observational study of US patients with unresectable or metastatic melanoma receiving ipilimumab (Yervoy) as first line therapy, a category 3 study in the RMP (MEA 030): to submit the final study report with 4-years of follow-up)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Albiglutide - EPERZAN (CAP) - EMEA/H/C/002735/II/0033

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Julie Williams

Scope: Update of the Package Leaflet in order to amend the layout and content of the instructions for use (IFU) for Eperzan (albiglutide). In addition, the RMP (version 8) is updated to implement additional pharmacovigilance and risk minimisation activities addressing the safety concern of 'medication errors/device issue potentially leading to lack of efficacy or inadequate diabetes control' and to add a PASS to investigate the effectiveness of the new IFU

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

5.3.2. Aliskiren - RASILEZ (CAP) - EMEA/H/C/000780/WS1026/0110; aliskiren, hydrochlorothiazide - RASILEZ HCT (CAP) - EMEA/H/C/000964/WS1026/0080

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Carmela Macchiarulo

Scope: Update of section 5.1 of the SmPC in order to reflect the results of study SPP100F2301 (ATMOSPHERE): a multicentre, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (New York Heart Association (NYHA) Class II-IV). The RMP (version 13) is updated accordingly

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

5.3.3. Atazanavir, atazanavir sulfate - REYATAZ (CAP) - EMEA/H/C/000494/II/0111

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Caroline Laborde

Scope: Update of sections 4.4 and 4.8 of the SmPC to add a warning on chronic kidney disease (CKD) observed in human immunodeficiency virus (HIV) infected patients during treatment with atazanavir (with or without ritonavir). This update is based on a review of the MAH safety database, a cohort study of patients with laboratory values from a large US administrative claims database and a review of published scientific literature. The Package Leaflet and the RMP (version 12.0) are updated accordingly

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

5.3.4. Avanafil - SPEDRA (CAP) - EMEA/H/C/002581/II/0027/G

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Grouped variation consisting of: 1) update of section 4.4 to reflect the results of clinical study TA-402: a double-blind, randomized, placebo-controlled, single-dose, parallel study to assess the effects of avanafil on multiple parameters of vision, including, but not limited to visual acuity, intraocular pressure, pupillometry, and colour vision discrimination, in healthy male subjects; 2) update of section 4.6 of the SmPC in order to reflect the results of clinical study TA-401: a randomized, double-blind, placebo-controlled, parallel group,

multicentre clinical trial of the effect of avanafil on spermatogenesis in healthy adult males and adult males with mild erectile dysfunction. The Package Leaflet and the RMP (version 5.1) are updated accordingly. In addition, the MAH took the opportunity to make an editorial correction on the approved SmPC by adding the missing adverse reaction epistaxis from the tabulated list of adverse reactions reported in section 4.8. Additionally, the MAH took the opportunity to align the information of Package Leaflet section 3 to SmPC section 4.2

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

5.3.5. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0002

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: Update of sections 4.5 and 5.2 of the SmPC, based on the final study report of an in vitro study investigating the inhibitory effect of baricitinib on the organic anion transporter 2 (OAT2) in fulfilment of MEA 001. The RMP (version 3.0) is updated accordingly

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

5.3.6. Belatacept - NULOJIX (CAP) - EMEA/H/C/002098/II/0045

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on the risk of venous thrombosis of the renal allograft when anti-thymocyte globulin (ATG) and belatacept are coadministered (at the same or nearly the same time) in patients with other predisposing risk factors for thrombosis. The update is based on a review of the potential increased risk for allograft thrombosis with belatacept given in close temporal relation to anti-thymocyte globulin (rabbit), as requested in the conclusion of the last PSUSA procedure (PSUSA/00000311/201606) finalised in January 2017. In addition, the MAH took the opportunity to update section 6 of the SmPC and the 'information for healthcare professionals (HCPs)' in the Package Leaflet (PL) with additional safety instructions for the co-administration of belatacept with anti-thymocyte globulin (rabbit). This variation fulfils LEG 021. The RMP (version 14) is updated accordingly

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

5.3.7. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/X/0046/G

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped application consisting of: 1) line extension to introduce a new pharmaceutical form (solution for injection), a new strength (200 mg) and a new route of administration (subcutaneous use); 2) update of sections 4.2, 4.8, 5.1 and 5.2 for the authorised presentations (Benlysta powder for concentrate for solution for infusion) as a consequence of the data package submitted to support the new proposed solution for injection subcutaneous. The RMP (version 21) is updated accordingly

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

5.3.8. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0049, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with data from study C25002: a phase 1/2, non-randomized single arm study of brentuximab vedotin (SGN-35) in paediatric patients with relapsed or refractory systemic anaplastic large cell lymphoma or Hodgkin lymphoma (listed in the agreed paediatric investigation plan (PIP) covering the conditions of Hodgkin lymphoma and anaplastic large cell lymphoma for Adcetris (EMEA-000980-PIP01-10-M04)). The RMP (version 11.0) is updated accordingly

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

5.3.9. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/II/0002/G

Applicant: Ipsen Pharma

PRAC Rapporteur: Sabine Straus

Scope: Update of section 5.1 of the SmPC to reflect the final study results from clinical study XL184-308: a phase 3, randomized, controlled study of cabozantinib (XL184) *vs* everolimus in subjects with metastatic renal cell carcinoma that has progressed after prior vascular endothelial growth factor (VEGFR) tyrosine kinase inhibitor therapy, to fulfil the condition to the marketing authorisation listed as a post-authorisation efficacy study (PAES) in Annex II. The RMP (version 2.0) is updated accordingly

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

5.3.10. Certolizumab pegol - CIMZIA (CAP) - EMEA/H/C/001037/II/0060

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to update the information on pregnancy and lactation based on two pharmacokinetic (PK) studies evaluating the transfer of Cimzia into breastmilk (UP0016 study: a multicentre, post-marketing study to evaluate the concentration of certolizumab pegol in the breast milk of mothers receiving treatment with Cimzia phase 1B (clinical pharmacology) study) and via the placenta (UP0017 study: a multicentre post-marketing study to evaluate the placental transfer of certolizumab pegol in pregnant women receiving treatment with Cimzia). The Package Leaflet and the RMP (version 12) are updated accordingly

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

5.3.11. Daptomycin - CUBICIN (CAP) - EMEA/H/C/000637/II/0061

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Julie Williams

Scope: Extension of indication to extend the *S. aureus* bacteraemia indication to include paediatric patients 1 to 17 years of age. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet, Labelling and the RMP (version 10.0) are updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template (version 10) and to combine the SmPCs for both strengths (350 and 500 mg)

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

5.3.12. Dasatinib - SPRYCEL (CAP) - EMEA/H/C/000709/X/0056/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Doris Stenver

Scope: Grouped application consisting of: 1) extension application (line extension) to introduce a new pharmaceutical form (powder for oral suspension) associated with a new strength (10 mg/ml); 2) extension of indication to include the treatment of children and adolescents aged 1 year to 18 years with Ph+ chronic phase in chronic myeloid leukaemia (CML). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated in order to add the new indication and its relevant posology, to add a warning on effects on growth and development in the paediatric population and to update the safety information. The Package Leaflet and the RMP (version 15.0) are updated accordingly

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

5.3.13. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/X/0054

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: Extension application (line extension) for a new pharmaceutical form (Exjade 90, 180 and 360 mg granules). The RMP (version 15.0) is updated accordingly

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

5.3.14. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0069

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC in order to update the safety information as cataract is no longer considered as a potential risk and/or adverse reaction associated with denosumab therapy following the completion of study 20080560: a phase 3, multicentre, randomized, double-blind, placebo-controlled study in men to evaluate new or worsening lens opacifications in subjects with non-metastatic prostate cancer receiving denosumab for bone loss due to androgen deprivation therapy and progression study using a slit-lamp-based evaluation system (lens opacities classification system III (LOCS III)). The Package Leaflet is updated accordingly. In addition, the RMP (version 20.0) is updated to remove the important potential risk of 'cataract in men with prostate cancer receiving androgen deprivation therapy'

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

5.3.15. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/II/0098, Orphan

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.6 and 5.3 of the SmPC in order to update the safety information related to pregnancy, lactation and fertility following the review of data in PSUR#13 and PSUR#14. Annex II, the Package Leaflet and the RMP (version 17) are updated accordingly

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

5.3.16. Eliglustat - CERDELGA (CAP) - EMEA/H/C/003724/II/0013, Orphan

Applicant: Genzyme Europe BV

PRAC Rapporteur: Dolores Montero Corominas

Scope: Update of section 4.8 of the SmPC in order to amend the safety information based on the analysis of adverse events from the following clinical trials: GZGD00304 (a phase 2, open-Label, multicentre study evaluating the efficacy, safety and pharmacokinetics of eliglustat (Genz-112638) in Gaucher type 1 patients), GZGD02507 (a phase 3, randomized, double-blind, placebo-controlled, multicentre study confirming the efficacy and safety of Genz-112638 in patients with Gaucher disease type 1 (ENGAGE)), GZGD02607 (a phase 3, randomized, multicentre, multinational, open-label, active comparator study to evaluate the efficacy and safety of Genz-112638 in patients with Gaucher disease type 1 who have reached therapeutic goals with enzyme replacement therapy (ENCORE)) and GZGD03109 (a phase 3, randomized, multicentre, multinational, double-blind study to evaluate the efficacy, safety and pharmacokinetics of once daily versus twice daily dosing of Genz-112638 in patients with Gaucher disease type 1 who have demonstrated clinical stability on a twice daily dose of Genz-112638 (EDGE)) to address post-authorisation MEA 011.1 included in the current approved RMP. The Labelling is updated in order to reflect the instructions for use for the sleeve of the intermediate packaging of the single blister. The RMP (version 4.0) is updated accordingly

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

5.3.17. 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

5.3.18. 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

5.3.19. Evolocumab - REPATHA (CAP) - EMEA/H/C/003766/II/0017/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped variation consisting of an extension of indication to include the reduction of atherosclerotic cardiovascular disease risk in adults with high cardiovascular risk based on the results from study 20110118: a double-blind, randomized, placebo-controlled, multicentre study assessing the impact of additional low-density lipoprotein (LDL)-cholesterol reduction on major cardiovascular events when evolocumab (AMG 145) is used in combination with statin therapy in patients with clinically evident cardiovascular disease (category 3 pharmacovigilance activity in the RMP, MEA 004). As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update section 5.1 of the SmPC to include important mechanistic information for healthcare professionals based on study 20120153 (a double-blind, randomized, multicentre, placebo-controlled, parallel group study to determine the effects of evolocumab (AMG 145) treatment on stherosclerotic disease burden as measured by intravascular ultrasound in subjects undergoing coronary catheterisation, a category 3 pharmacovigilance activity, MEA 006). The RMP (version 2.0) is also updated in order to add two category 3 studies in the RMP (study 20160250: a multicentre, open-label, single-arm, extension study to assess long-term safety of evolocumab therapy in subjects with clinically evident cardiovascular disease in selected European countries and study 20150338: a multicentre, controlled, open-label extension (OLE) study to assess the long-term safety and efficacy of evolocumab (AMG 145)) as well as to update the milestones of five category 3 studies (study 20110110: multicentre, controlled, OLE study to assess the long-term safety and efficacy of evolocumab; study 20110271: multicentre, open-label study to assess the long-term safety, tolerability, and efficacy of evolocumab on low-density lipoprotein cholesterol (LDL-C) in subjects with

severe familial hypercholesterolaemia (including homozygous familial hypercholesterolemia (HoFH)); study 20120138: a multicentre, controlled, OLE study to assess the long-term safety and efficacy of evolocumab; study 20130286: a double blind, randomized, placebo controlled, multicentre study to evaluate safety, tolerability, and efficacy on LDL-C of evolocumab in human immunodeficiency virus (HIV) positive patients with hyperlipidemia and mixed dyslipidemia; and study 20130295: a multicentre, OLE study to assess long-term safety and efficacy of evolocumab therapy in patients with clinically evident cardiovascular disease (FOURIER-OLE))

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

5.3.20. Exenatide - BYDUREON (CAP) - EMEA/H/C/002020/II/0045

Applicant: AstraZeneca AB

PRAC Rapporteur: Qun-Ying Yue

Scope: Extension of indication to include treatment in combination with basal insulin for Bydureon. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated based on study D5553C00002: a multicentre, randomized, double-blind, placebo-controlled, parallel group, phase 3 study to evaluate the safety and efficacy of once weekly exenatide therapy added to titrated basal insulin glargine compared to placebo added to titrated basal insulin glargine in patients with type 2 diabetes mellitus (T2DM) who have inadequate glycemic control on basal insulin glargine with or without metformin (Duration 7). The Package Leaflet and the RMP (version 25) are updated accordingly. In addition, the MAH took the opportunity to make minor corrections in sections 4.8 and 5.1 of the SmPC

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

5.3.21. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0047

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to reflect the results of preclinical study MRPO-2015-PKM-005: 'a pharmacokinetic study of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol' and clinical study REP-POPPK-MRP-2015-PKM-005: 'a population pharmacokinetic analysis from study titled pharmacokinetic of azathioprine in the rat after one-week daily oral treatment at three different dosages and with the concomitant oral administration of febuxostat or allopurinol', investigating the drug-drug interaction with azathioprine when co-administered with febuxostat. The RMP (version 6.0) is updated accordingly. In addition, the MAH took the opportunity to correct typing errors 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

5.3.22. 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

5.3.23. 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

5.3.24. Idarucizumab - PRAXBIND (CAP) - EMEA/H/C/003986/II/0007

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to reflect the final results from study 1321.3, the RE-VERSE-AD study (re-versal effects of idarucizumab on active dabigatran): a phase 3 case series clinical study of the reversal of the anticoagulant effects of dabigatran by intravenous administration of 5.0 g idarucizumab (BI 655075) in patients treated with dabigatran etexilate who have uncontrolled bleeding or require emergency surgery or procedures - RMP category 3 study (MEA 001)). The RMP (version 3.0) is updated accordingly. In addition, the MAH took the opportunity to update the immunogenicity section in 5.1 of SmPC and to bring the product information (PI) 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. 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

5.3.26. Insulin degludec - TRESIBA (CAP) - EMEA/H/C/002498/II/0028

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Qun-Ying Yue

Scope: Update of section 5.1 of the SmPC based on new clinical data from a cardiovascular outcome trial EX1250-4080 (DEVOTE): a randomised, double-blind and event-driven clinical study with a median duration of 2 years comparing the cardiovascular safety of Tresiba (insulin degludec) versus insulin glargine (100 units/mL) in patients with type 2 diabetes mellitus (T2DM) at high risk of cardiovascular events. The RMP (version 8) is updated accordingly

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

5.3.27. Insulin glargine - ABASAGLAR (CAP) - EMEA/H/C/002835/II/0014

Applicant: Eli Lilly Regional Operations GmbH

PRAC Rapporteur: Carmela Macchiarulo

Scope: Submission of the final report from study I4L-MC-ABER (ABER): 'a prospective, randomized, open-label comparison of long-acting basal insulin analog Abasaglar (LY2963016) to the reference product (Lantus (insulin glargine)) in adult patients with type 2 diabetes mellitus (T2DM): the ELEMENT 5 study' conducted in non-European countries. This study replaces the cancelled studies initially planned to be conducted in China and other countries. The RMP (version 1.6) is updated accordingly

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

5.3.28. 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 worksharing 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

5.3.29. 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

5.3.30. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0044

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Extension of indication to include the treatment of advanced (unresectable or metastatic) melanoma in children and adolescents 12 years of age and older. As a consequence sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and the RMP (version 15) are updated accordingly

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

5.3.31. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/II/0047/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sabine Straus

Scope: Grouped variations consisting of: 1) update of section 4.4 to revise the current warning on concurrent administration with vemurafenib to enhance awareness on the potential of hypersensitivity reactions when ipilimumab is used sequentially with vemurafenib as requested by the PRAC following the assessment of PSUSA/00009200/201603 completed in October 2016; 2) update of section 4.8 of the SmPC to amend the frequency of the adverse drug reaction (ADR) 'Vogt-Konyanagi-Haranda syndrome' from 'not know' to 'very rare'. The RMP (version 16) is updated accordingly. In addition, the MAH took the opportunity to implement some editorial changes to sections 4.2 and 4.4 of the SmPC to update the dose modification information for hepatotoxicity management guidelines in line with the National Cancer Institute (NCI) common terminology criteria for adverse events (CTCAE) recommendations (version 4)

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

5.3.32. Ivabradine - CORLENTOR (CAP) - EMEA/H/C/000598/WS1180/0047; IVABRADINE ANPHARM (CAP) - EMEA/H/C/004187/WS1180/0006; PROCORALAN (CAP) - EMEA/H/C/000597/WS1180/0046

Applicants: Anpharm Przedsiebiorstwo Farmaceutyczne (Ivabradine Anpharm), Les

Laboratoires Servier (Corlentor, Procorolan)

PRAC Rapporteur: Menno van der Elst

Scope: Update of section 4.8 of the SmPC with new adverse drug reactions (ADRs): ventricular tachycardia, ventricular fibrillation and Torsade de Pointes. The Package Leaflet and the RMP (version 6) are updated accordingly. In addition, the MAH took the opportunity to align the Product Information 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

5.3.33. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/II/0009

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include alone or in combination with conventional disease-modifying anti-rheumatic drug (cDMARD) the treatment of active psoriatic arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more DMARD therapies. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated to reflect the new safety and efficacy information. The Package Leaflet and the RMP (version 5) are updated accordingly

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

5.3.34. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/II/0044/G, Orphan

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Update of section 4.4 of the SmPC in order to amend the warning regarding antibody response to injected insulin-like growth factor 1 (IGF-1). The RMP (version 9) is updated accordingly, including changes to the educational materials and changes to the instructions for antibody testing

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

5.3.35. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0017

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from phase 1 study NaltrexBuprop-1001 (TQT) to evaluate the potential effect of naltrexone/bupropion extended-release combination on cardiac repolarisation in healthy subjects. The RMP (version 10) is updated to include study NaltrexBuprop-1001 and additional studies recently completed (NB-CVOT (a multicentre, randomized, double-blind, placebo-controlled study assessing the occurrence of major adverse cardiovascular events (MACE) in overweight and obese subjects with cardiovascular risk factors receiving naltrexone sustained release (SR)/bupropion SR), NaltrexBuprop-4001 (a multicentre, randomized, double-blind, placebo-controlled, phase 4 study to assess the effect of naltrexone hydrochloride and bupropion hydrochloride extended release (ER)

combination on the occurrence of MACE in overweight and obese subjects with cardiovascular disease), NaltrexBuprop-1004 (a phase 1, open-label, sequential design study to evaluate the potential effect of multiple oral doses of ER combination of naltrexone and bupropion on the pharmacokinetics (PK) of a single oral dose of metformin in healthy subjects) and NB-404 (a multicentre, randomized, open-label, controlled, method-of-use study assessing the effect of naltrexone SR/bupropion SR on body weight and cardiovascular risk factors in overweight and obese subjects (the Ignite study)). The MAH also took the opportunity to update the RMP to include references to the PASS protocols currently under discussion at PRAC

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

5.3.36. 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

5.3.37. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0036/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce new dosing regimens and schedule; 2) update of sections 4.2, 5.1, 5.2 and 6.6 of the SmPC in order to introduce a change in the infusion time from 60 minutes to 30 minutes. These changes are based on interim results from study CA209153: a phase IIIb/IV safety trial of nivolumab in subjects with advanced or metastatic non-small cell lung cancer (NSCLC) who have progressed during or after receiving at least one prior systemic regimen. The Package Leaflet and the RMP (version 10.0) are updated accordingly

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

5.3.38. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0038

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.8 of the SmPC with longer follow-up for subjects proceeding to allogeneic transplant following nivolumab treatment and update of section 5.1 of the SmPC with efficacy data from longer follow-up based on final results from study CA209205 (listed as a post-authorisation efficacy study (PAES) in Annex II): a phase 2, non-comparative,

multi-cohort, single-arm, open-label study of nivolumab (BMS-936558) in classical Hodgkin lymphoma (cHL) subjects after failure of autologous stem cell transplant (ASCT). Annex II is updated to remove the commitment. The RMP (version 7.5) is updated accordingly

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

5.3.39. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/X/0016/G, Orphan

Applicant: AstraZeneca AB

PRAC Rapporteur: Carmela Macchiarulo

Scope: Grouped application consisting of: 1) extension application (line extension) to add a new pharmaceutical form (film-coated tablets) associated with a new strength (100 mg and 150 mg); 2) Alignment of the Product Information (PI) for the approved capsule presentation with the PI proposed for the tablet presentation. The RMP (version 15) is updated accordingly

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

5.3.40. Palbociclib - IBRANCE (CAP) - EMEA/H/C/003853/II/0007

Applicant: Pfizer Limited

PRAC Rapporteur: Torbjorn Callreus

Scope: Update of sections 4.2, 4.4 and 5.2 of the SmPC to reflect the results of study A5481013: a phase 1, open-label, single dose 75 mg palbociclib), parallel-cohort study to evaluate the pharmacokinetics of palbociclib in subjects with impaired hepatic function, and study A5481014: a phase 1, open-label, single dose (125 mg palbociclib), parallel-group study to evaluate the pharmacokinetics of palbociclib in subjects with impaired renal function. The RMP (version 1.4) is updated accordingly

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

5.3.41. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/II/0093/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Patrick Batty

Scope: Grouped variation consisting of: 1) addition of a new device: the on-body injector (Onpro kit) to be used with Neulasta, 6mg solution for injection, pre-filled syringe; 2) change the fill volume for Neulasta, 6 mg, solution for injection pre-filled syringe co-packed with the on-body injector (Onpro kit). In addition, the MAH took the opportunity to introduce editorial changes to module 3.2.P.2.4 on container closure system. As a consequence, sections 3, 4.2, 5.1, 6.4, 6.5, 6.6 and 8 of the SmPC are updated. The Labelling, Package Leaflet and the RMP (version 4.2) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to include some editorial changes and correct some typos throughout the product information. Finally, the MAH brought 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

5.3.42. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0004/G, Orphan

Applicant: Bioprojet Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations to update sections 4.4, 4.5, 4.6 and 5.2 of the SmPC based on the final clinical study report (CSR) of study P15-02 assessing the mass balance recovery, metabolite profile and metabolite identification of [^{14}C] pitolisant at steady state conditions, in healthy cytochrome P450 2D6 (CYP2D6) phenotyped subjects, study P14-07 evaluating the pharmacokinetic interaction of pitolisant with sodium oxybate and modafinil in healthy male volunteers and study P15-15 evaluating the pharmacokinetic (PK) interaction of pitolisant with cytochrome P450 3A4 (CYP3A4) substrates (midazolam), cytochrome P450 2B6 (CYP2B6) substrates (bupropion), UDP-Glucuronosyltransferase-2B7 (UGT2B7) inhibitors (probenecide)) in fulfilment of PAM (MEA 02, 03 and 04). The Package Leaflet and the RMP (version 5.0) are updated accordingly. In addition, the MAH took the opportunity to make minor editorial change in section 4.8 of the SmPC

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

5.3.43. Plerixafor - MOZOBIL (CAP) - EMEA/H/C/001030/II/0032, Orphan

Applicant: Genzyme Europe BV

PRAC Rapporteur: Sabine Straus

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to reflect the results of the completed study MSC12830 (MOZ11809): a phase 4, multicentre, randomized, comparator trial evaluating the standard weight-based dose (0.24 mg/kg) compared to a fixed dose (20 mg) of plerixafor injection in combination with granulocyte-colony stimulating factor (G-CSF) to mobilize and collect ≥5 x 10^6 $CD34^+$ cells/kg in ≤4 days and to evaluate the difference in total systemic exposure in patients with non-Hodgkin's lymphoma weighing ≤70 kg' listed as a category 3 study in the RMP. The Package Leaflet and the RMP (version 9.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

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

5.3.44. Rasagiline - AZILECT (CAP) - EMEA/H/C/000574/WS1168/0077; RASAGILINE RATIOPHARM (CAP) - EMEA/H/C/003957/WS1168/0010

Applicant: Teva B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.4, 4.7 and 4.8 to include a new warning on excessive daytime sleepiness and sudden sleep onset episodes as well as update of section 4.9 to remove 'dysphoria' as a symptom reported following overdose of rasagiline based on a company core data sheet (CCDS) update. The Package Leaflet and the RMP (version 2.0) are updated accordingly. In addition, the MAH took the opportunity to make editorial changes throughout the Product Information to correct the invented name for Rasagiline Ratiopharm in the Czech annexes and to bring the Product Information (PI) in line with the latest QRD template (version 10)

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

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

Applicant: Bayer 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 accordingly; 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, semi-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[7] 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

5.3.46. Romiplostim - NPLATE (CAP) - EMEA/H/C/000942/II/0060/G, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Grouped variation consisting of: 1) extension of indication to include the paediatric population for the use in the paediatric chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients from 1 year of age and older. As a consequence, sections 1, 2, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 6.3 6.5, 6.6 and 8 of the SmPC are updated accordingly. The RMP (version 18) is updated accordingly. Furthermore, the Product information is brought in line with the latest QRD template (version 10); 2) addition of a low-dose romiplostim 125 microgram vial presentation for powder for solution for injection (4 vials pack); 3) addition of a 1 vial pack size of a low-dose romiplostim 125 microgram presentation

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

5.3.47. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/X/0020

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application (line extension) to add new strengths of 2500 IU, 3000 IU, 4000 IU for Nuwiq, powder and solvent for solution for injection. The RMP (version 5.4) is updated accordingly

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

[7] Medical Dictionary for Regulatory Activities

5.3.48. Simoctocog alfa - NUWIQ (CAP) - EMEA/H/C/002813/II/0017/G

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variation consisting of an update of sections 4.2, 4.8 and 5.1 of the SmPC to reflect available data from previously untreated patients (PUP) based on the interim report of interventional GENA-05 study: an immunogenicity, efficacy and safety of treatment with human cell line-derived recombinant factor VIII (human-cl-rhFVIII) in previously untreated patients with severe haemophilia A. The Package Leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to update the Product Information throughout to bring it in line with the core Summary of Product Characteristics for human plasma-derived and recombinant coagulation factor VIII products (EMA/CHMP/BPWP/1619/1999 rev. 2) and with the latest QRD template (version 10). Moreover, the MAH proposed to combine the SmPC for all strengths and to update Annex A with detailed information on the packaging

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

5.3.49. Sitagliptin - JANUVIA (CAP) - EMEA/H/C/000722/WS1211/0059; RISTABEN (CAP) - EMEA/H/C/001234/WS1211/0051; TESAVEL (CAP) - EMEA/H/C/000910/WS1211/0059; XELEVIA (CAP) - EMEA/H/C/000762/WS1211/0063

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to modify the information on dosing, an existing warning and administration instructions, respectively for use of sitagliptin in patients with type 2 diabetes mellitus (T2DM) and renal impairment. The RMP (version 8) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet for Tesavel and to bring the Product Information in line with the latest QRD template (version 10). Minor editorial changes are also introduced in the Product Information

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

5.3.50. Sitagliptin, metformin hydrochloride - EFFICIB (CAP) - EMEA/H/C/000896/WS1212/0085/G; JANUMET (CAP) - EMEA/H/C/000861/WS1212/0085/G; RISTFOR (CAP) - EMEA/H/C/001235/WS1212/0072/G; VELMETIA (CAP) - EMEA/H/C/000862/WS1212/0088/G

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2. and 5.2 of the SmPC in order to modify the information on dosing, and administration instructions respectively for use of sitagliptin/metformin in patients with type 2 diabetes mellitus (T2DM) and moderate renal impairment. The RMP (version 8) is updated accordingly. In addition, section 4.5 of the SmPC is updated to include information on the concomitant use of ranolazine, vandetanib, dolutegravir and cimetidine. Furthermore, the MAH took the opportunity to update the list of local

representatives in the Package Leaflet for Efficib and to bring the product information (PI) in line with the latest QRD template (version 10). Minor editorial changes are also introduced in the Product Information

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Abatacept - ORENCIA (CAP) - PSUSA/00000013/201612

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Adalimumab - HUMIRA (CAP) - PSUSA/00000057/201612

Applicant: AbbVie Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Agomelatine - THYMANAX (CAP); VALDOXAN (CAP) - PSUSA/00000071/201702

Applicant: Servier (Ireland) Industries Ltd. (Thymanax), Les Laboratoires Servier (Valdoxan)

PRAC Rapporteur: Kristin Thorseng Kvande

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Asfotase alfa - STRENSIQ (CAP) - PSUSA/00010421/201701

Applicant: Alexion Europe SAS

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Asparaginase[8] - SPECTRILA (CAP) - PSUSA/00010445/201701

Applicant: Medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/201701

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Atazanavir, cobicistat - EVOTAZ (CAP) - PSUSA/00010404/201701 (with RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Axitinib - INLYTA (CAP) - PSUSA/00010022/201701

Applicant: Pfizer Limited

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Besilesomab - SCINTIMUN (CAP) - PSUSA/00000385/201701 (with RMP)

Applicant: Cis Bio International

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Birch bark extract - EPISALVAN (CAP) - PSUSA/00010446/201701

Applicant: Birken AG

PRAC Rapporteur: Zane Neikena

[8] Centrally authorised product only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Brimonidine[9] - MIRVASO (CAP) - PSUSA/00010093/201702 (with RMP)

Applicant: Galderma International

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Brivaracetam - BRIVIACT (CAP) - PSUSA/00010447/201701

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Carfilzomib - KYPROLIS (CAP) - PSUSA/00010448/201701

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Colistimethate sodium[10] - COLOBREATHE (CAP) - PSUSA/00009112/201702

Applicant: Teva B.V.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dapagliflozin, metformin - EBYMECT (CAP); XIGDUO (CAP) - PSUSA/00010294/201701 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Centrally authorised product only
[10] Dry inhalation powder only

6.1.16. Dasabuvir - EXVIERA (CAP) - PSUSA/00010363/201701

Applicant: AbbVie Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Dexamethasone[11] - OZURDEX (CAP) - PSUSA/00000985/201701 (with RMP)

Applicant: Allergan Pharmaceuticals Ireland

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Dolutegravir - TIVICAY (CAP); dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - PSUSA/00010075/201701

Applicant: ViiV Healthcare UK Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Elbasvir, grazoprevir - ZEPATIER (CAP) - PSUSA/00010519/201701

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Elosulfase alfa - VIMIZIM (CAP) - PSUSA/00010218/201702

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Eluxadoline - TRUBERZI (CAP) - PSUSA/00010528/201703

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

[11] Uveitis and macular oedema indication only

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.22. Eptifibatide - INTEGRILIN (CAP) - PSUSA/00001246/201701

Applicant: Glaxo Group Ltd

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Etanercept - ENBREL (CAP) - PSUSA/00001295/201702

Applicant: Pfizer Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Etanercept - BENEPALI (CAP) - PSUSA/00010452/201701

Applicant: Samsung Bioepis UK Limited (SBUK)

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Evolocumab - REPATHA (CAP) - PSUSA/00010405/201701

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Fampridine - FAMPYRA (CAP) - PSUSA/00001352/201701

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Florbetaben (^{18}F) - NEURACEQ (CAP) - PSUSA/00010094/201702

Applicant: Piramal Imaging Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Gadoversetamide - OPTIMARK[12] - PSUSA/00001508/201701

Applicant: Guerbet

PRAC Rapporteur: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For information

6.1.29. Gimeracil, oteracil monopotassium, tegafur - TEYSUNO (CAP) - PSUSA/00002875/201701

Applicant: Nordic Group B.V.

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Idelalisib - ZYDELIG (CAP) - PSUSA/00010303/201701

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Infliximab[13] - FLIXABI (CAP); INFLECTRA (CAP); REMSIMA (CAP) - PSUSA/00010106/201701

Applicant: Samsung Bioepis UK Limited (SBUK) (Flixabi), Hospira UK Limited (Inflectra), Celltrion Healthcare Hungary Kft. (Remsima)

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Ingenol mebutate - PICATO (CAP) - PSUSA/00010035/201701

Applicant: Leo Laboratories Ltd

PRAC Rapporteur: Julie Williams

[12] Marketing authorisation(s) expiry date: 25 July 2017
[13] Biosimilars only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Ivacaftor - KALYDECO (CAP) - PSUSA/00009204/201701

Applicant: Vertex Pharmaceuticals (Europe) Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Lenvatinib - KISPLYX (CAP); LENVIMA (CAP) - PSUSA/00010380/201702

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Lixisenatide - LYXUMIA (CAP) - PSUSA/00010017/201701

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Meningococcal group-B vaccine (rDNA, component, adsorbed) - BEXSERO (CAP) - PSUSA/00010043/201701

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Modified vaccinia Ankara virus - IMVANEX (CAP) - PSUSA/00010119/201701 (with RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Nilotinib - TASIGNA (CAP) - PSUSA/00002162/201701

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - PSUSA/00010367/201701

Applicant: AbbVie Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Pegaspargase - ONCASPAR (CAP) - PSUSA/00010457/201701

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Peginterferon beta-1a - PLEGRIDY (CAP) - PSUSA/00010275/201701

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Perampanel - FYCOMPA (CAP) - PSUSA/00009255/201701

Applicant: Eisai Europe Ltd.

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/201701

Applicant: Omeros London Limited

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) - PREVENAR 13 (CAP) - PSUSA/00009263/201701

Applicant: Pfizer Limited

PRAC Rapporteur: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Pomalidomide - IMNOVID (CAP) - PSUSA/00010127/201702

Applicant: Celgene Europe Limited

PRAC Rapporteur: Patrick Batty

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Pregabalin - LYRICA (CAP); PREGABALIN PFIZER (CAP) - PSUSA/00002511/201701

Applicant: Pfizer Limited

PRAC Rapporteur: Sabine Straus

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Pyronaridine, artesunate - PYRAMAX (Art 58[14]) - EMEA/H/W/002319/PSUV/0016

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.48. Roflumilast - DALIRESP (CAP); DAXAS (CAP); LIBERTEK (CAP) - PSUSA/00002658/201701

Applicant: AstraZeneca AB

PRAC Rapporteur: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.1.49. Rufinamide - INOVELON (CAP) - PSUSA/00002671/201701

Applicant: Eisai Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Sacubitril, valsartan - ENTRESTO (CAP); NEPARVIS (CAP) - PSUSA/00010438/201701

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Saxagliptin, dapagliflozin - QTERN (CAP) - PSUSA/00010520/201701

Applicant: AstraZeneca AB

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Silodosin - SILODYX (CAP); UROREC (CAP) - PSUSA/00002701/201701

Applicant: Recordati Ireland Ltd

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Simoctocog alfa - NUWIQ (CAP) - PSUSA/00010276/201701

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Sorafenib - NEXAVAR (CAP) - PSUSA/00002773/201612

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Tipranavir - APTIVUS (CAP) - PSUSA/00002973/201612

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Vismodegib - ERIVEDGE (CAP) - PSUSA/00010140/201701

Applicant: Roche Registration Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.57. Vorapaxar - ZONTIVITY (CAP) - PSUSA/00010357/201701

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Abacavir - ZIAGEN (CAP); NAP - PSUSA/00000010/201612

Applicants: ViiV Healthcare UK Limited (Ziagen), various

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Abacavir, lamivudine - KIVEXA (CAP); NAP - PSUSA/00000011/201612

Applicants: ViiV Healthcare UK Limited (Kivexa), various

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Abacavir, lamivudine, zidovudine - TRIZIVIR (CAP); NAP - PSUSA/00003144/201612

Applicants: ViiV Healthcare UK Limited (Trizivir), various

PRAC Rapporteur: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Alitretinoin - PANRETIN (CAP); NAP - PSUSA/00000090/201701

Applicants: Eisai Ltd (Panretin), various

PRAC Rapporteur: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Caspofungin - CANCIDAS (CAP); CASPOFUNGIN ACCORD (CAP); NAP - PSUSA/00000576/201612

Applicants: Merck Sharp & Dohme Limited (Cancidas), Accord Healthcare Ltd (Caspofungin Accord), various

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Docetaxel - DOCETAXEL WINTHROP (CAP); TAXOTERE (CAP); NAP - PSUSA/00001152/201611

Applicants: Aventis Pharma S.A. (Docetaxel Winthrop, Taxotere), various

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.7. Sildenafil[15] - VIAGRA (CAP); NAP - PSUSA/00002699/201612

Applicants: Pfizer Limited (Viagra), various

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Erectile dysfunction indication only

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

6.3.1. Allergen for therapy[16]: Dactylis Glomerata L., Phleum Pratense L., Anthoxanthum Odoratum L., Lolium Perenne L., Poa Pratensis L. (NAP) - PSUSA/00010465/201612

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Allopurinol (NAP) - PSUSA/00000095/201612

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Amino acid combinations, glucose, triglyceride combinations[17]- NUMETA (NAP) - PSUSA/00010190/201612

Applicant(s): Baxter Healthcare Limited

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Amlodipine, lisinopril (NAP) - PSUSA/00010192/201612

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Antithrombin III (NAP) - PSUSA/00003159/201612

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[16] Sublingual tablet only
[17] Only for Numeta (e.g. olive oil, soya bean oil, fish oil), with or without electrolytes, mineral compounds (intravenous (IV) application)

6.3.6. Aprotinin, calcium chloride, human factor XIII, human fibrinogen, human thrombin (NAP); aprotinin, fibrinogen, fibronectin, human coagulation factor XIII, plasma protein fraction, plasminogen, thrombin (NAP); aprotinin, human fibrinogen, thrombin, calcium chloride (NAP); aprotinin, calcium chloride, factor XIII, human thrombin, human clottable protein containing mainly fibrinogen and fibronectin (NAP); bovine aprotinin, calcium chloride, human fibrinogen, factor XIII, fibronectin, plasminogen, human thrombin (NAP); bovine aprotinin, calcium chloride, human fibrinogen, factor XIII, fibronectin, human thrombin (NAP); bovine aprotinin, human fibrinogen, calcium chloride dihydrate, plasma fibronectin, thrombin, human coagulation factor XIII (NAP), bovine aprotinin, human fibrinogen, calcium chloride dihydrate, plasma protein fraction, fibronectin, thrombin, human coagulation factor XIII (NAP); bovine aprotinin, human fibrinogen, plasminogen, human thrombin, human coagulation factor XIII, human fibronectin (NAP) - PSUSA/00010346/201611

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Bacillus clausii multi-antibioresistant spores (NAP) - PSUSA/00000284/201611

Applicant(s): various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Beclometasone (NAP) - PSUSA/00000306/201612

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Beclometasone, salbutamol (NAP) - PSUSA/00000309/201701

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Bendamustine hydrochloride (NAP) - PSUSA/00003162/201701

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Brotizolam (NAP) - PSUSA/00000444/201612

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Cefazolin (NAP) - PSUSA/00000589/201611

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Chlormadinone (NAP) - PSUSA/00000677/201611

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Chlormadinone acetate, ethinylestradiol (NAP) - PSUSA/00000679/201611

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Ciprofibrate (NAP) - PSUSA/00000771/201612

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Citalopram (NAP) - PSUSA/00000779/201612

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Dexlansoprazole (NAP), lansoprazole (NAP) - PSUSA/00001827/201612

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Diacerein (NAP) - PSUSA/00001026/201612

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Dienogest (NAP) - PSUSA/00003167/201612

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Donepezil (NAP) - PSUSA/00001160/201611

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Escitalopram (NAP) - PSUSA/00001265/201612

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Flurbiprofen (NAP) - PSUSA/00001450/201611

Applicant(s): various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Furosemide, spironolactone (NAP) - PSUSA/00001493/201612

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Gaxilose (NAP) - PSUSA/00010283/201701

Applicant(s): various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Idarubicin (NAP) - PSUSA/00001720/201611

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Indapamide, perindopril (NAP) - PSUSA/00010230/201611

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Iron[18] (NAP) - PSUSA/00010236/201701

Applicant(s): various

PRAC Lead: Zane Neikena

[18] Parenteral preparations only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Levobunolol[19] (NAP) - PSUSA/00010109/201701

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Levonorgestrel, ethinylestradiol (NAP); ethinylestradiol[20] (NAP) - PSUSA/00010442/201701

Applicant(s): various

PRAC Lead: Caroline Laborde

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide (NAP) - PSUSA/00010390/201701

Applicant(s): various

PRAC Lead: Doris Stenver

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.31. Lubiprostone (NAP) - PSUSA/00010290/201701

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Octenidine dihydrochloride, phenoxyethanol (NAP) - PSUSA/00002199/201701

Applicant(s): various

PRAC Lead: Jolanta Gulbinovic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[19] Ophthalmic indication only
[20] Combination pack

6.3.33. Pergolide (NAP) - PSUSA/00002351/201612

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.34. Quinine (NAP) - PSUSA/00002598/201611

Applicant(s): various

PRAC Lead: Almath Spooner

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.35. Roxithromycin (NAP) - PSUSA/00002669/201612

Applicant(s): various

PRAC Lead: Carmela Macchiarulo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.36. Rupatadine (NAP) - PSUSA/00002673/201612

Applicant(s): various

PRAC Lead: Dolores Montero Corominas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.37. Sertindole (NAP) - PSUSA/00002695/201701

Applicant(s): various

PRAC Lead: Julie Williams

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.38. Sulbactam (NAP) - PSUSA/00002800/201611

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.39. Terbutaline (NAP) - PSUSA/00002897/201612

Applicant(s): various

PRAC Lead: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.40. Testosterone undecanoate[21] (NAP) - PSUSA/00010161/201612

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.41. Tibolone (NAP) - PSUSA/00002947/201612

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.42. Topiramate (NAP) - PSUSA/00002996/201701

Applicant(s): various

PRAC Lead: Qun-Ying Yue

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.43. Ursodeoxycholic acid (NAP) - PSUSA/00003084/201611

Applicant(s): various

PRAC Lead: Amy Tanti

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.44. Varicella zoster-immunoglobin (NAP) - PSUSA/00010266/201612

Applicant(s): various

[21] Injection route only

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.45. Vecuronium bromide (NAP) - PSUSA/00003102/201611

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.46. Yellow fever vaccine (live) (NAP) - PSUSA/00003135/201612

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/LEG 034.1

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to LEG 034 [cumulative review of data from all sources on the risk of rebound multiple sclerosis (MS) with fingolimod, as requested in the conclusions of EMEA/H/C/PSUSA/00001393/201602 adopted by PRAC in October 2016] as adopted in March 2017 further to the submission of a cumulative review of data from all per the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

6.4.2. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/LEG 084.1

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to LEG 084 [cumulative review on the teratogenic risk and the risk of neurodevelopmental disorders associated with the use of levetiracetam during pregnancy, based on data from all available sources as requested in the conclusions of EMEA/H/C/PSUSA/00001846/201511 adopted by PRAC in September 2016] as per the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

6.4.3. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/LEG 065

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Detailed review of fatal events in line with the MedDRA[22] hierarchy terms sorted by country of origin as requested in the conclusions of PSUSA/2127/201608/0099 adopted by PRAC in March 2017

Action: For adoption of advice to CHMP

6.4.4. Vardenafil - LEVITRA (CAP) - EMEA/H/C/000475/LEG 026.1

Applicant: Bayer AG

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to LEG 026 [submission of a cumulative review and a discussion on cerebrovascular disorders with data from all available sources (clinical trials, post-marketing experience, literature) including information regarding time to onset, age of patients, dose of vardenafil, confounding or risk factors as well as any information on dechallenge/rechallenge as requested in the conclusions of PSUSA/00003098/201603 adopted by PRAC in November 2016] as per the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

6.4.5. Vardenafil - VIVANZA (CAP) - EMEA/H/C/000488/LEG 026.1

Applicant: Bayer AG

PRAC Rapporteur: Dolores Montero Corominas

Scope: MAH's response to LEG 026 [submission of a cumulative review and a discussion on cerebrovascular disorders with data from all available sources (clinical trials, post-marketing experience, literature) including information regarding time to onset, age of patients, dose of vardenafil, confounding or risk factors as well as any information on dechallenge/rechallenge as requested in the conclusions of PSUSA/00003098/201603 adopted by PRAC in November 2016] as per the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

[22] Medical Dictionary for Regulatory Activities

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[23]

7.1.1. Cholic acid – KOLBAM (CAP) - EMEA/H/C/PSA/S/0021

Applicant: Retrophin Europe Limited

PRAC Rapporteur: Patrick Batty

Scope: Amendment to PASS protocol for a prospective, observational, non-interventional, post-marketing, patient registry to collect data on routine clinical care in patients treated with Kolbam (cholic acid) [protocol previously adopted within procedure EMEA/H/C/PSP/0017.2 at November 2016 PRAC meeting]

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

7.1.2. Direct acting antivirals (DAAV) indicated for the treatment of hepatitis C: Daclatasvir – DAKLINZA (CAP); dasabuvir - EXVIERA (CAP); elbasvir, grazoprevir – ZEPATIER (CAP); ledipasvir, sofosbuvir - HARVONI (CAP); ombitasvir, periteprevir, ritonavir – VIEKIRAX (CAP); simeprevir - OLYSIO (CAP); sofosbuvir – SOVALDI (CAP); sofosbuvir, velpatasvir – EPCLUSA (CAP) - EMEA/H/N/PSP/J/0056

Applicant(s): AbbVie Limited (Exviera, Viekirax), Bristol-Myers Squibb Pharma EEIG (Daklinza), Gilead Sciences International Ltd (Epclusa, Harvoni, Sovaldi), Janssen-Cilag International NV (Olysio), Merck Sharp & Dohme Limited (Zepatier)

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Joint PASS protocol for a prospective, non-interventional study evaluating the risk of early recurrence of hepatocellular carcinoma (HCC) in hepatitis C virus (HCV)-infected patients after direct-acting antiviral (DAAV) therapy compared to HCV-infected patients without previous DAA therapy during routine clinical care with previous successfully treated HCC, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on DAAV indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

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

7.1.3. Iron intravenous (IV) (NAP) - EMEA/H/N/PSP/J/0053.1

Applicant: Mesama Consulting

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to EMEA/H/N/PSP/J/0053.1 [PASS protocol for a study evaluating the risk of severe hypersensitivity reactions and assessing the risk of anaphylactic or severe immediate hypersensitivity reactions on the day of or the day after first IV iron use] as per the request for supplementary information (RSI) adopted in March 2017

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

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

7.1.4. Ketoconazole – KETOCONAZOLE HRA (CAP) - EMEA/H/C/PSP/S/0040.4

Applicant: Laboratoire HRA Pharma

PRAC Rapporteur: Željana Margan Koletić

Scope: MAH's response to PSP/S/0040.3 [revised PASS protocol for a prospective, multinational, observational registry to collect clinical information on patients with endogenous Cushing's syndrome exposed to ketoconazole (using the existing European Registry on Cushing's syndrome (ERCUSYN)), to assess drug utilisation pattern and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of ketoconazole] as per the request for supplementary information (RSI) adopted in June 2017

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

7.1.5. Ethinylestradiol (NAP), levonorgestrel, ethinylestradiol (NAP) - EMEA/H/N/PSP/J/0054.1

Applicant: Teva Pharma B.V. (Seasonique)

PRAC Rapporteur: Caroline Laborde

Scope: MAH's response to PSP/J/0054 [PASS protocol for a drug utilisation study of Seasonique (ethinylestradiol, levonorgestrel) in Europe aiming at assessing both safety outcomes and drug utilisation patterns] as per the request for supplementary information (RSI) adopted in April 2017

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

7.1.6. Parathyroid hormone – NATPAR (CAP) - EMEA/H/C/PSP/S/0058

Applicant: Shire Pharmaceuticals Ireland

PRAC Rapporteur: Almath Spooner

Scope: PASS protocol for a registry for subjects with chronic hypoparathyroidism (PARADIGHM: physicians advancing disease knowledge in hypoparathyroidism)

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

7.1.7. Valproate (NAP) - EMEA/H/N/PSA/J/0015.1

Applicant: Sanofi

PRAC Rapporteur: Sabine Straus

Scope: MAH's response to PSA/J/0015 including a revised protocol [updated protocol for a joint drug utilisation study (DUS) using EU databases to study the effectiveness of the imposed risk minimisation measures following the conclusion of the referral procedure under Article 31 of Directive 2001/83/EC completed in 2014 (EMEA/H/A-31/1387) and to further characterise the prescribing patterns for valproate] as per the request for supplementary information (RSI) adopted in March 2017

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[24]

7.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.4

Applicant: Genzyme Therapeutics Ltd

PRAC Rapporteur: Torbjorn Callreus

Scope: MAH's response to MEA 007.2 and MEA 007.3 [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 April 2017

Action: For adoption of advice to CHMP

7.2.2. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 002

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Patrick Batty

Scope: PASS protocol for study I4V-MC-B003: a prospective observational US post-marketing registry study to assess the long-term safety of baricitinib compared with other therapies used in the treatment of adults with moderate-to-severe rheumatoid arthritis in the course of routine clinical care [final report expected by March 2031] (as requested in the initial opinion)

Action: For adoption of advice to CHMP

7.2.3. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 012.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: MAH's response to MEA 012.1 [PASS protocol for an epidemiological study to evaluate the risk of acute pancreatitis in patients with type 2 diabetes mellitus (T2DM) newly exposed to canagliflozin-containing products compared to patients with T2DM exposed to non-sodium-glucose co-transporter-2 (SGLT2) inhibitor anti-hyperglycaemic agents: a retrospective cohort study using large claims databases in the United States] as requested in the request for supplementary information (RSI) adopted in April 2017

Action: For adoption of advice to CHMP

7.2.4. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 013

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Valerie Strassmann

Scope: PASS protocol for a US epidemiology database study l to further characterise the incidence of lower limb amputation in patients taking canagliflozin (category 3 PASS) as well

[24] 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

as a feasibility assessment report for the conduct of a similar observational database study in the EU (category 3 PASS) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442)

Action: For adoption of advice to CHMP

7.2.5. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 011.1

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 011 [PASS protocol for an epidemiological study to evaluate the risk of acute pancreatitis in patients with type 2 diabetes mellitus (T2DM) newly exposed to canagliflozin-containing products compared to patients with T2DM exposed to non-sodium-glucose co-transporter-2 (SGLT2) inhibitor anti-hyperglycaemic agents: a retrospective cohort study using large claims databases in the United States] as requested in the request for supplementary information (RSI) adopted in April 2017

Action: For adoption of advice to CHMP

7.2.6. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 012

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: PASS protocol for a US epidemiology database study to further characterise the incidence of lower limb amputation in patients taking canagliflozin (category 3 PASS) as well as a feasibility assessment report for the conduct of a similar observational database study in the EU (category 3 PASS) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442)

Action: For adoption of advice to CHMP

7.2.7. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/MEA 024

Applicant: Pfizer Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Amendment of a protocol for study A8081062: a PASS descriptive study evaluating the frequency of risk factors for and sequelae of potential sight threatening event and severe visual loss among patients being treated with crizotinib following exposure to Xalkori (crizotinib) required by the US FDA (RMP category 3 study) (from the outcome of II/39 variation procedure)

Action: For adoption of advice to CHMP

7.2.8. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/MEA 001.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: MAH's response to MEA 001.1 [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 the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.2.9. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/MEA 067.2

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 067.1 [revised PASS protocol and questionnaire for a cross sectional physician survey (study N6987) to assess the impact of educational materials on prescribers' awareness of doses and biological monitoring recommendations and also to assess the awareness and appropriate use of both formulations (orodispersible tablets and film-coated tablets) as per request for supplementary information (RSI) adopted in April 2017

Action: For adoption of advice to CHMP

7.2.10. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 009

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Martin Huber

Scope: PASS protocol for study 109MS303: a dose-blind, multicentre, extension study to determine the long-term safety and efficacy of two doses of BG00012 monotherapy in subjects with relapsing-remitting multiple sclerosis (ENDORSE) [final clinical study report expected in Q1 2024]

Action: For adoption of advice to CHMP

7.2.11. Eluxadoline - TRUBERZI (CAP) - EMEA/H/C/004098/MEA 005.1

Applicant: Allergan Pharmaceuticals International Ltd

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's responses to MEA 005 [PASS protocol for study EVM-19596-00-001: a drug utilisation study (DUS) (RMP category 3) using relevant healthcare databases at two different time periods in order to define the compliance to contraindications over time and the number of subjects diagnosed with pancreatitis after eluxadoline treatment] as requested in the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

7.2.12. Fenofibrate, simvastatin - CHOLIB (CAP) - EMEA/H/C/002559/MEA 002.6

Applicant: Mylan Products Limited

PRAC Rapporteur: Julie Williams

Scope: MAH's responses to MEA 002.5 [PASS protocol to assess the clinical practice regarding concomitant use of fenofibrate and simvastatin both as free and fixed combination (Cholib): a European study in Austria, Croatia, Czech Republic, Portugal, Slovakia and Slovenia and a corresponding study web questionnaire] as per the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

7.2.13. Idelalisib - ZYDELIG (CAP) - EMEA/H/C/003843/MEA 015.1

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Patrick Batty

Scope: MAH's responses to MEA 015 [PASS protocol for study GS-EU-313-4172: a non-interventional study to assess the safety profile of idelalisib in patients with refractory follicular lymphoma (FL)] as per the request for supplementary information (RSI) adopted in March 2017

Action: For adoption of advice to CHMP

7.2.14. Lidocaine, prilocaine - FORTACIN (CAP) - EMEA/H/C/002693/MEA 004

Applicant: Plethora Solutions Ltd.

PRAC Rapporteur: Dolores Montero Corominas

Scope: Protocol for a drug utilisation study (DUS) of Fortacin (lidocaine, prilocaine) in Europe: a retrospective cohort study using electronic medical records database aiming at characterising the population of patients who are prescribed the medicinal product and at describing the real-life prescribing patterns (listed as a category 3 study in RMP)

Action: For adoption of advice to CHMP

7.2.15. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/MEA 014.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Proposed amendment to the drug utilisation study (DUS), study NN8022-4241 evaluating in-market utilisation of Saxenda (liraglutide) used for weight management in Europe: a retrospective medical record review study to be conducted in Italy and Germany [PASS protocol agreed in September 2015 and protocol amendment agreed in February 2016], relating to a smaller sample size of patients in Germany for a pilot study to be conducted prior to the DUS

Action: For adoption of advice to CHMP

7.2.16. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 004.1

Applicant: Teva Pharmaceuticals Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 004 [PASS protocol for study C38072-AS-50026, a non-interventional phase IV study active pregnancy surveillance: effect of reslizumab exposure on pregnancy outcomes] as per the request for supplementary information (RSI) adopted in April 2017

Action: For adoption of advice to CHMP

7.2.17. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 005.1

Applicant: Teva Pharmaceuticals Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 005 [submission of a protocol for study C38072-AS-50027: a long-term non-interventional cohort study comparing the risk of malignancy in severe asthma patients treated with reslizumab and patients not treated with reslizumab using secondary administrative healthcare data (RMP category 3)] as per the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.2.18. Sodium oxybate - XYREM (CAP) - EMEA/H/C/000593/MEA 019.1

Applicant: UCB Pharma Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 019 [Protocol for study NA0001 (EU PAS register EUPAS15024): a non-interventional PASS on the effectiveness of the educational materials] as per the request for supplementary information (RSI) adopted in April 2017

Action: For adoption of advice to CHMP

7.2.19. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/MEA 025.2

Applicant: Shire Pharmaceuticals Ireland Ltd

PRAC Rapporteur: Valerie Strassmann

Scope: MAH's response to MEA 025.1 [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 the request for supplementary information (RSI) adopted in May 2017

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[25]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[26]

7.4.1. Adalimumab - AMGEVITA (CAP) - EMEA/H/C/004212/WS1182/0001; SOLYMBIC (CAP) - EMEA/H/C/004373/WS1182/0001

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report for study 20130258: an open-label, single-arm extension study to evaluate the long-term safety and efficacy of ABP 501 (adalimumab biosimilar) in subjects with moderate to severe rheumatoid arthritis (listed as a category 3 study in the RMP (MEA 002)). The RMP (version 2.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Apixaban - ELIQUIS (CAP) - EMEA/H/C/002148/II/0043

Applicant: Bristol-Myers Squibb, Pfizer EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report for study CV185-365: a PASS evaluating the effectiveness of Eliquis (apixaban) risk minimisation tools in the European Economic Area countries (listed as a category 3 study in the RMP). The RMP (version 17.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/II/0204

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final registry report from C0168T71 study: a review and analysis of birth outcomes from Swedish, Danish and Finish medical birth registers and an evaluation of pregnancy data from multiple sources. As a consequence, section 4.6 of the SmPC is updated. The Package Leaflet and the RMP (version 13.2) are updated accordingly. In addition, the MAH took the opportunity to bring the product in line with the latest QRD template and update the local representative section of the Package Leaflet

Action: For adoption of PRAC Assessment Report

[25] In accordance with Article 107p-q of Directive 2001/83/EC
[26] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.4.4. Insulin lispro - HUMALOG (CAP) - EMEA/H/C/000088/WS1188/0157; LIPROLOG (CAP) - EMEA/H/C/000393/WS1188/0120

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Julie Williams

Scope: Submission of the final report for a non-interventional PASS EUPAS 13422 evaluating the impact of additional risk minimisation measures on healthcare professionals and on patients' understanding and their behaviour regarding the risk of hypoglycaemia and/or hyperglycaemia due to medication errors associated with administration of Humalog 200 U/mL KwikPen or Liprolog 200 U/mL KwikPen

Action: For adoption of PRAC Assessment Report

7.4.5. Paliperidone - XEPLION (CAP) - EMEA/H/C/002105/II/0031

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Qun-Ying Yue

Scope: Submission of the final study report for a PASS using European Union databases to assess the risk of cardiovascular and cerebrovascular adverse events in elderly patients treated with paliperidone palmitate, paliperidone prolonged-release, and other antipsychotics

Action: For adoption of PRAC Assessment Report

7.4.6. Sodium oxybate - XYREM (CAP) - EMEA/H/C/000593/II/0066

Applicant: UCB Pharma Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study C00302 (post marketing non-interventional surveillance pharmacoepidemiology study (PMSS) to evaluate long-term safety, tolerability and compliance in administration of Xyrem (sodium oxybate) oral solution in patients who receive treatment with this medication in regular clinical practice) listed as a category 3 study in the RMP. The RMP (version 8) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0182

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Caroline Laborde

Scope: Submission of the final report for study GX-US-174-0172: a 5-year observational (non-interventional) renal safety registry conducted to provide further safety data in hepatitis B virus (HBV)-infected patients with decompensated liver disease (listed as a category 3 study in the RMP)

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. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/ANX 038.8

Applicant: Novartis Europharm Ltd

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to ANX 038.7 [third annual interim report for study CICL670E2422: an observational, multicentre study to evaluate the safety of deferasirox in the treatment of paediatric patients with non-transfusion-dependent iron overload] as per the request for supplementary information (RSI) adopted in April 2017

Action: For adoption of advice to CHMP

7.5.2. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 002.4

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Second annual interim report for study 1245.96: an observational cohort study using existing data including urinary tract infection (UTI) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors [final report expected in July 2020]

Action: For adoption of advice to CHMP

7.5.3. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/MEA 004

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Julie Williams

Scope: Second annual interim report for study 1245.96: an observational cohort study using existing data including urinary tract infection (UTI) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl peptidase-4 (DPP-4) inhibitors [final report expected in July 2020]

Action: For adoption of advice to CHMP

7.5.4. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 003.1

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Second annual interim report for study 1245.96: an observational cohort study using existing data including urinary tract infection (UTI) as a safety topic of interest assessing a number of risks in patients treated with empagliflozin compared with patients treated with other sodium-glucose cotransporter-2 (SGLT2) inhibitors or with dipeptidyl

peptidase-4 (DPP-4) inhibitors [final report expected in July 2020]

Action: For adoption of advice to CHMP

7.5.5. Epoetin beta - NEORECORMON (CAP) - EMEA/H/C/000116/MEA 045.6

Applicant: Roche Registration Limited

PRAC Rapporteur: Valerie Strassmann

Scope: Sixth interim report summarising the progress on studies to assess the functional activity of epoetin receptors in different tumour types, and at different stages in the life-cycle of tumour evaluation

Action: For adoption of advice to CHMP

7.5.6. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/MEA 007.2

Applicant: Hospira UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Third annual interim safety and efficacy report for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra (infliximab) in patients with rheumatoid arthritis (EU and Korea) and MAH's responses to EMEA/H/C/002778/MEA 007.1 procedure as per the request for supplementary information (RSI) adopted in September 2016 [final report expected by May 2026]

Action: For adoption of advice to CHMP

7.5.7. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/MEA 010.2

Applicant: Hospira UK Limited

PRAC Rapporteur: Patrick Batty

Scope: Annual interim safety and efficacy report for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Inflectra (infliximab) in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) and MAH's responses to EMEA/H/C/002778/MEA 010.1 procedure as per the request for supplementary information (RSI) adopted in September 2016 [final report expected by May 2026]

Action: For adoption of advice to CHMP

7.5.8. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 007.2

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: Third annual interim safety and efficacy report for registry CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Remsima (infliximab) in patients with rheumatoid arthritis (EU and Korea) and MAH's responses to EMEA/H/C/002576/MEA 007.1 procedure as per the request for supplementary information (RSI) adopted in September 2016 [final report expected by May 2026]

Action: For adoption of advice to CHMP

7.5.9. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/MEA 010.2

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Patrick Batty

Scope: Annual interim safety and efficacy report for registry CT-P13 4.3: an observational, prospective cohort study to evaluate the safety and efficacy of Remsima (infliximab) in patients with Crohn's disease (CD), and ulcerative colitis (UC) (EU and Korea) and MAH's responses to EMEA/H/C/002576/MEA 010.1 procedure as per the request for supplementary information (RSI) adopted in September 2016 [final report expected by May 2026]

Action: For adoption of advice to CHMP

7.5.10. Influenza vaccine (live attenuated, nasal) - FLUENZ TETRA (CAP) - EMEA/H/C/002617/MEA 004.7

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual interim report for the passive enhanced safety surveillance study (ESS) D2560C00008: a postmarketing non-interventional cohort study of the safety of live attenuated influenza vaccine (LAIV) in subjects 2 through 17 years of age

Action: For adoption of advice to CHMP

7.5.11. Meningococcal group B vaccine(rDNA, component, adsorbed) - BEXSERO (CAP) - EMEA/H/C/002333/MEA 017.3

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Qun-Ying Yue

Scope: Third interim report for study V72_36OB: a post-licensure observational safety study after meningococcal B vaccine 4CMenB (Bexsero) vaccination in routine UK care [final report expected in December 2019]

Action: For adoption of advice to CHMP

7.5.12. Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/MEA 013.4

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 013.3 [annual interim report from an observational database-assisted comparative cohort study to investigate the risk of hepatotoxicity and

hepatocellular carcinoma (protocol number: ISN 9463-CL-140): a multicentre cohort study of the short and long-term safety of micafungin and other parenteral antifungal agents (MYCOS)] as per the request for supplementary information (RSI) adopted in January 2017

Action: For adoption of advice to CHMP

7.5.13. Mixture of polynuclear iron(III)-oxyhydroxide, sucrose and starches - VELPHORO (CAP) - EMEA/H/C/002705/MEA 002.4

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Julie Williams

Scope: Second biannual interim report for the VERIFIE study (VFMCRP-MEAF-PA21-01-EU): a non-interventional study to investigate the short and long-term real-life safety, effectiveness, and adherence of Velphoro in patients with hyperphosphataemia undergoing haemodialysis or peritoneal dialysis (PD) and MAH's responses to the request for supplementary information (RSI) for MEA 002.3 adopted in February 2017 on the first interim study report

Action: For adoption of advice to CHMP

7.5.14. Nomegestrol acetate, estradiol - ZOELY (CAP) - EMEA/H/C/001213/ANX 011.3

Applicant: Teva B.V.

PRAC Rapporteur: Caroline Laborde

Scope: Third interim report (covering the period from the start of recruitment in August 2014 until April 2017) for a prospective PASS observational study (ZEG2013_08) to assess the risk of venous thromboembolic events (VTE) and arterial thromboembolic events (ATE) in nomegestrol/estradiol users compared with the VTE risk in users of combined oral contraceptives containing levonorgestrel (as imposed in accordance with Article 10(a) of Regulation (EC) No 726/2004

Action: For adoption of advice to CHMP

7.5.15. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/ANX 001.3

Applicant: Shionogi Limited

PRAC Rapporteur: Julie Williams

Scope: Second annual interim report for PASS ENCEPP/SDPP/8585: an observational retrospective cohort study for ospemifene utilising existing databases in Germany, Italy, Spain, and the United States to evaluate the incidence of venous thromboembolism and other adverse events, as agreed in the RMP, in vulvar and vaginal atrophy (VVA) patients treated with ospemifene as compared to: 1) patients newly prescribed selective estrogen receptor modulators (SERMs) for oestrogen-deficiency conditions or breast cancer prevention and; 2) the incidence in untreated VVA patients (category 1) [final report expected in February 2021]

Action: For adoption of advice to CHMP

7.5.16. Pegvisomant - SOMAVERT (CAP) - EMEA/H/C/000409/MEA 061

Applicant: Pfizer Limited

PRAC Rapporteur: Caroline Laborde

Scope: Interim report from study A6291010 (ACROSTUDY): a multicentre, post marketing surveillance study of pegvisomant therapy in patients with acromegaly as agreed in the opinion for the initial MAA [due date: final report due in 2018, extended to 2019 (MEA 059)]

Action: For adoption of advice to CHMP

7.5.17. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/MEA 011.3

Applicant: Roche Registration Limited

PRAC Rapporteur: Doris Stenver

Scope: Fourth annual interim report for study H4621g (MotHER pregnancy register): an observational study of pregnancy and pregnancy outcomes in women with breast cancer treated with Herceptin (trastuzumab), Perjeta (pertuzumab) in combination with Herceptin, or Kadcyla during pregnancy or within 7 months prior to conception [final report expected by May 2024]

Action: For adoption of advice to CHMP

7.5.18. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 023.9

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Seventh annual interim report for study CNTO1275PSO4005 (Nordic database initiative): a prospective cohort registry, five-year observational study of adverse events (AEs) observed in patients exposed to ustekinumab

Action: For adoption of advice to CHMP

7.5.19. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 024.10

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Seventh annual interim report for study CNTO1275PSO4007 (pregnancy research initiative) (C0743T): exposure to ustekinumab during pregnancy in patients with psoriasis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers. In addition, the submission includes a summary document on pregnancy outcomes from study CNT01275PS04037: pregnancy exposure registry OTIS (Organisation of Teratology Information Specialists) study conducted in North America on autoimmune diseases in pregnancy; study C0168Z03: a multicentre, prospective, observational PSOLAR (Psoriasis Longitudinal Assessment and Registry) study tracking the long-term safety experience and clinical status of patients with psoriasis who are eligible to receive (or are actively receiving) systemic therapies for psoriasis; and study CNT01275PS04007: a prospective, observational, exposure-based cohort Nordic Pregnancy Registry study analysing maternal and birth outcome data obtained from the Swedish Medical Birth Register (SMBR), Danish Medical Birth Register (DMBR) and Finnish Medical Birth Register (FMBR)

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Bazedoxifene - CONBRIZA (CAP) - EMEA/H/C/000913/MEA 012.10

Applicant: Pfizer Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of a statistical analysis plan (SAP) for PASS B1781044: a cohort study of venous thromboembolism and other clinical endpoints among osteoporotic women prescribed bazedoxifene, bisphosphonates or raloxifene in Europe, as per the request for supplementary information (RSI) agreed in the conclusion of MEA 012.9 adopted in May 2017

Action: For adoption of advice to CHMP

7.6.2. Daclatasvir - DAKLINZA (CAP) - EMEA/H/C/003768/MEA 019

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of advice to CHMP

7.6.3. Daclizumab - ZINBRYTA (CAP) - EMEA/H/C/003862/MEA 004

Applicant: Biogen Idec Ltd

PRAC Rapporteur: Eva Segovia

Scope: Feasibility study for conducting a PASS using multiple sclerosis registries to address specific safety concerns or to measure effectiveness of risk minimisation measures (from initial opinion)

Action: For adoption of advice to CHMP

7.6.4. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/MEA 007

Applicant: AbbVie Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C

(interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of advice to CHMP

7.6.5. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/MEA 004

Applicant: Merck Sharp & Dohme Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of advice to CHMP

7.6.6. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 011

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Statistical analysis plan (SAP) outlining the meta-analysis of three clinical trials: 1) study 1245.25: a phase 3, multicentre, international, randomised, parallel group, double-blind cardiovascular safety study of empagliflozin (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk (EMPA REG); 2) study 1245.110: a phase 3 randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic heart failure with preserved ejection fraction (HFpEF) (EMPEROR-Preserved) and 3) study 1245.121: a randomized study on efficacy and safety of empagliflozin compared to placebo in patients with heart failure with reduced ejection fraction (EMPEROR-Reduced), including a graph of the cumulative incidence of amputation events and relevant preceding adverse events of special interest (AESI including gangrene, osteomyelitis) over time, to further characterise the important potential risk of lower limb amputation, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442)

Action: For adoption of advice to CHMP

7.6.7. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/MEA 003

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Julie Williams

Scope: Statistical analysis plan (SAP) outlining the meta-analysis of three clinical trials: 1) study 1245.25: a phase 3, multicentre, international, randomised, parallel group, double-blind cardiovascular safety study of empagliflozin (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk (EMPA REG); 2) study 1245.110: a phase 3 randomised, double-blind

trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic heart failure with preserved ejection fraction (HFpEF) (EMPEROR-Preserved) and 3) study 1245.121: a randomized study on efficacy and safety of empagliflozin compared to placebo in patients with heart failure with reduced ejection fraction (EMPEROR-Reduced), including a graph of the cumulative incidence of amputation events and relevant preceding adverse events of special interest (AESI including gangrene, osteomyelitis) over time, to further characterise the important potential risk of lower limb amputation, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442)

Action: For adoption of advice to CHMP

7.6.8. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 007

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Dolores Montero Corominas

Scope: Statistical analysis plan (SAP) outlining the meta-analysis of three clinical trials: 1) study 1245.25: a phase 3, multicentre, international, randomised, parallel group, double-blind cardiovascular safety study of empagliflozin (10 mg and 25 mg administered orally once daily) compared to usual care in type 2 diabetes mellitus patients with increased cardiovascular risk (EMPA REG); 2) study 1245.110: a phase 3 randomised, double-blind trial to evaluate efficacy and safety of once daily empagliflozin 10 mg compared to placebo, in patients with chronic heart failure with preserved ejection fraction (HFpEF) (EMPEROR-Preserved) and 3) study 1245.121: a randomized study on efficacy and safety of empagliflozin compared to placebo in patients with heart failure with reduced ejection fraction (EMPEROR-Reduced), including a graph of the cumulative incidence of amputation events and relevant preceding adverse events of special interest (AESI including gangrene, osteomyelitis) over time, to further characterise the important potential risk of lower limb amputation, as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on lower limb amputation in relation to the use of sodium-glucose co-transporter-2 (SGLT-2) inhibitors completed in February 2017 (EMEA/H/A-20/1442)

Action: For adoption of advice to CHMP

7.6.9. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/MEA 017

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of advice to CHMP

7.6.10. Palonosetron - PALONOSETRON ACCORD (CAP) - EMEA/H/C/004129/LEG 002.1

Applicant: Accord Healthcare Ltd

PRAC Rapporteur: Almath Spooner

Scope: Six-monthly cumulative review of cases of injection site reactions classified as an important potential risk (1 October 2016-31 March 2017) as requested at the time of the opinion for marketing authorisation(s) for Palonosetron Accord 250 micrograms solution for injection until further market experience is acquired

Action: For adoption of advice to CHMP

7.6.11. Simeprevir - OLYSIO (CAP) - EMEA/H/C/002777/MEA 013

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Julie Williams

Scope: Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of advice to CHMP

7.6.12. Ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/MEA 007

Applicant: AbbVie Limited

PRAC Rapporteur: Dolores Montero Corominas

Scope: Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of advice to CHMP

7.6.13. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/MEA 024

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Julie Williams

Scope: Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of advice to CHMP

7.6.14. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/MEA 008

Applicant: Gilead Sciences International Ltd

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Feasibility assessment for a prospective cohort study in hepatitis C virus (HCV) infected patients with compensated cirrhosis (CPT-A) without history of hepatocellular carcinoma (HCC) and treated with direct-acting antivirals (DAAV) (listed as category 3 study in RMP) as per the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 on direct-acting antivirals (DAAV) indicated for treatment of hepatitis C (interferon-free) completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of advice to CHMP

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

8.1.1. Amifampridine - FIRDAPSE (CAP) - EMEA/H/C/001032/S/0049 (without RMP)

Applicant: BioMarin Europe Ltd

PRAC Rapporteur: Julie Williams

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/R/0051 (with RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/R/0002 (without RMP), Orphan

Applicant: Intercept Pharma Ltd

PRAC Rapporteur: Sabine Straus

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/R/0005 (without RMP)

Applicant: AbbVie Ltd.

PRAC Rapporteur: Patrick Batty

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - EMEA/H/C/002246/R/0031 (with RMP)

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Valerie Strassmann

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/R/0105 (with RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Torbjorn Callreus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Loxapine - ADASUVE (CAP) - EMEA/H/C/002400/R/0024 (with RMP)

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Sabine Straus

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Nalmefene - SELINCRO (CAP) - EMEA/H/C/002583/R/0022 (without RMP)

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Ocriplasmin - JETREA (CAP) - EMEA/H/C/002381/R/0033 (without RMP)

Applicant: ThromboGenics NV

PRAC Rapporteur: Julie Williams

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Pioglitazone, metformin hydrochloride - GLUBRAVA (CAP) - EMEA/H/C/000893/R/0054 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Almath Spooner

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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. Darbepoetin alfa – ARANESP (CAP) - EMEA/H/C/000332/II/0143

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Valerie Strassmann

Scope: PRAC consultation on a type II variation to update section 4.8 the SmPC in order to add a warning on injection site bruise and haemorrhage with frequency unknown and to provide additional instructions on the use of the device in the Package Leaflet following signal procedure EMEA/H/C000332/SDA/090 on cases of incorrect device use / device malfunction

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

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

11.1.1. Moxifloxacin (NAP) - DE/H/xxxx/WS/387; DE/H/xxxx/WS/388

Applicant: Bayer AG (Avelox, Avalox); various

PRAC Lead: Martin Huber

Scope: PRAC consultation on variation (DE/H/xxxx/WS/387) on uveitis and bilateral acute iris transillumination and on a variation (DE/H/xxxx/WS/388) on increased intracranial pressure (including benign intracranial hypertension) submitted at national level following conclusions of procedure PSUSA/00009231/201605 adopted in January 2017

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC Brexit ancillary working group

PRAC lead: Almath Spooner

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh

12.2.1. Advanced therapy medicinal products (ATMP) - Revision of procedural advice on the evaluation of ATMP in accordance with Article 8 of Regulation (EC) No 1394/2007

Action: For discussion

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. EMA reflection paper on extrapolation across age groups

PRAC lead: Jolanta Gulbinovič

Action: For adoption

12.4.2. Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE) - update

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan for 2017 - update

PRAC lead: June Raine

Action: For discussion

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

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

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality - EudraVigilance auditable requirement project – update on going live

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation safety studies – Results[27] of PASS imposed in the marketing authorisation(s) for nationally approved products – proposal for PRAC involvement in assessing MAH(s)' request for submission delays

Action: For discussion

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

12.17.1. Renewals, conditional renewals, annual re-assessments and type II variations - update of assessment report templates

Action: For discussion

12.18. Risk communication and transparency

12.18.1. Good pharmacovigilance practice (GVP) Module XV on 'safety communication' – revision 1

PRAC lead: Amelia Cupelli, Sabine Straus

Action: For discussion

12.18.2. Public participation in pharmacovigilance

None

[27] In accordance with Article 107p of Directive 2001/83/EC

12.18.3. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Good Pharmacovigilance Practices (GVP) - revised PRAC process for GVP modules in 2017 - update on GVP status overview

Action: For discussion

12.20.2. Initial marketing authorisation(s) - update to CHMP rapporteur assessment report – due date in the first phase of initial marketing authorisation application (MAA)

Action: For discussion

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/