11 May 2020
EMA/PRAC/257460/2020
Human Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 11-14 May 2020

Chair: Sabine Straus – Vice-Chair: Martin Huber

11 May 2020, 10:30 – 19:30, via teleconference

12 May 2020, 08:30 – 19:30, via teleconference

13 May 2020, 08:30 – 19:30, via teleconference

14 May 2020, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

28 May 2020, 09:00-12:00, via teleconference

Disclaimers

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

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

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006, Rev. 1).

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 11-14 May 2020. See May 2020 PRAC minutes (to be published post June 2020 PRAC meeting).

1.2. Agenda of the meeting on 11-14 May 2020

Action: For adoption

1.3. Minutes of the previous meeting on 14-17 April 2020

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

None

3.3. Procedures for finalisation

3.3.1. Leuprorelin[1] (NAP) – EMEA/H/A-31/1486

Applicant(s): various

PRAC Rapporteur: Željana Margan Koletić; PRAC Co-rapporteur: Eva Segovia

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

Action: For adoption of recommendation to CMDh

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Mirtazapine (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

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

Action: For adoption of PRAC recommendation

EPITT 19565 – New signal

Lead Member State(s): NL

4.1.2. Olaparib - LYNPARZA (CAP)

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of angioedema

Action: For adoption of PRAC recommendation

EPITT 19558 – New signal

Lead Member State(s): IT

[1] Depot formulation(s)
[2] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[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

4.1.3. Pembrolizumab – KEYTRUDA (CAP)

Applicant(s): Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Signal of Sjogren's syndrome

Action: For adoption of PRAC recommendation

EPITT 19564 – New signal

Lead Member State(s): NL

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Andexanet alfa – ONDEXXYA (CAP) - EMEA/H/C/004108/SDA/010

Applicant(s): Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Signal of erroneous assay results for levels of anti-factor Xa activity with use of andexanet alfa

Action: For adoption of PRAC recommendation

EPITT 19493 – Follow-up to April 2020

4.3.2. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/SDA/010

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

PRAC Rapporteur: Adam Przybylkowski

Scope: Signal of diverticulitis

Action: For adoption of PRAC recommendation

EPITT 19496 – Follow-up to January 2020

4.3.3. Buprenorphine – BUVIDAL (CAP) - EMEA/H/C/004651/SDA 002, SIXMO (CAP) - EMEA/H/C/004743/SDA 003, NAP; buprenorphine, naloxone – SUBOXONE (CAP) - EMEA/H/C/000697/SDA 028, ZUBSOLV (CAP), NAP; Selective serotonin reuptake inhibitors (SSRIs): citalopram (NAP); escitalopram (NAP); fluvoxamine (NAP); fluoxetine (NAP); paroxetine (NAP); sertraline (NAP); Serotonin norepinephrine reuptake inhibitors (SNRIs): desvenlafaxine (NAP); duloxetine – CYMBALTA (CAP), DULOXETINE LILLY (CAP), DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), XERISTAR (CAP), YENTREVE (CAP), NAP; milnacipran (NAP); venlafaxine (NAP); Tricyclic antidepressants (TCAs): amitriptyline (NAP); clomipramine (NAP); doxepin (NAP); imipramine (NAP); nortriptyline (NAP); trimipramine (NAP); Monoamine oxidase inhibitors (MAOIs): isocarboxazid (NAP); phenelzine (NAP); selegiline (NAP); tranylcypromine (NAP); Other psychiatric medicines: amoxapine (NAP); buspirone (NAP); lithium (NAP);

maprotiline (NAP); mirtazapine (NAP); trazodone (NAP);
Serotonin receptor agonists: almotriptan (NAP); frovatriptan (NAP); naratriptan(NAP); rizatriptan (NAP); sumatriptan (NAP); zolmitriptan (NAP);
Antiemetics: granisetron - SANCUSO (CAP), NAP; ondansetron (NAP); palonosetron – ALOXI (CAP), PALONOSETRON ACCORD (CAP), NAP; netupitant, palonosetron – AKYNZEO (CAP); tropisetron (NAP);
Other serotonergic drugs: cyclobenzaprine (NAP); dextromethorphan (NAP); hypericum perforatum (NAP); linezolid (NAP); methylene blue (NAP); tryptophan (NAP)

Applicant(s): Accord Healthcare S.L.U. (Palonosetron Accord), Camurus AB (Buvidal), Eli Lilly Nederland B.V. (Cymbalta, Duloxetine Lilly, Xeristar, Yentreve), Helsinn Birex Pharmaceuticals (Aloxi, Akynzeo), Indivior Europe Limited (Suboxone), Kyowa Kirin Holdings B.V. (Sancuso), L. Molteni & C. dei Fratelli Alitti (Sixmo), Mundipharma Corporation (Nyxoid), Mylan S.A.S (Duloxetine Mylan), Orexo AB (Zubsolv), Zentiva k.s. (Duloxetine Zentiva), various

PRAC Rapporteur: Martin Huber

Scope: Signal of drug-drug interaction with serotonergic drugs leading to serotonin syndrome

Action: For adoption of PRAC recommendation

EPITT 19475 – Follow-up to March 2020

4.3.4. Dabrafenib – TAFINLAR (CAP) - EMEA/H/C/002604/SDA/016; trametinib – MEKINIST (CAP) - EMEA/H/C/002643/SDA/011

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Signal of disseminated intravascular coagulation (DIC)

Action: For adoption of PRAC recommendation

EPITT 19510 – Follow-up to January 2020

4.3.5. Dipeptidyl peptidase-4 (DPP4) inhibitors: alogliptin - VIPIDIA (CAP) - EMEA/H/C/002182/SDA/012.1; alogliptin, metformin hydrochloride - VIPDOMET (CAP) - EMEA/H/C/002654/SDA/009.1; alogliptin, pioglitazone - INCRESYNC (CAP) - EMEA/H/C/002178/SDA/009.1; linagliptin - TRAJENTA (CAP) - EMEA/H/C/002110/SDA/019.1; saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/SDA/044.1; saxagliptin, dapagliflozin - QTERN (CAP) - EMEA/H/C/004057/SDA/007.1; saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/SDA/019.1; sitagliptin – JANUVIA (CAP) - EMEA/H/C/000722/SDA/039.1, RISTABEN (CAP) - EMEA/H/C/001234/SDA/017.1, TESAVEL (CAP) - EMEA/H/C/000910/SDA/033.1, XELEVIA (CAP) - EMEA/H/C/000762/SDA/038.1; NAP; sitagliptin, ertugliflozin – STEGLUJAN (CAP); sitagliptin, metformin – EFFICIB (CAP); JANUMET (CAP); VELMETIA (CAP);NAP; vildagliptin - GALVUS (CAP) - EMEA/H/C/000771/SDA/048.1, JALRA (CAP) - EMEA/H/C/001048/SDA/032.1, XILIARX (CAP) - EMEA/H/C/001051/SDA/032.1; vildagliptin, metformin hydrochloride - EUCREAS (CAP) - EMEA/H/C/000807/SDA/026.1, ICANDRA (CAP) - EMEA/H/C/001050/SDA/024.1, ZOMARIST (CAP) - EMEA/H/C/001049/SDA/024.1; NAP

Applicant(s): AstraZeneca AB (Kombogzyle, Onglyza, Qtern), Boehringer Ingelheim International GmbH (Trajenta), Merck Sharp & Dohme B.V. (Efficib, Janumet, Januvia, Ristaben, Steglujan, Tesavel, Velmetia, Xelevia), Takeda Pharma A/S (Incresync, Vipidia,

Vipdomet), Novartis Europharm Limited (Eucreas, Galvus, Icandra, Jalra, Xiliarx, Zomarist), various

PRAC Rapporteur: Menno van der Elst

Scope: Signal of rhabdomyolysis

Action: For adoption of PRAC recommendation

EPITT 19466 – Follow-up to January 2020

4.3.6. Fluoroquinolones: ciprofloxacin (NAP); delafloxacin – QUOFENIX (CAP); levofloxacin – QUINSAIR (CAP), NAP; lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP)

Applicant(s): A. Menarini Industrie Farmaceutiche Riunite (Quofenix), Chiesi Farmaceutici S.p.A. (Quinsair), various

PRAC Rapporteur: Martin Huber

Scope: Signal of heart valve regurgitation, cervical artery dissection, and aortic aneurysm and dissection

Action: For adoption of PRAC recommendation

EPITT 19522 – Follow-up to January 2020

4.3.7. Hormone replacement therapy (HRT): chlorotrianisene (NAP); conjugated estrogens (NAP); conjugated estrogens, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C002314/SDA 005; dienestrol (NAP); diethylstilbestrol (NAP); estradiol (NAP); estradiol, norethisterone (NAP); estriol (NAP); estrone (NAP); ethinylestradiol (NAP); methallenestril (NAP); moxestrol (NAP); promestriene (NAP); tibolone (NAP)

Applicant(s): Pfizer Europe MA EEIG (Duavive), various

PRAC Rapporteur: Menno van der Elst

Scope: New information on the known risk of breast cancer

Action: For adoption of PRAC recommendation

EPITT 19482 – Follow-up to March 2020

4.3.8. Mirtazapine (NAP)

Applicant(s): various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of amnesia

Action: For adoption of PRAC recommendation

EPITT 19506 – Follow-up to January 2020

4.3.9. Sertraline (NAP)

Applicant(s): various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Signal of microscopic colitis

Action: For adoption of PRAC recommendation

EPITT 19513 – Follow-up to January 2020

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Cobicistat - TYBOST (CAP) - EMEA/H/C/002572/II/0054

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to add a new contraindication regarding drug-drug interactions between cobicistat-containing products and thienopyridines, based on a cumulative safety review conducted by the MAH and related to the final signal recommendation adopted in May 2019 (EPITT 19325) regarding the interaction of clopidogrel with boosted antiviral human immunodeficiency virus (HIV)-therapy leading to insufficient inhibition of platelet aggregation. In addition, the MAH took the opportunity to amend section 2 of the SmPC regarding the amount of sunset yellow FCF aluminium lake (E110) per tablet. Moreover, the MAH took the opportunity to update the product information in accordance with the European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' and to introduce minor linguistic amendments in the product information. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Abicipar pegol - EMEA/H/C/005103

Scope: Treatment of neovascular (wet) age-related macular degeneration (AMD)

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

5.1.2. Acalabrutinib - EMEA/H/C/005299, Orphan

Applicant: AstraZeneca AB

Scope: Treatment of adult patients with chronic lymphocytic leukaemia (CLL), small lymphocytic lymphoma (SLL)

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

5.1.3. Arsenic trioxide - EMEA/H/C/005218

Scope: Treatment of relapsed acute promyelocytic leukaemia (APL)

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

5.1.4. Autologous peripheral blood T cells CD[4]4 and CD 8 selected and CD 3 and CD 28 activated transduced with retroviral vector expressing anti-CD19, CD28/CD3-zeta chimeric antigen receptor and cultured - EMEA/H/C/005102, Orphan

Applicant: Kite Pharma EU B.V, ATMP[5]

Scope (accelerated assessment): Treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)

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

5.1.5. Bevacizumab - EMEA/H/C/005181

Scope: Treatment of metastatic carcinoma of the colon or rectum, metastatic breast cancer and recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer, for the first-line treatment of patients with unresectable advanced, metastatic or recurrent non-small cell lung cancer (NSCLC) as well as the first line treatment of patients with advanced and/or metastatic renal cell cancer

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

5.1.6. Caffeine citrate - EMEA/H/C/005435

Scope: Treatment of primary apnoea

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

5.1.7. Deferiprone - EMEA/H/C/005004, Orphan

Applicant: Apotex B.V

Scope: Treatment of neurodegeneration with brain iron accumulation

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

5.1.8. Eladocagene exuparvovec - EMEA/H/C/005352, Orphan

Applicant: PTC Therapeutics International Limited, ATMP[6]

Scope: Treatment of aromatic L-amino acid decarboxylase (AADC) deficiency

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

5.1.9. Elexacaftor, tezacaftor, ivacaftor - EMEA/H/C/005269, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

Scope (accelerated assessment): Treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one F508del[7] mutation in the CF transmembrane conductance regulator (CFTR) gene

[4] Cluster of differentiation
[5] Advanced therapy medicinal product
[6] Advanced therapy medicinal product
[7] Deletion of a phenylalanine at residue

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

5.1.10. Fampridine - EMEA/H/C/005359

Scope: Treatment of multiple sclerosis

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

5.1.11. Filgotinib - EMEA/H/C/005113

Scope: Treatment of adult patients with moderately to severely active rheumatoid arthritis

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

5.1.12. Rivaroxaban - EMEA/H/C/005279

Scope: Prevention of atherothrombotic events

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

5.1.13. Satralizumab - EMEA/H/C/004788, Orphan

Applicant: Roche Registration GmbH

Scope (accelerated assessment): Treatment of adult and adolescent patients from 12 years of age with neuromyelitis optica spectrum disorders (NMOSD)

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. Asparaginase - SPECTRILA (CAP) - EMEA/H/C/002661/II/0017

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of an updated RMP (version 12) in line with revision 2 of GVP module V on 'Risk management systems' and in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). The milestones and timelines for study MC-Spectrila.1/ALL: a clinical phase 2 trial to describe pharmacokinetics, pharmacodynamics, safety and immunogenicity of Spectrila (asparaginase) with the pharmaceutical active ingredient recombinant L asparaginase in adult subjects with newly diagnosed acute B-Cell lymphoblastic leukaemia are updated in accordance with the newly applied data lock point (DLP) for the RMP

Action: For adoption of PRAC Assessment Report

5.2.2. Autologous $CD34^+$ enriched cell fraction that contains $CD34^+$ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) complementary deoxyribonucleic acid (cDNA) sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/II/0026, Orphan

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP[8]

[8] Advanced therapy medicinal product

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 4.1) to introduce changes to the design of post-authorisation study STRIM-002: a methodology study to investigate the utility of retroviral insertion site analysis in samples from subjects treated with Strimvelis gene therapy, in order to reflect a change in the analysis methodology and shifting the timelines

Action: For adoption of PRAC Assessment Report

5.2.3. Epoetin zeta - RETACRIT (CAP) - EMEA/H/C/000872/II/0094

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 11.1) in order to align the safety concerns of Retacrit (epoetin zeta – biosimilar) to the medicinal product of reference containing epoetin alfa (Eprex). The RMP (version 15.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.4. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/II/0024

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 3.0) in order to include amended study milestones and to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.5. Galsulfase - NAGLAZYME (CAP) - EMEA/H/C/000640/II/0081

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 6.0) in order to update the safety specifications based on a review of the preclinical, clinical, post-marketing and literature data. In addition, the MAH took the opportunity to update the RMP in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

Action: For adoption of PRAC Assessment Report

5.2.6. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/II/0052

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 11.0) to replace the prospective observational cohort study of Flixabi (infliximab) in patients with Crohn's disease (CD) (SB2-G42-CD), with real-world data from the following studies: 1) PERFUSE: a French cohort study with the primary aim to evaluate the persistence of Flixabi (infliximab) treatment over one year; 2) CREDIT: a nationwide German inflammatory bowel disease (IBD) registry: a long term

observation of IBD patients; 3) CEDUR: Czech register of IBD patients on biological therapy

Action: For adoption of PRAC Assessment Report

5.2.7. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/II/0029/G

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Grouped variations consisting of the submission of an updated RMP (version 6.0) in order to: 1) update the list of safety concerns in line with revision 2 of GVP module V on 'Risk management systems'; 2) reclassify the risk of gastrointestinal (GI) perforation as requested in the conclusions of the PSUR single assessment (PSUSA) (PSUSA/00010317/201809) concluded in April 2019

Action: For adoption of PRAC Assessment Report

5.2.8. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - EMEA/H/C/002736/II/0016

Applicant: CO.DON AG, ATMP[9]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 6.0) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). The educational materials described in Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly

Action: For adoption of PRAC Assessment Report

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

5.3.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0033, Orphan

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to revise the frequencies of adverse drug reactions (ADRs) based on safety reports and to add new ADRs based on post-marketing spontaneous reports as requested in the conclusions of the renewal procedure (R/0026) finalised in September 2019. The package leaflet and the RMP (version 9.0) are updated accordingly. The RMP is also brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to introduce minor editorial changes in section 2 of the SmPC and Annex III-A on labelling

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

5.3.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0039

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

[9] Advanced therapy medicinal product

Scope: Extension of indication to include in combination with bevacizumab the treatment of patients with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy, based on the results of pivotal study YO40245 (IMbrave150): a phase 3, open-label, randomised study of atezolizumab in combination with bevacizumab compared with sorafenib in patients with untreated locally advanced or metastatic hepatocellular carcinoma, as well as data from arms A and F of the supportive Phase Ib study GO30140: an open-label, multicentre phase 1b study of the safety and efficacy of atezolizumab administered in combination with bevacizumab and/or other treatments in patients with solid tumours. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the Tecentriq (atezolizumab) 1200 mg concentrate for solution for infusion SmPC are updated. The package leaflet and the RMP (version 13.0) are updated in accordance

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

5.3.3. Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/II/0004/G

Applicant: Dova Pharmaceuticals Ireland Limited

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) extension of indication to include the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments. 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 addition, section 5.3 of the SmPC is updated with data from juvenile toxicity studies; 2) addition of a pack size of 30 tablets with subsequent updates of sections 6.5 and 8 of the SmPC. The package leaflet, labelling and the RMP (version 2.1) are updated in accordance. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.4. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/II/0013

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Update of section 5.1 of the SmPC in order to update efficacy information following results from study EMR100070-003 Part B (listed as a specific obligation in Annex II): a phase 2, open-label, multicentre trial to investigate the clinical activity and safety of avelumab (MSB0010718C) in subjects with Merkel cell carcinoma. The MAH took the opportunity to update Annex II proposing the deletion of the specific obligation and proposing the switch from conditional to full marketing authorisation. The package leaflet and the RMP (version 2.1) are updated accordingly

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

5.3.5. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0021, Orphan

Applicant: Kite Pharma EU B.V., ATMP[10]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Update of sections 4.2, 4.4 and 6.6 of the SmPC to allow clinicians to administer

[10] Advanced therapy medicinal product

Yescarta (axicabtagene ciloleucel) to seriously ill patients with relapsed/refractory non-Hodgkin lymphoma while having on site an adequate supply of tocilizumab (i.e. to ensure that one dose of tocilizumab per patient is available at the treating centres to manage cytokine release syndrome (CRS), in addition, treatment centres should have access to an additional dose within 8 hours of each previous dose). Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product', the package leaflet and the RMP (version 2.4) are updated accordingly

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

5.3.6. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0016

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include a new indication in the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 8.1) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to introduce minor editorial changes to the labelling. Furthermore, Annex II is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.7. Bortezomib - BORTEZOMIB FRESENIUS KABI (CAP) - EMEA/H/C/005074/II/0001/G

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Grouped variations consisting of: 1) addition of a new pack size (EU number- EU/1/19/1397/002) for the sterile parenteral biological medicinal product Bortezomib Fresenius Kabi (bortezomib) powder for solution for injection with a fill volume for a single dose vial of 1 mg per vial in addition to the authorised 3.5 mg per vial; 2) addition of a new pack size within a range (EU number- EU/1/19/1397/003) for the sterile parenteral biological medicinal product Bortezomib Fresenius Kabi (bortezomib) powder for solution for injection with a fill volume for a single dose vial of 2.5 mg per vial in addition to the authorised 3.5 mg per vial. The RMP (version 2.0) is updated accordingly

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

5.3.8. Botulinum toxin type A - NUCEIVA (CAP) - EMEA/H/C/004587/X/0005

Applicant: Evolus Pharma Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to add a new strength of 50 U for botulinum toxin type A for powder for solution for injection in vial (glass) for intramuscular administration. The RMP (version 3.0) is updated accordingly

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

5.3.9. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/X/0058/G

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: 1) extension application to add a new pharmaceutical form associated with new strength (5mg dispersible tablet). The new presentation is indicated for the treatment of human immunodeficiency virus (HIV) infected children from 4 weeks of life and weighing at least 3 kg; 2) update of the currently approved SmPC, labelling and package leaflet for the existing film-coated tablets (10mg, 25mg and 50mg) for children of 6 years and older and weighing at least 15 kg, based on pharmacokinetic (PK), safety, and efficacy data from study P1093: a phase 1/2, multicentre, open-label pharmacokinetic, safety, tolerability and antiviral activity of dolutegravir, a novel integrase inhibitor, in combination regimens in HIV-1 infected infants, children and adolescents and PK and safety data from relevant sub-studies nested within study ODYSSEY (PENTA 20): a phase 2/3 randomised trial of dolutegravir (DTG)-based antiretroviral therapy vs. standard of care (SOC) in children with HIV infection starting first-line or switching to second-line antiretroviral therapy (ART). In addition, the MAH took the opportunity to amend section 4.1 of SmPC to clarify that children should be 'aged at least 6 years' as the current approved indication is inclusive of those aged 6 years. The RMP (version 16) is updated in accordance

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

5.3.10. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0014/G

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Grouped variations consisting of: 1) extension of indication to include the use of Imfinzi (durvalumab) in combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC). The proposed indication is supported by study D419QC00001 (CASPIAN): an ongoing phase 3 randomised, multicentre, open-label, comparative study designed to determine the efficacy and safety of durvalumab, or durvalumab and tremelimumab, in combination with etoposide and platinum-based chemotherapy (EP) for the first-line treatment of patients with ES-SCLC; 2) update of sections 4.4 and 4.8 of the SmPC to update the safety information based on the durvalumab pan-tumour pool: a safety dataset comprising of 9 clinical studies building on the existing safety database and summarising the safety information for durvalumab monotherapy characterised across tumour types in the durvalumab clinical programme to date, The package leaflet and the RMP (version 2.1) are updated in accordance

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

5.3.11. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/II/0047/G

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Grouped variations consisting of: 1) extension of indication to include the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) for Xtandi (enzalutamide) in combination with androgen deprivation therapy (ADT). As a consequence,

sections 4.1, 4.7, 4.8, 5.1, 5.3 and 6.6 of the SmPC are updated. Furthermore the MAH took the opportunity to introduce minor corrections to section 4.7 of the SmPC. The package leaflet and the RMP (version 13.0) are updated accordingly; 2) update of section 5.1 of the SmPC based on the 5-year overall survival (OS) results obtained from study MDV310003 (PREVAIL), a phase 3 study of enzalutamide in chemotherapy naïve patients with metastatic prostate cancer that progressed on ADT

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

5.3.12. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0020

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC to include anaphylactic reactions as an adverse drug reaction. The package leaflet and the RMP (version 5.2) are updated accordingly

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

5.3.13. Human normal immunoglobulin - HYQVIA (CAP) - EMEA/H/C/002491/II/0056

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to replace the therapeutic indications of replacement therapy in hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia and multiple myeloma and hypogammaglobulinaemia in patients with hematopoietic stem cell transplantation (HSCT), by the therapeutic indication of replacement therapy in secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either proven specific antibody failure (PSAF) or serum immunoglobulin G (IgG) level of <4 g/L. As a consequence, sections 4.1 and 4.2 of the SmPC are updated. The package leaflet and the RMP (version 10.0) are updated in accordance

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

5.3.14. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - EMEA/H/C/000721/II/0106

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.4 and 5.1 of the SmPC based on final results from study HPV-019 (listed as a category 3 study in the RMP) (in fulfilment of MEA 080): a safety and immunogenicity study of Cervarix (human papillomavirus vaccine) in human immunodeficiency virus (HIV)-positive female subjects aged 15-25 years as compared to human papillomavirus 4 (HPV-4). In addition, the MAH took the opportunity to reflect an update in section 4.2 of the SmPC to indicate that limited clinical data is now available in 4-6 years old children based on study HPV-073: a safety and immunogenicity study of Cervarix (human papillomavirus vaccine) in girls aged 4-6 years, as an alternative to the current adolescent HPV vaccination schedule. The RMP (version 21.0) is updated accordingly and also reflect the removal of the use of Cervarix (human papillomavirus vaccine) in HIV-infected

subjects or subjects with known immune deficiencies as missing information. Furthermore, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.15. Iron - VELPHORO (CAP) - EMEA/H/C/002705/II/0021

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 5.1 of the SmPC in order to add information related to the results of the VERIFIE study (listed as a category 3 study in the RMP): a non-interventional voluntary PASS trial to investigate the short and long-term real-life safety, effectiveness, and adherence of Velphoro (iron) in patients with hyperphosphataemia undergoing haemodialysis or peritoneal dialysis. Furthermore, minor editorial changes in section 4.2 of the SmPC were introduced to provide consistent information between the SmPC, the labelling and the package leaflet. The RMP (version 8.0) is updated accordingly. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.16. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/II/0026

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment as an adjunct to a healthy nutrition and physical activity counselling for weight management in adolescent patients from the age of 12 years and above with body weight above 60 kg and obesity (body mass index (BMI) corresponding to ≥30 kg/m^2 for adults) based on study NN8022-4180: effect of liraglutide for weight management in pubertal adolescent subjects with obesity, 56-week, double-blind, randomised, parallel-group, placebo-controlled multi-national trial followed by a 26-week period off study-drug. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 32.0) are updated in accordance. The application relates to paediatric studies submitted according to Article 46 of the paediatric regulation

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

5.3.17. Measles, mumps, rubella and varicella vaccine (live) - PROQUAD (CAP) - EMEA/H/C/000622/II/0139

Applicant: MSD Vaccins

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC to amend the safety information and further characterise the risk of secondary transmission following MAH's evaluation of new significant pharmacovigilance data. The package leaflet and the RMP (version 7.1) are updated accordingly. The MAH took the opportunity to implement some changes in section 6.5 of the SmPC with information on the glass type for the immediate container in accordance with the

European Commission (EC) guideline on 'excipients in the labelling and package leaflet of medicinal products for human use' and the guideline on 'quality aspects included in the product information for vaccines for human use'. Annex A is updated accordingly. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1) taking into account the 'compilation of QRD decisions on stylistic matters in product information'. Finally, the MAH took the opportunity to align some wordings with other MAH's measles, mumps, rubella, and varicella (MMRV) vaccines, in particular section 6.6 of the SmPC

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

5.3.18. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/II/0023

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and immunogenicity information based on final results from study B1971033 (listed as a category 3 study in the RMP) (in fulfilment of MEA 007): a duration of immunity study to assess persistence of hSBA (serum bactericidal activity using human complement) response for up to 48 months after completion of vaccination with Trumenba (meningococcal group B vaccine) and the immunogenicity, safety, and tolerability of a booster dose of Trumenba (meningococcal group B vaccine). The RMP (version 3) is updated accordingly and includes changes agreed in variation II/13 as well as editorial changes. In addition, the MAH took the opportunity to introduce editorial changes in Annex II, in the labelling and in the package leaflet

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

5.3.19. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/II/0027, Orphan

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype based on the results of pharmacology studies and the double-blind, randomised, placebo-controlled phase 3 trial (INBUILD). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 9.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor formatting changes in the product information. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.20. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/II/0019, Orphan

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

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

advanced high-grade ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy. As a consequence, sections 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated in accordance. The RMP is also brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template) and includes updated due dates for category 3 studies. Finally, the MAH took the opportunity to introduce minor corrections throughout the product information

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

5.3.21. Nitisinone - ORFADIN (CAP) - EMEA/H/C/000555/II/0071

Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of adult patients with alkaptonuria (AKU). As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1 and 10 of the SmPC are updated. The package leaflet and the RMP (version 5.2) are updated in accordance. The RMP is also brought in line with revision 2 of GVP module V on 'Risk management systems'

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

5.3.22. Prucalopride - RESOLOR (CAP) - EMEA/H/C/001012/II/0051

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of Section 4.4 of the SmPC with suicidal ideation and behaviour and to add 'suicidal ideation and behaviour' to the list of safety concerns as an important potential risk in the RMP based on post-marketing reports. The package leaflet and the RMP (version 16.0) are updated accordingly. The MAH took to opportunity to introduce editorial changes to the RMP and SmPC

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

5.3.23. Ribociclib - KISQALI (CAP) - EMEA/H/C/004213/II/0021

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to add a warning on interstitial lung disease (ILD)/pneumonitis and related dose modification recommendations. The package leaflet and the RMP (version 4.0) are updated accordingly

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

5.3.24. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0057

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include the treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy

for Cosentyx (secukinumab). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 of the SmPC are updated. Section 6.6 of the SmPC for the solution for injection is also updated. The package leaflet and the RMP (version 6.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, Annex II is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.25. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/X/0059

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension application to add a new strength of 300mg (in 2mL) solution for injection in pre-filled syringe and pre-filled pen. The RMP (version 7.0) is updated in accordance

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

5.3.26. Sodium oxybate - XYREM (CAP) - EMEA/H/C/000593/II/0076

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include adolescents and children older than 7 years to the existing indication of treatment of narcolepsy with cataplexy in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 9.0) are updated accordingly

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

5.3.27. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/II/0016, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the information based on final results from study VX14-661-110 (listed as a category 3 study in the RMP): a phase 3, multicentre, open label, rollover study for studies 103, 106, 107, 108, 109, 111, 112 and 114 designed to evaluate the long-term safety and tolerability of tezacaftor/ivacaftor (TEZ/IVA) treatment for 96 weeks in cystic fibrosis (CF) subjects 12 years and older, homozygous or heterozygous for the phenylalanine in position 508 of the cystic fibrosis transmembrane conductance regulator (F508del CFTR) mutation. In addition, the MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1). The RMP (version 2.2) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Alglucosidase alfa - MYOZYME (CAP) - PSUSA/00000086/201909

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Andexanet alfa - ONDEXXYA (CAP) - PSUSA/00010764/201910

Applicant: Portola Netherlands B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Axicabtagene ciloleucel - YESCARTA (CAP) - PSUSA/00010703/201910

Applicant: Kite Pharma EU B.V., ATMP[11]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.4. Bezlotoxumab - ZINPLAVA (CAP) - PSUSA/00010576/201910

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Brigatinib - ALUNBRIG (CAP) - PSUSA/00010728/201910

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[11] Advanced therapy medicinal product

6.1.6. Ceftaroline fosamil - ZINFORO (CAP) - PSUSA/00010013/201910

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Ceritinib - ZYKADIA (CAP) - PSUSA/00010372/201910

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Cerliponase alfa - BRINEURA (CAP) - PSUSA/00010596/201910

Applicant: BioMarin International Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Conestat alfa - RUCONEST (CAP) - PSUSA/00000873/201910

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Deferasirox - EXJADE (CAP) - PSUSA/00000939/201910

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Defibrotide - DEFITELIO (CAP) - PSUSA/00010086/201910 (with RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Delamanid - DELTYBA (CAP) - PSUSA/00010213/201910

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Durvalumab - IMFINZI (CAP) - PSUSA/00010723/201910 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Eculizumab - SOLIRIS (CAP) - PSUSA/00001198/201910

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Edoxaban - LIXIANA (CAP); ROTEAS (CAP) - PSUSA/00010387/201910

Applicant: Daiichi Sankyo Europe GmbH (Lixiana), Berlin Chemie AG (Roteas)

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Glycopyrronium bromide[12] - ENUREV BREEZHALER (CAP); SEEBRI BREEZHALER (CAP); TOVANOR BREEZHALER (CAP) - PSUSA/00010047/201909

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Glycopyrronium bromide, formoterol - BEVESPI AEROSPHERE (CAP) - PSUSA/00010739/201910

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

[12] Centrally authorised product(s) indicated for chronic obstructive pulmonary disease

Action: For adoption of recommendation to CHMP

6.1.18. Granisetron[13] - SANCUSO (CAP) - PSUSA/00010101/201910

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - PSUSA/00010678/201910

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Idarucizumab - PRAXBIND (CAP) - PSUSA/00010435/201910

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Irinotecan[14] - ONIVYDE PEGYLATED LIPOSOMAL (CAP) - PSUSA/00010534/201910

Applicant: Les Laboratoires Servier

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - PSUSA/00010607/201910

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Midostaurin - RYDAPT (CAP) - PSUSA/00010638/201910

Applicant: Novartis Europharm Limited

[13] Transdermal patch
[14] Liposomal formulation(s)

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Nintedanib[15] - OFEV (CAP) - PSUSA/00010319/201910

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Nintedanib[16] - VARGATEF (CAP) - PSUSA/00010318/201910

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Agni Kapou

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Obinutuzumab - GAZYVARO (CAP) - PSUSA/00010279/201910

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Ocriplasmin - JETREA (CAP) - PSUSA/00010122/201910

Applicant: Oxurion NV

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) – FOCLIVIA (CAP); prepandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - PSUSA/00010008/201910

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Respiratory indication(s)
[16] Oncology indication(s)

6.1.29. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/201910

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Pasireotide - SIGNIFOR (CAP) - PSUSA/00009253/201910

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Patiromer - VELTASSA (CAP) - PSUSA/00010618/201910

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Pazopanib - VOTRIENT (CAP) - PSUSA/00002321/201910

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Hans Christian Siersted

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Ranibizumab - LUCENTIS (CAP) - PSUSA/00002609/201910

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Sotagliflozin - ZYNQUISTA (CAP) - PSUSA/00010766/201910

Applicant: Navigant Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Talazoparib - TALZENNA (CAP) - PSUSA/00010781/201910

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/201910

Applicant: Amgen Europe B.V., ATMP[17]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.37. Turoctocog alfa - NOVOEIGHT (CAP) - PSUSA/00010138/201910

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

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. Buprenorphine, naloxone - SUBOXONE (CAP); ZUBSOLV (CAP); NAP - PSUSA/00002113/201909

Applicants: Indivior Europe Limited (Suboxone), Orexo AB (Zubsolv), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Methotrexate - JYLAMVO (CAP); NORDIMET (CAP); NAP - PSUSA/00002014/201910

Applicants: Nordic Group B.V. (Nordimet), Therakind (Europe) Limited (Jylamvo), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[17] Advanced therapy medicinal product

6.2.3. Midazolam[18] [19] - BUCCOLAM (CAP); NAP - PSUSA/00010118/201909

Applicants: Shire Services BVBA (Buccolam), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Sodium oxybate[20] - XYREM (CAP); NAP - PSUSA/00010612/201910

Applicants: UCB Pharma S.A. (Xyrem), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Acitretin (NAP) - PSUSA/00000051/201910

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Ambrosia artemisiifolia[21] [22] [23] [24] (NAP) - PSUSA/00010693/201910

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Ambroxol (NAP) - PSUSA/00000130/201909

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[18] Oromucosal solution
[19] Indicated for the treatment of prolonged, acute, convulsive seizures
[20] Oral use
[21] Allergen for therapy
[22] (302)
[23] Sublingual use
[24] Medicinal product(s) authorised via decentralised procedure

6.3.4. Ambroxol, clenbuterol (NAP) - PSUSA/00000131/201909

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Aminosalicylate sodium (NAP) - PSUSA/00000165/201910

Applicant(s): various

PRAC Lead: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Artemether, lumefantrine[25] (NAP) - PSUSA/00000236/201910

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Atenolol, chlortalidone (NAP) - PSUSA/00000260/201909

Applicant(s): various

PRAC Lead: Marek Juračka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Betamethasone, tetryzoline (NAP) - PSUSA/00010072/201909

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Bromhexine (NAP) - PSUSA/00000437/201909

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[25] All except dispersible tablet(s)

6.3.10. Carbidopa, levodopa (NAP) - PSUSA/00000548/201910

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Chlorquinaldol[26], promestriene (NAP) - PSUSA/00009272/201909

Applicant(s): various

PRAC Lead: Roxana Stefania Stroe

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Clenbuterol (NAP) - PSUSA/00000794/201909

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Dinoprostone (NAP) - PSUSA/00001104/201909

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Drospirenone, ethinylestradiol (NAP) - PSUSA/00010217/201909

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Felbamate (NAP) - PSUSA/00010155/201909

Applicant(s): various

PRAC Lead: Ghania Chamouni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[26] Vaginal tablet(s)

6.3.16. Hexaminolevulinate hydrochloride (NAP) - PSUSA/00001606/201909

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Levosimendan (NAP) - PSUSA/00001858/201909

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Methylphenidate (NAP) - PSUSA/00002024/201910

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Opium (NAP) - PSUSA/00010670/201909

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Pramiracetam (NAP) - PSUSA/00002492/201909

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. 1-Propanol, 2-propanol, lactic acid (NAP) - PSUSA/00010414/201909

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Sumatriptan (NAP) - PSUSA/00002832/201909

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Technetium (^{99m}Tc) bicisate (NAP) - PSUSA/00002856/201910

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Valsartan, rosuvastatin (NAP) - PSUSA/00010735/201910

Applicant(s): various

PRAC Lead: Gabriela Jazbec

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Aflibercept - EYLEA (CAP) - EMEA/H/C/002392/LEG 018

Applicant: Bayer AG

PRAC Rapporteur: Ghania Chamouni

Scope: Detailed review of available epidemiological and clinical data to estimate background incidence of retinal artery occlusion (RAO) in the population with similar risk profile as that treated with Eylea (aflibercept) together with a discussion on potential pathophysiological mechanisms for development of RAO, an overview of pharmacokinetic (PK) and pharmacodynamic (PD) data on systemic exposure including the potential for occurrence of systemic adverse reactions as well as an updated causality assessment of all RAO events as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010020/201811) adopted by PRAC in June 2019

Action: For adoption of advice to CHMP

6.4.2. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/LEG 016

Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Analysis of available mortality data from controlled clinical trials in the dexmedetomidine development programme as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000998/201903) adopted in November 2019

Action: For adoption of advice to CHMP

6.4.3. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/LEG 012.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 012 [detailed review on weight gain as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/201901) adopted by PRAC in September 2019] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

6.4.4. Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/LEG 009.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 009 [detailed review on weight gain as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/201901) adopted by PRAC in September 2019] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

6.4.5. Dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/LEG 004.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: MAH's response to LEG 004 [detailed review on weight gain as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/201901) adopted by PRAC in September 2019] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

6.4.6. Levetiracetam - KEPPRA (CAP) - EMEA/H/C/000277/LEG 088.1

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Laurence de Fays

Scope: MAH's response to LEG 088 [cumulative review of cases of cardiac arrhythmia and cases of torsades de pointes/QT prolongation as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001846/201811) adopted in July 2019] as per the request for supplementary information (RSI) adopted in February 2020

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Dupilumab - DUPIXENT (CAP) – EMEA/H/C/004390/II/0030

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.8 of the SmPC to include arthralgia as a new adverse drug reaction (ADR) with a frequency not known, based on a safety review of post marketing data and as per the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010645/201909) adopted in April 2020

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[27]

7.1.1. Cholic acid – ORPHACOL (CAP) - EMEA/H/C/PSA/S/0051

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Amendment to a protocol previously agreed in the initial marketing authorisation procedure for a patient surveillance database to monitor accumulating data on efficacy and safety in the treatment of inborn errors in primary bile acid synthesis due to 3β-hydroxy-Δ5-C27-steroid oxidoreductase deficiency or Δ4-3-oxosteroid-5β-reductase deficiency with Orphacol (cholic acid) in infants, children, adolescents and adults

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

7.1.2. Deferasirox – EXJADE (CAP) - EMEA/H/C/PSA/S/0052

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Ghania Chamouni

Scope: Amendment to a protocol previously agreed in March 2016 (PSP/0010.4.A.2) 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

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[28]

7.2.1. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/MEA 092

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

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

Scope: Protocol for study 20190404: a retrospective cohort study to assess the use of erythropoiesis stimulating agents (ESAs) in subjects receiving myelosuppressive chemotherapy in Europe

Action: For adoption of advice to CHMP

7.2.2. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 006.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: MAH's response to MEA 006 [protocol for study H9X-MC-B013 (listed as a category 3 study in the RMP): a non-interventional retrospective study to estimate the incidence rates of events of interest among type 2 diabetes mellitus (T2DM) patients treated with dulaglutide compared to other glucagon-like peptide 1 (GLP-1) receptor agonists in order to better characterise the safety profile of dulaglutide in terms of acute pancreatitis, pancreatic and thyroid malignancies] as per the request for supplementary information (RSI) adopted in October 2019

Action: For adoption of advice to CHMP

7.2.3. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/MEA 002.14

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002.13 [substantial amendment to a protocol previously agreed in May 2015 for ongoing US study B2311060 (listed as a category 3 study in the RMP): a study to estimate the incidence and to compare the risks of endometrial hyperplasia and endometrial cancer in postmenopausal women initiating either Duavive (estrogens conjugated/bazedoxifene) or estrogen + progestin (E+P) combination hormone replacement therapy (HRT)] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

7.2.4. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/MEA 002.5

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002.4 [amendment to protocol previously agreed in January 2019 for study INSLIC08571 (listed as a category 3 study in the RMP): a cross-sectional multinational, multichannel survey conducted among healthcare professionals and patients to measure the effectiveness of Suliqua (insulin glargine/lixisenatide) educational materials set up to evaluate the knowledge and understanding of the key safety messages in the healthcare professional guide and the patient guide] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.2.5. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/MEA 046.4

Applicant: Celgene Europe BV

PRAC Rapporteur: Ghania Chamouni

Scope: MAH's response to MEA 046.3 [substantial amendment (version 4.0) to a protocol previously endorsed in November 2017 for study CC-5013-MCL-005 to further investigate and characterise the association of lenalidomide and tumour flare reaction (TFR)/high tumour burden following the extension of indication for the treatment of adult patients with relapsed and/or refractory mantle cell lymphoma (RRMCL) [final clinical study report (CSR) expected in December 2022] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

7.2.6. Micafungin - MYCAMINE (CAP) - EMEA/H/C/000734/MEA 015.11

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Protocol for study 9463-PV-0002 (listed ads a category 3 study in the RMP): a non-interventional PASS on the effectiveness of the updated prescriber checklist for Mycamine (micafungin)

Action: For adoption of advice to CHMP

7.2.7. Naldemedine - RIZMOIC (CAP) - EMEA/H/C/004256/MEA 001.1

Applicant: Shionogi B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 001 [protocol for an observational PASS of patients with chronic opioid use for non-cancer and cancer pain who have opioid-induced constipation (OIC) [final clinical study report (CSR) expected in January 2026)] as per the request for supplementary information (RSI) adopted in December 2019

Action: For adoption of advice to CHMP

7.2.8. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 003.1

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 003 [protocol for study PUMA-NER-7402: a non-interventional study exploring the safety of neratinib among breast cancer patients to characterise the incidence and duration of diarrhoea in a real world setting, to describe patient characteristics, incidence rates and duration of diarrhoea, to describe use of loperamide and other concomitant anti-diarrhoeal medication, describe adherence to neratinib therapy, assess the impact of neratinib therapy on patient self-reported, health related quality of life and their ability to perform their activities of daily living and to further assess and characterise adverse events hepatic, cardiac, pulmonary, reproductive and developmental toxicity] as per the request for supplementary information (RSI) adopted in July 2019

Action: For adoption of advice to CHMP

7.2.9. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 004.1

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 004 [protocol for study PUMA-NER-7403: a study to evaluate the availability, interpretability, and impact of Nerlynx (neratinib) educational materials] as per the request for supplementary information (RSI) adopted in July 2019

Action: For adoption of advice to CHMP

7.2.10. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 013

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study A3921344 (listed as a category 3 study in the RMP): an active surveillance, post-authorisation study to characterise the safety of tofacitinib in patients with moderately to severely active ulcerative colitis (UC) in the real-world setting using data from the Swedish Quality Register for Inflammatory Bowel Disease (SWIBREG) registry as requested in the conclusions of procedure X/0005/G finalised in May 2018 and in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[29]

7.3.1. Brentuximab vedotin – ADCETRIS (CAP) - EMEA/H/C/PSR/S/0022

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to PSR/S/002 [results for study MA25101: an observational cohort study of the safety of brentuximab vedotin in the treatment of relapsed or refractory CD30+ Hodgkin lymphoma and relapsed or refractory systemic anaplastic large cell lymphoma (sALCL) evaluating the occurrence of serious adverse events (SAEs) and adverse events of special interest (AESIs) and identifying and describing potential risk factors for peripheral neuropathy] as per the request for supplementary information (RSI) adopted January 2020

Action: For adoption of recommendation to CHMP

7.3.2. Teicoplanin (NAP) - EMEA/H/N/PSR/S/0025

Applicant: Sanofi (Targocid)

PRAC Rapporteur: Martin Huber

Scope: Results for a PASS study: a prospective, observational cohort, evaluating the incidence of nephrotoxicity and other adverse events of interest in patients treated with the higher

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

recommended teicoplanin loading dose (12mg/kg twice a day), and comparison with external historical comparator data

Action: For adoption of recommendation to CHMP

7.4. Results of PASS non-imposed in the marketing authorisation(s)[30]

7.4.1. Anakinra - KINERET (CAP) - EMEA/H/C/000363/II/0073

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Hans Christian Siersted

Scope: Submission of the final report from study Sobi.ANAKIN-302 (listed as a category 3 study in the RMP): a non-interventional PASS to evaluate the long-term safety of Kineret (anakinra) in patients with systemic juvenile idiopathic arthritis. The RMP (version 5.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - EMEA/H/C/002246/II/0047, Orphan

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study MW2013-06-01 (listed as a category 3 study in the RMP): an international, observational retrospective, data-collection study assessing efficacy of applied risk-minimisation measures in burn patients treated with NexoBrid (concentrate of proteolytic enzymes enriched in bromelain). The RMP (version 7.0) is updated accordingly. In addition, the MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and to change the due dates for: 1) study MW2013-06-01 (listed as a category 3 study in the RMP): a drug utilisation study (DUS) for further evaluation of the effectiveness of the risk minimisation activities; 2) study MW2010-03-02 (DETECT) (listed as a category 3 study in the RMP): a multicentre, multinational, randomized, controlled, open-label study, performed in subjects with thermal burns, to evaluate the efficacy and safety of NexoBrid (concentrate of proteolytic enzymes enriched in bromelain) as compared to standard of care (SOC) treatment

Action: For adoption of PRAC Assessment Report

7.4.3. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1742/0037; FORXIGA (CAP) - EMEA/H/C/002322/WS1742/0056; dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS1742/0043; XIGDUO (CAP) - EMEA/H/C/002672/WS1742/0054

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Update of section 4.4 of the SmPC based on the final results of a PASS (listed as a category 3 study in the RMPs): a meta-analysis across the following studies: 1) study D1690C00018: a 24-week, multicentre, randomised, double-blind, age-stratified, placebo

[30] 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

controlled, phase 3 study with a 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg once daily in patients with type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD) and hypertension who exhibit inadequate glycaemic control on usual care; 2) study D1690C00019: A 24-week, multicentre, randomised, double-blind, age-stratified, placebo controlled phase 3 study with an 80-week extension period to evaluate the efficacy and safety of dapagliflozin 10 mg once daily in patients with T2DM and CVD, who exhibit inadequate glycaemic control on usual care; 3) study D1693C00001 (DECLARE): a multicentre, randomized, double-blind, placebo-controlled trial to evaluate the effect of dapagliflozin 10 mg once daily on the incidence of cardiovascular death, myocardial infarction or ischemic stroke in patients with T2DM, for analysis of lower limb amputation and relevant preceding adverse events. The package leaflets are updated accordingly. In addition, the MAH took the opportunity to implement a minor editorial change in the product information of Edistride (dapagliflozin). The RMPs (version 19 for Edistride/Forxiga (dapagliflozin) and version 12 for Ebymect/Xigduo (dapagliflozin/metformin) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.4. Degarelix - FIRMAGON (CAP) - EMEA/H/C/000986/II/0037

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Ghania Chamouni

Scope: Update of Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' in order to revise the additional risk minimisation measures (educational programme) based on previous assessment and results from study FE 200486 CS39: a prospective observational safety study in patients with advanced prostate cancer treated with Firmagon (degarelix) or a gonadotropin-releasing hormone (GnRH) agonist conducted in multiple countries in the European Economic Area (EEA). As a consequence, the RMP (version 16.0) is updated accordingly. The MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems', to bring the product information in line with the latest quality review of documents (QRD) template (version 10.1) and to propose a combination of different strengths in the product information

Action: For adoption of PRAC Assessment Report

7.4.5. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS1760/0024; ROTEAS (CAP) - EMEA/H/C/004339/WS1760/0011

Applicant(s): Daiichi Sankyo Europe GmbH (Lixiana), Berlin Chemie AG (Roteas)

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final study report from study ETNA-DUS (listed as a category 3 study in the RMP): the edoxaban treatment in routine clinical practice drug utilisation study, a retrospective drug utilisation chart review study to gain insight on how edoxaban is used in real practice, to identify prescription patterns and to measure the effectiveness of the educational programmes

Action: For adoption of PRAC Assessment Report

7.4.6. Safinamide - XADAGO (CAP) - EMEA/H/C/002396/II/0035

Applicant: Zambon S.p.A.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final clinical study report (CSR) for study Z7219N02 (listed as a category 3 study in the RMP): a European multicentre retrospective-prospective cohort study to observe safinamide safety profile and pattern of use in clinical practice during the first post-commercialisation phase (SYNAPSES). The RMP (version 6.2) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Aclidinium - BRETARIS GENUAIR (CAP) - EMEA/H/C/002706/ANX 001.8

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to ANX 001.7 [second interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of aclidinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients in the UK. This is a sub-study report addressing the heart failure component of the PASS programme. It also includes stroke and acute myocardial infarction (AMI) incidence rate descriptive analysis] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.5.2. Aclidinium - EKLIRA GENUAIR (CAP) - EMEA/H/C/002211/ANX 001.8

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to ANX 001.7 [second interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of aclidinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients in the UK. This is a sub-study report addressing the heart failure component of the PASS programme. It also includes stroke and acute myocardial infarction (AMI) incidence rate descriptive analysis] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.5.3. Aclidinium, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP) - EMEA/H/C/003969/ANX 003.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to ANX 003.4 [second interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of aclidinium bromide-containing products

versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients in the UK. This is a sub-study report addressing the heart failure component of the PASS programme. It also includes stroke and acute myocardial infarction (AMI) incidence rate descriptive analysis] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.5.4. Aclidinium, formoterol fumarate dihydrate - DUAKLIR GENUAIR (CAP) - EMEA/H/C/003745/ANX 003.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to ANX 003.4 [second interim report for study D6560R00004, formerly M/34273/44, (listed as a category 1 in Annex II and the RMP): an observational study evaluating the risk of cardiovascular endpoints of aclidinium bromide-containing products versus other chronic obstructive pulmonary disease (COPD) medications in COPD patients in the UK. This is a sub-study report addressing the heart failure component of the PASS programme. It also includes stroke and acute myocardial infarction (AMI) incidence rate descriptive analysis] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.5.5. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 065.10

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Eleventh interim annual report for study P10-023, a psoriasis patient registry: a 10-year, post-marketing observational study to assess the long term safety of Humira (adalimumab) in adult patients with chronic plaque psoriasis (PS) [final registry report expected in February 2023] together with MAH’s response to MEA 065.9 adopted in May 2019

Action: For adoption of advice to CHMP

7.5.6. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 048.8

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual update report on recruitment for study IM101240 (listed as a category 3 study in the RMP): an observational registry of abatacept in patients with juvenile idiopathic arthritis (JIA registry) to explore the long-term safety of abatacept treatment for JIA in routine clinical practice by quantifying the incidence rates of serious infections, autoimmune disorders and malignancies [final registry report expected by 2029]

Action: For adoption of advice to CHMP

7.5.7. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/MEA 002.2

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: First yearly interim progress update report for study MS100070-0031 (listed as a category 3 study in the RMP): a non-interventional cohort study to assess characteristics and management of patients with Merkel cell carcinoma (MCC) in Germany [final study report expected in Q1/2024]

Action: For adoption of advice to CHMP

7.5.8. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/MEA 001.3

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 001.2 [interim report for study F-FR-60000-001 (CASSIOPE): a prospective non-interventional study of the utilisation of cabozantinib tablets in adults with advanced renal cell carcinoma (RCC) following prior vascular endothelial growth factor (VEGF)-targeted therapy in real life settings in terms of dose modifications due to adverse events (AEs) when used as a second line therapy or third and later line therapy] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.5.9. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/MEA 003

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Tenth annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.10. Lesinurad - ZURAMPIC (CAP) - EMEA/H/C/003932/ANX 002.3

Applicant: Grunenthal GmbH

PRAC Rapporteur: Eva Segovia

Scope: Annual progress report for study D5310R00016: an observational PASS of lesinurad patients (SATURATES) to further assess cardiovascular (CV) safety with a focus on major adverse cardiovascular events (MACE) in gout patients treated with Zurampic (lesinurad) in combination with a xanthine oxidase inhibitor (XOI)

Action: For adoption of advice to CHMP

7.5.11. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/002789/ANX 004.4

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Second annual interim report for a post-marketing, open-label, observational safety

study of Quinsair (nebulised levofloxacin hemihydrate) in patients with cystic fibrosis and chronic *Pseudomonas aeruginosa* infection, using data collected through European cystic fibrosis registries [final clinical study report (CSR) expected in June 2022]

Action: For adoption of advice to CHMP

7.5.12. Nomegestrol acetate, estradiol - ZOELY (CAP) - EMEA/H/C/001213/ANX 011.5

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Adrien Inoubli

Scope: Fourth interim report for a prospective observational study to assess the risk of venous thromboembolic events (VTE) and arterial thromboembolic events (ATE) in nomegestrel/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

7.5.13. Octocog alfa - KOGENATE BAYER (CAP) - EMEA/H/C/000275/MEA 086.8

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Tenth annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.14. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/MEA 004.2

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Tenth annual European Haemophilia Safety Surveillance (EUHASS) report for study 14149 (listed as a category 3 study in the RMP): evaluation of cases with adverse events (AEs) of special interest in the EUHASS registry [final clinical study report (CSR) expected in December 2021]

Action: For adoption of advice to CHMP

7.5.15. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 006.2

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Third interim clinical study report (CSR) for study M12-175 (listed as a category 3 study in the RMP): a phase 1 study evaluating the safety and pharmacokinetics of venetoclax (ABT-199) in subjects with relapsed or refractory chronic lymphocytic leukaemia and non-Hodgkin lymphoma; together with MAH's response to MEA 006.1 adopted in December 2019

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 031

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Feasibility report for study D2019-6798: review of the possibility to undertake a PASS within established registries, to further characterise the safety of Benlysta (belimumab) in children with systemic lupus erythematosus (SLE) with particular focus on infections (from the conclusions of variation II/0062 on the extension of the indication to include patients with systemic lupus erythematosus (SLE) aged 5 years and older adopted in September 2019)

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)

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/S/0033 (without RMP)

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/R/0057 (without RMP)

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/R/0017 (without RMP)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Hans Christian Siersted

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Larotrectinib - VITRAKVI (CAP) - EMEA/H/C/004919/R/0006 (without RMP)

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Aripiprazole - ARIPIPRAZOLE ACCORD (CAP) - EMEA/H/C/004021/R/0019 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Brivaracetam - BRIVIACT (CAP) - EMEA/H/C/003898/R/0025 (without RMP)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Cinacalcet - CINACALCET MYLAN (CAP) - EMEA/H/C/004014/R/0011 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/R/0038 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/R/0046 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - EMEA/H/C/004042/R/0069 (with RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Everolimus - VOTUBIA (CAP) - EMEA/H/C/002311/R/0065 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Guanfacine - INTUNIV (CAP) - EMEA/H/C/003759/R/0022 (without RMP)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Idarucizumab - PRAXBIND (CAP) - EMEA/H/C/003986/R/0019 (with RMP)

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/R/0020 (without RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Isavuconazole - CRESEMBA (CAP) - EMEA/H/C/002734/R/0027 (without RMP)

Applicant: Basilea Pharmaceutica Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Lumacaftor, ivacaftor - ORKAMBI (CAP) - EMEA/H/C/003954/R/0056 (with RMP)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Pemetrexed - CIAMBRA (CAP) - EMEA/H/C/003788/R/0006 (without RMP)

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Ghania Chamouni

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/R/0033 (with RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.15. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/R/0039 (without RMP)

Applicant: Amgen Europe B.V., ATMP[31]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

[31] Advanced therapy medicinal product

8.3.16. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/R/0045 (without RMP)

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0063

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: PRAC consultation on an update of sections 4.4 and 4.8 of the SmPC to reflect progressive multifocal leukoencephalopathy (PML) in the setting of mild lymphopenia based on data submitted in the ongoing PSUSA/00010143/201903 due for recommendation at the November 2019 PRAC meeting. The package leaflet is updated accordingly. Additionally, the Product Information has been updated in line with the quality review of documents (QRD) template (version 10.1)

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. Paracetamol[32], tramadol (NAP) - HU/H/0190/003/II/035

Applicant: Krka, d.d., Novo mesto (Doreta SR)

PRAC Lead: Julia Pallos

Scope: PRAC consultation on a type II variation procedure in the decentralised procedure (DCP) to update the RMP (version 3.0) for tramadol/paracetamol 75 mg/650 mg prolonged-release tablet to provide evidence in support of proportionate, feasible and effective measures to prevent the risk of overdose and minimise the risk of hepatic injury following intentional or accidental overdoses with the medicinal product to lift the suspension concluded in the referral procedure under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1445) finalised in December 2017, on request of Hungary

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 working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals -Q1 2020

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

[32] modified release

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic – update

Action: For discussion

12.4.2. PRAC strategic review and learning meeting (SRLM) under the Croatian presidency of the European Union (EU) Council - Split, Croatia, 02-04 June 2020 - cancellation

PRAC lead: Nikica Mirošević Skvrce, Željana Margan Koletić

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

None

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system – quarterly workload measures and performance indicators - Q1 2020 and predictions

PRAC lead: Ulla Wändel Liminga, Martin Huber, Menno van der Elst, Ghania Chamouni, Jan Neuhauser

Action: For discussion

12.8.2. PRAC workload statistics – Q1 2020

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, 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: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.15.3. Good pharmacovigilance practices (GVP) module VIII on 'Post-authorisation safety studies (PASS)' – Addendum I - revision 3

Action: For adoption

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Others

12.20.1. Drug-induced hepatotoxicity - PRAC assessors' guide - draft

PRAC lead: Menno van der Elst, Martin Huber

Action: For adoption

12.20.2. Good Pharmacovigilance Practice (GVP) - update on GVP status overview

Action: For discussion

12.20.3. Serious cutaneous adverse reactions (SCARs) - PRAC assessors' guide - update

PRAC lead: Sabine Straus, Zane Neikena

Action: For adoption

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/