07 March 2022
EMA/PRAC/76497/2022
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 07-10 March 2022

Chair: Sabine Straus – Vice-Chair: Martin Huber

07 March 2022, 10:30 – 19:30, via teleconference

08 March 2022, 08:30 – 19:30, via teleconference

09 March 2022, 08:30 – 19:30, via teleconference

10 March 2022, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

24 March 2022, 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 07-10 March 2022. See March 2022 PRAC minutes (to be published post April 2022 PRAC meeting).

1.2. Agenda of the meeting on 07-10 March 2022

Action: For adoption

1.3. Minutes of the previous meeting on 07-10 February 2022

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

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Selective serotonin reuptake transporter inhibitors (SSRIs): citalopram (NAP); escitalopram (NAP); fluoxetine (NAP); fluvoxamine (NAP); paroxetine (NAP); sertraline (NAP)
serotonin-norepinephrine reuptake inhibitor (SNRIs): desvenlafaxine (NAP); duloxetine – CYMBALTA (CAP), DULOXETINE LILLY (CAP), DULOXETINE MYLAN (CAP), DULOXETINE ZENTIVA (CAP), YENTREVE (CAP), NAP; milnacipran (NAP); venlafaxine (NAP)
mirtazapine (NAP); vortioxetine - BRINTELLIX (CAP)

Applicant(s): Eli Lilly Nederland B.V. (Cymbalta, Duloxetine Lilly, Yentreve), H. Lundbeck A/S (Brintellix), Mylan Pharmaceuticals Limited (Duloxetine Mylan), Zentiva k.s. (Duloxetine Zentiva), various

PRAC Rapporteur: To be appointed

Scope: Signal of pulmonary hypertension

Action: For adoption of PRAC recommendation

EPITT 19772 – New signal

Lead Member State(s): BE, ES, FR, LT, NL, SE

4.2. New signals detected from other sources

4.2.1. Pneumococcal polysaccharide vaccine (23 serotypes) (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

[1] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[2] Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

Scope: Signal of extensive swelling of vaccinated limb

Action: For adoption of PRAC recommendation

EPITT 19768 – New signal

Lead Member State(s): DE

4.2.2. Tocilizumab - ROACTEMRA (CAP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of pancreatitis

Action: For adoption of PRAC recommendation

EPITT 19777 – New signal

Lead Member State(s): DE

4.3. Signals follow-up and prioritisation

4.3.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/SDA/012

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of vitiligo

Action: For adoption of PRAC recommendation

EPITT 19737 – Follow-up to November 2021

4.3.2. Cannabidiol – EPIDYOLEX (CAP); calcineurin inhibitors[3]: ciclosporin (NAP); tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/SDA/031, ENVARSUS (CAP) - EMEA/H/C/002655/SDA/003, MODIGRAF (CAP) - EMEA/H/C/000954/SDA/023, TACFORIUS (CAP) - EMEA/H/C/004435/SDA/004, NAP mammalian target of rapamycin (mTOR) inhibitors[4]: everolimus – AFINITOR (CAP) - EMEA/H/C/001038/SDA/033, VOTUBIA (CAP) - EMEA/H/C/002311/SDA/033, NAP; sirolimus – RAPAMUNE (CAP) - EMEA/H/C/002311/SDA/055; temsirolimus – TORISEL (CAP) - EMEA/H/C/000799/SDA/038, NAP

Applicant(s): Astellas Pharma Europe B.V. (Advagraf, Modigraf), Chiesi Farmaceutici S.p.A. (Envarsus), GW Pharma (International) B.V. (Epidyolex), Novartis Europharm Limited (Afinitor, Votubia), Pfizer Europe MA EEIG (Rapamune, Torisel), Teva B.V. (Tacforius), various

PRAC Rapporteur: Ronan Grimes

Scope: Signal of drug interaction with cannabidiol leading to calcineurin inhibitors and

[3] For systemic use
[4] For systemic use

mTOR inhibitors serum levels increased and toxicity

Action: For adoption of PRAC recommendation

EPITT 19614 – Follow-up to June 2021

4.3.3. Elasomeran (previously coronavirus (COVID-19) mRNA[5] vaccine (nucleoside-modified))- SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/052.1; tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/051

Applicant: BioNTech Manufacturing GmbH (Comirnaty), Moderna Biotech Spain, S.L. (Spikevax)

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of capillary leak syndrome

Action: For adoption of PRAC recommendation

EPITT 19743 – Follow-up to January 2022

4.3.4. Sacubitril, valsartan – ENTRESTO (CAP) - EMEA/H/C/004062/SDA/010, NEPARVIS (CAP) - EMEA/H/C/004343/SDA/008

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of vasoplegia syndrome

Action: For adoption of PRAC recommendation

EPITT 19739 – Follow-up to November 2021

4.4. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Doxorubicin hydrochloride - EMEA/H/C/005330

Scope: Treatment of breast cancer, ovarian cancer, multiple myeloma, and acquired immunodeficiency syndrome (AIDS) related Kaposi's sarcoma

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

[5] Messenger ribonucleic acid

5.1.2. Eptacog beta (activated) - EMEA/H/C/005655

Scope: Treatment of bleeding episodes and prevention of bleeding in patients undergoing surgery or invasive procedures, in children and adults congenital haemophilia A or B patients

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

5.1.3. Ertapenem - EMEA/H/C/005815

Scope: Treatment of bacterial infections and prophylaxis of surgical site infection following elective colorectal surgery

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

5.1.4. Ganirelix - EMEA/H/C/005641

Scope: Prevention of premature luteinising hormone (LH) surges in women undergoing controlled ovarian hyperstimulation (COH) for assisted reproduction techniques (ART)

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

5.1.5. Melphalan flufenamide - EMEA/H/C/005681, Orphan

Applicant: Oncopeptides AB

Scope: Treatment of multiple myeloma

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

5.1.6. Mitapivat - EMEA/H/C/005540, Orphan

Applicant: Agios Netherlands B.V.

Scope: Treatment of pyruvate kinase deficiency

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

5.1.7. Sitagliptin, metformin hydrochloride - EMEA/H/C/005850

Scope: Treatment of type 2 diabetes mellitus

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

5.1.8. Sugammadex - EMEA/H/C/005760

Scope: Reversal of neuromuscular blockade induced by rocuronium or vecuronium

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

5.1.9. Tabelecleucel - EMEA/H/C/004577, PRIME, Orphan

Applicant: Atara Biotherapeutics Ireland Limited, ATMP[6]

Scope (accelerated assessment): Treatment of Epstein-Barr virus positive post-transplant lymphoproliferative disease (EBV$^+$ PTLD)

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

5.1.10. Tezepelumab - EMEA/H/C/005588

Scope: Add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma

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

5.1.11. Tixagevimab, cilgavimab - EMEA/H/C/005788

Scope: Prophylaxis of coronavirus disease 2019 (COVID-19) in adults 18 years of age and older

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. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/WS2210/0076; dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/WS2210/0100; dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/WS2210/0028; dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/WS2210/0041

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Submisson of updated RMPs for Tivicay (dolutegravir - RMP version 17), Triumeq (dolutegravir/abacavir/lamivudine – RMP version 18), Dovato (dolutegravir/lamivudine – RMP version 2) and Juluca (dolutegravir/rilpivirine – RMP version 3) following the completion of worksharing variation WS1810 finalised in January 2021 that assessed the final report for study 201177 (EuroSIDA) (listed as a category 3 study in the RMP): a prospective observational cohort study on clinical and virological outcome of European patients infected with human immunodeficiency virus (HIV). In addition, the MAH took the opportunity to propose a harmonisation of the risks across all 4 dolutegravir-containing product RMPs and other minor updates (including study details and epidemiology data)

Action: For adoption of PRAC Assessment Report

5.2.2. Duloxetine - DULOXETINE MYLAN (CAP), NAP - EMEA/H/C/003981/WS2214/0029

Applicant: Mylan Pharmaceuticals Limited

[6] Advanced therapy medicinal product

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of an updated RMP (version 5.0) in order to align the RMP with that of the originator duloxetine-containing product. The MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and to achieve one RMP covering multiple different marketing authorisations containing the same active substance for which the MAH has an approved RMP. The RMP is also updated with the results of a follow-up questionnaire pertaining to suicidality as recommended in renewal procedure (R/0021) finalised in December 2019

Action: For adoption of PRAC Assessment Report

5.2.3. Fentanyl - EFFENTORA (CAP), NAP - EMEA/H/C/000833/WS2212/0060

Applicant: Teva B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 5.1) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and to implement PRAC requests arising from previous assessments as follows: 1) revision of the list of safety concerns; 2) update of the key messages of the educational materials in line with another centrally authorised product containing fentanyl. As a result, Annex II on additional risk minimisation measures is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.4. Fentanyl - PECFENT (CAP) - EMEA/H/C/001164/II/0054

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 7.1) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA 00001369/202004) finalised in January 2021 in order to update the key messages of the educational materials in line with another centrally authorised product containing fentanyl. As a result, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. Finally, the MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and the product information in line with the latest quality review of documents (QRD) template (version 10.2)

Action: For adoption of PRAC Assessment Report

5.2.5. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/II/0026, Orphan

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 3.1) to remove carcinogenicity in rats as missing information and to add a targeted questionnaire as routine pharmacovigilance measure and a patient alert card as additional risk minimisation for liver transplant rejection. In addition, the RMP is updated to add 'injection site reactions' and

'immunogenicity' as risks not considered important for inclusion in the list of safety concerns (S.VII.1.1) and to update the patient alert card with additional warnings on hepatic monitoring and ocular toxicity. The MAH took the opportunity to include further minor updates to the RMP

Action: For adoption of PRAC Assessment Report

5.2.6. Lurasidone - LATUDA (CAP) - EMEA/H/C/002713/II/0037

Applicant: Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 9.0) to update the list of safety concerns and to discontinue the use of targeted adverse event follow-up questionnaire (FUQ) for angioedema following the completion of variation II/0033 finalised in March 2021 that assessed the final study report for a non-interventional PASS on the evaluation of the safety profile of lurasidone: a PASS using United States administrative claims databases in order to compare the incidence of important identified risks and important potential risks in patients treated with lurasidone to patients treated with other second-generation oral atypical antipsychotics (OAAs)

Action: For adoption of PRAC Assessment Report

5.2.7. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/II/0038

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 7.2) to remove study D3820R00009 (listed as a category 3 study in the RMP): an observational drug utilisation PASS of Moventig (naloxegol) in selected European populations, following the completion of procedure MEA 006.11 in November 2021

Action: For adoption of PRAC Assessment Report

5.2.8. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/II/0087

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 2.6) to include data from the booster/third dose, including data in patients who have undergone a solid organ transplantation, following the outcome of procedures II/0062 (third dose in immunocompromise as part of the primary vaccination) and II/0067 (booster dose) finalised in October 2021. The MAH took the opportunity to update the RMP regarding the discontinuation of enrolment in study C4591015: a phase 2/3 study to evaluate the safety, tolerability, and immunogenicity in healthy pregnant women 18 years of age and older and the final clinical study report (CSR) milestones

Action: For adoption of PRAC Assessment Report

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

5.3.1. Agalsidase alfa - REPLAGAL (CAP) - EMEA/H/C/000369/II/0117

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.2 and 6.6 of the SmPC in order to add self-administration by a trained patient and/or a caregiver as a new method of administration. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information. The RMP (version 0.1) is updated accordingly

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/0064

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include adjuvant treatment of non-small cell lung cancer (NSCLC) following resection and platinum-based chemotherapy for adult patients whose tumours have programmed death-ligand 1 (PD-L1) expression on ≥ 1% of tumour cells (TC) for Tecentriq (atezolizumab) as monotherapy based on the results from pivotal study GO29527 (IMpower010): a phase 3, open-label, randomized study to investigate the efficacy and safety of atezolizumab compared with best supportive care following adjuvant cisplatin-based chemotherapy in patients with completely resected stage IB-IIIA NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of Tecentriq (atezolizumab) 840 mg concentrate for solution for infusion SmPC and Tecentriq (atezolizumab) 1,200 mg concentrate for solution for infusion SmPC are updated. The package leaflet and the RMP (version 21.0) are updated. The MAH took the opportunity to introduce minor editorial updates throughout the product information

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

5.3.3. Autologous peripheral blood T cells CD[7]4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta chimeric antigen receptor and cultured - TECARTUS (CAP) - EMEA/H/C/005102/II/0008/G, Orphan

Applicant: Kite Pharma EU B.V, ATMP[8]

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) extension of indication to include treatment of adult patients with relapsed or refractory (r/r) B-cell acute lymphoblastic leukaemia (B-ALL); 2) change the drug product dose specification for the new indication. As a consequence, sections 2.2, 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet, labelling and the RMP (version 1.1) are updated in accordance. Furthermore, the product information is brought in line with the latest quality review of

[7] Cluster of differentiation
[8] Advanced therapy medicinal product

documents (QRD) template (version 10.2)

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

5.3.4. Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - EMEA/H/C/004449/X/0040/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped application consisting of: 1) extension application to introduce a new strength 30/120/15 mg; 2) extension of indication to include a paediatric indication by adding the use in patients of 2 years of age and older and weighing at least 14 kg. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet are updated to support the extension of indication. The RMP (version 3.1) is updated in accordance

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

5.3.5. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0099, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.8 and 5.1 of the SmPC based on final results from study C25006 (listed as a category 2 study in the RMP (SOB 010)): a multicentre open-label, phase 4 study of 50 patients with relapsed/refractory systemic anaplastic large cell lymphoma (ALCL) undertaken to further evaluate the efficacy and safety of brentuximab vedotin as a single agent in adult patients who had previously received at least 1 multiagent chemotherapy regimen. In addition, the MAH took the opportunity to delete SOB 010 from Annex II and to delete the mention of conditional approval from Annex II and the package leaflet. The RMP (version 16.1) is updated accordingly

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

5.3.6. Clopidogrel - ISCOVER (CAP) - EMEA/H/C/000175/WS2150/0146; PLAVIX (CAP) - EMEA/H/C/000174/WS2150/0145; clopidogrel, acetylsalicylic acid - DUOPLAVIN (CAP) - EMEA/H/C/001143/WS2150/0060

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI). As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The RMP (version 1.5) for Iscover/Plavix (clopidogrel) is updated accordingly. In addition, the MAH took the opportunity to introduce an editorial update in the labelling

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

5.3.7. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - EMEA/H/C/004282/II/0018/G, Orphan

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Grouped variations consisting of: 1) extension of indication to add treatment of relapsed/refractory acute myeloid leukaemia (AML) in paediatric patients. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated based on the new safety and efficacy data from the paediatric clinical study AAML1421: a phase 1/2 study of liposomal daunorubicin/cytarabine alone followed by fludarabine, cytarabine, and granulocyte colony-stimulating factor (G-CSF) (FLAG) for children with relapsed AML. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the product information is updated in line with the latest quality review of documents (QRD) template (version 10.2); 2) submission of the final data from paediatric clinical study CPX-MA-1201: a phase 1/pilot study of liposomal daunorubicin/cytarabine for children, adolescents and young adults with recurrent or refractory hematologic malignancies, in support of the extension of indication

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

5.3.8. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0056, Orphan

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 15-007 (listed as a specific obligation in Annex II): a phase 3, randomised, adaptive study of defibrotide vs. best supportive care in the prevention of hepatic veno-occlusive disease in adult and paediatric patients undergoing hematopoietic stem cell transplant (HSCT). The RMP (version 9) is updated accordingly. The MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) (template 10.2). In addition, the MAH introduced some minor correction throughout the product information

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

5.3.9. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/II/0035

Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC in order to add a new warning on mortality in intensive care unit patients ≤ 65 years old, based on results from study SPICE III: an open-label, randomized trial on early sedation with dexmedetomidine in ventilated critically ill patients and heterogeneity of treatment effect and based on the completion of post-authorisation measure LEG 16.4 finalised in November 2021. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. A proposal for a direct healthcare professional communication (DHPC) and a communication plan is submitted. The RMP (version 9) is updated accordingly

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

5.3.10. Elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - EMEA/H/C/004042/X/0079/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength (90 mg/90 mg/120 mg/6 mg film-coated tablets); 2) extension of indication to include treatment of human immunodeficiency virus 1 (HIV 1) infection without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir in paediatric patients aged from 2 years and with body weight at least 14 kg. As a consequence, sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated to support the extended indication. The package leaflet and the RMP (version 5.1) 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/0057

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to reflect updated safety and efficacy data from the final analysis of study 9785-CCL-0335 (ARCHES): a phase 3 randomized, double-blind, placebo-controlled study that evaluated the safety and efficacy of enzalutamide plus androgen deprivation therapy (ADT) vs placebo plus ADT in men with metastatic hormone-sensitive prostate cancer (mHSPC). The package leaflet and the RMP (version 17.0) are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the SmPC

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

5.3.12. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0010/G, Orphan

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of an update of section 5.3 of the SmPC in order to update the non-clinical information based on data from: 1) study 20147822: a 6-month carcinogenicity study of fenfluramine hydrochloride in mice; 2) study 8001993: a 2-year oral gavage carcinogenicity study of fenfluramine hydrochloride in rats, together with the final reports for dose range finding studies 20147821 and 20166554 and the final report for study 2021006-Z001-01: in-vitro evaluation of potential melanin binding by fenfluramine and norfenfluramine. The RMP (version 3.1) is updated accordingly

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

5.3.13. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0011/G, Orphan

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 4.2 and 5.2 of the SmPC to include the relevant information regarding patients with renal impairment following the study 1902: a pharmacokinetic study of fenfluramine hydrochloride in subjects with varying degrees of impaired and normal renal function; 2) update of section 4.4 and 4.5 of the SmPC in order to reflect the relevant information on cytochrome (CYP)1A2 or CYP2B6 or CYP2D6 inducers following study 1904: a pharmacokinetic drug-drug interaction study of fenfluramine hydrochloride with and without fluvoxamine (CYP1A2 inhibitor), paroxetine (CYP2D6 inhibitor) and rifampin (CYP2B6 inducer) in healthy subjects. The RMP (version 2.2) is updated accordingly

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

5.3.14. Gemtuzumab ozogamicin - MYLOTARG (CAP) - EMEA/H/C/004204/II/0024, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC based on the final results from study B176103: a single-arm, open-label, phase 4 study evaluating the QT interval, pharmacokinetics, and safety of gemtuzumab ozogamicin as a single-agent regimen in patients with relapsed or refractory CD[9]33-positive acute myeloid leukaemia. The RMP (version 2.0) is updated in accordance. In addition, the MAH took the opportunity to introduce some editorial changes in the product information

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

5.3.15. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0006, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to add 'blood homocysteine increase' as a new adverse drug reaction (ADR) and update of section 4.4 of the SmPC to add a related warning. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, the MAH took the opportunity to make editorial changes to the product information and to update the local representative details for Malta and Cyprus

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

5.3.16. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0070

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of the existing indication on chronic lymphocytic leukaemia (CLL) to include combination treatment with venetoclax for previously untreated patients based on efficacy and safety data from: 1) study GLOW: a phase 3 trial testing ibrutinib and venetoclax for people with untreated CLL or small lymphocytic lymphoma (SLL); 2) study PCYC-1142-CA (CAPTIVATE): a phase 2 study of the combination of ibrutinib plus

[9] Cluster of differenciation

venetoclax in subjects with treatment-naïve CLL/SLL. The SmPC sections 4.1, 4.2, 4.8 and 5.1 are updated in accordance. The package leaflet and the RMP (version 18.4) are updated accordingly. the MAH also included a justification to support one year-extension of the marketing protection period

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

5.3.17. Lonoctocog alfa - AFSTYLA (CAP) - EMEA/H/C/004075/II/0042

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 3001 (listed as a category 3 study in the RMP): an open label, multicentre extension study to assess the safety and efficacy of Afstyla (lonoctocog alfa) in subjects with severe haemophilia A. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. The RMP (version 6.0) is updated accordingly

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

5.3.18. Metreleptin - MYALEPTA (CAP) - EMEA/H/C/004218/II/0025, Orphan

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Proposal for an alternative study to the currently agreed protocol for study AEGR-734-002 (specific obligation SOB002): a 24-month, multicentre, open label phase 4 post-authorisation efficacy study (PAES) to evaluate the efficacy, safety and immunogenicity of daily subcutaneous metreleptin treatment in patients with partial lipodystrophy due to the challenges of implementing the existing protocol. Annex II and the RMP (version 2.1) are updated accordingly. The MAH took the opportunity to update the RMP in line with the outcome of previous procedures and to include editorial changes

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

5.3.19. Midostaurin - RYDAPT (CAP) - EMEA/H/C/004095/II/0024, Orphan

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of the final report from study CPKC412E2301 (listed as an obligation in the Annex II): a phase 3 study to investigate the efficacy in elderly patients. A final pharmacogenomic report is also provided (in fulfilment of MEA 004). Annex II and the RMP (version 7.0) are updated accordingly

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

5.3.20. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0056

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated study design and a protocol synopsis for study CVOT-2 (listed as a category 1 study in Annex II-D (ANX/001.7)): a multicentre, randomised, double-blind, placebo-controlled phase 4 study to assess the effect of naltrexone extended release (ER)/bupropion ER on the occurrence of major adverse cardiovascular events (MACE) in overweight and obese subjects with cardiovascular disease, as requested by CHMP in the conclusions of procedure ANX 001.6 adopted in April 2021. Annex II and the RMP (version 13) are updated accordingly

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

5.3.21. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/II/0030, Orphan

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on pivotal study NETTER-1: a multicentre, stratified, open, randomized, comparator-controlled, parallel-group phase 3 study comparing treatment with Luthatera ((^{177}Lu) oxodotreotide) to octreotide long acting release (LAR) in patients with inoperable, progressive, somatostatin receptor positive midgut carcinoid tumours. Additionally, updates are proposed in the product information to correct some information based on currently approved data. The package leaflet and the RMP (version 2.0) are updated accordingly. The MAH took the opportunity to update the details of local representatives in the package leaflet

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

5.3.22. Pegcetacoplan - ASPAVELI (CAP) - EMEA/H/C/005553/II/0002, Orphan

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC based on final results from study APL2-302 (Pegasus) (listed as a category 3 study in the RMP): a global, phase 3, prospective, randomised, multicentre, open-label, active-comparator–controlled study in 80 subjects. The objective was to confirm treatment efficacy and safety of pegcetacoplan monotherapy for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) (in fulfilment of MEA 001). The package leaflet and the RMP (version 5.) are updated accordingly

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

5.3.23. Pemigatinib - PEMAZYRE (CAP) - EMEA/H/C/005266/II/0005, Orphan

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from study INCB054828 (FIGHT-202) (listed as a specific obligation in the Annex II (SOB/002)): a phase 2 study investigating the efficacy and safety of pemigatinib in adults with advanced/metastatic or surgically unresectable cholangiocarcinoma including fibroblast growth factor receptor 2 (FGFR2) translocations who failed previous therapy. The RMP (version 2.0) and Annex II are updated accordingly

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

5.3.24. Ponatinib - ICLUSIG (CAP) - EMEA/H/C/002695/II/0061, Orphan

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Annika Folin

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC based on results from study AP24534-14-203 (OPTIC) (listed as a specific obligation (SOB002) in Annex II): a randomised, open-label, phase 2 trial of ponatinib in patients with chronic myeloid leukaemia to characterise the efficacy and safety of ponatinib over a range of doses. The package leaflet and the RMP (version 21.0) are updated accordingly. The RMP (version 21.0) is updated as a response to the request for supplementary information (RSI)

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

5.3.25. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/II/0002/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic rearranged during transfection (RET)-mutant medullary thyroid cancer for Gavreto (pralsetinib) based on the efficacy and safety data obtained from pivotal study BO42863 (ARROW): a phase 1/2 study of the highly-selective RET inhibitor, BLU-667, in patients with thyroid cancer, non-small cell lung cancer (NSCLC) and other advanced solid tumours. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. Furthermore, some minor changes to the product information have been implemented in line with the latest anticancer guidelines recommendations; 2) extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic RET fusion-positive thyroid cancer for Gavreto (pralsetinib) based on the efficacy and safety data obtained from pivotal study BO42863 (ARROW). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly

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

5.3.26. Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/II/0026

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of adult patients with generalised

myasthenia gravis (gMG). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 4.0) are updated accordingly. The MAH took the opportunity to introduce minor editorial corrections throughout the SmPC and package leaflet. The MAH also requested 1 year of market protection for a new indication

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

5.3.27. Relugolix, estradiol, norethisterone acetate - RYEQO (CAP) - EMEA/H/C/005267/II/0006

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study MVT-601-035 (listed as a category 3 study in the RMP): an international phase 3 double-blind, placebo-controlled, randomised withdrawal study of relugolix co-administered with estradiol and norethisterone in women with heavy menstrual bleeding associated with uterine fibroids to evaluate the efficacy and safety of long-term use of this medicinal product. The RMP (version 1.0) is updated accordingly

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

5.3.28. Rituximab - MABTHERA (CAP) - EMEA/H/C/000165/II/0188

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from study MA28150 (RITAZAREM) (listed as an interventional category 3 study in the RMP): an international, open label, randomised controlled trial comparing rituximab with azathioprine as therapy for maintenance of remission for anti-neutrophilcytoplasm antibody (ANCA)-associated vasculitis. The RMP (version 23.0) is updated accordingly

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

5.3.29. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/II/0053

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Extension of indication to include treatment of patients with graft versus host disease (GvHD) aged 12 years and older who have inadequate response to corticosteroids or other systemic therapies. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8. 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 13.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives for the Netherlands in the package leaflet

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

5.3.30. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/II/0044, Orphan

Applicant: Novartis Europharm Limited, ATMP[10]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of adult patients with follicular lymphoma (FL) after two or more lines of therapy who are refractory, or relapsed during or within 6 months after completion of anti-CD[11]20 antibody maintenance, or relapsed after autologous haematopoietic stem cell transplantation (HSCT). 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 4.0) are updated accordingly. The MAH took the opportunity to introduce minor editorial corrections throughout the product information to bring in line with the latest quality review of documents (QRD) template (version 10.2).

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

5.3.31. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/II/0014

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include treatment of adult patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer who have received one or more prior anti-HER2-based regimens. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and RMP (version 1.2) are updated accordingly

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

5.3.32. Turoctocog alfa pegol - ESPEROCT (CAP) - EMEA/H/C/004883/II/0010, Orphan

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC to add a new warning and update the list of adverse drug reactions (ADRs) based on post-marketing data concerning a lack of factor VIII activity in patients switching from a similar factor VIII product to Esperoct (turoctocog alfa pegol). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and to bring the product information in line with the latest quality review of documents (QRD) (template 10.2). The RMP (version 2.0) is updated accordingly

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

5.3.33. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/II/0015/G

Applicant: AbbVie Deutschland GmbH & Co. KG

[10] Advanced therapy medicinal product
[11] Cluster of differentiation

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Grouped variation consisting of: 1) update of sections 4.8 to add neutropenia and 5.1 of the SmPC in order to update efficacy information of Rinvoq (upadacitinib) in ankylosing spondylitis (AS) patients who are biologic disease modifying anti rheumatic drug (DMARD) inadequate responders (bDMARD-IR) based on interim results from study M19-944: a phase 3, randomized, double-blind, study evaluating the long-term safety, tolerability, and efficacy of upadacitinib 15 mg QD in subjects with active ankylosing spondylitis (AS) who have an inadequate response (IR) to bDMARD; 2) update of section 5.1 of the SmPC in order to include long term (through week 104) data in AS patients who are naïve to previous treatment with a bDMARD based on interim results from study M16-098: a multicentre, randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of upadacitinib in subjects with active AS. The RMP (version 7.0) is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes in the product information

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

5.3.34. Volanesorsen - WAYLIVRA (CAP) - EMEA/H/C/004538/II/0017/G, Orphan

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.8 and 5.1 of the SmPC based on the final results from study ISIS 304801 CS7: a multicentre open label extension study of volanesorsen administered subcutaneously to patients with familial chylomicronemia syndrome. The package leaflet and the RMP (version 2.1) are updated accordingly. The RMP is updated: 1) to reflect a change in the distribution methodology of the educational materials and to clarify what is meant by the prescriber kit; 2) to reflect the final results from study ISIS 304801 (CS17): a phase 2/3 double blind, randomized, placebo controlled study, with an open label extension of volanesorsen (ISIS 304801) administered subcutaneously to patients with familial partial lipodystrophy. In addition, the MAH took the opportunity to implement editorial changes to the product information in order to align with the latest quality review of documents (QRD) template and to introduce minor linguistic update to Annex III of the product information to support product launch

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. Aflibercept[12] - ZALTRAP (CAP) - PSUSA/00010019/202108

Applicant: sanofi-aventis groupe

[12] Oncological indication(s) only

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Agalsidase alfa - REPLAGAL (CAP) - PSUSA/00000069/202108

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Apalutamide - ERLEADA (CAP) - PSUSA/00010745/202108

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/202107

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Baloxavir marboxil - XOFLUZA (CAP) - PSUSA/00010895/202108

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Baricitinib - OLUMIANT (CAP) - PSUSA/00010578/202108

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Belantamab mafodotin - BLENREP (CAP) - PSUSA/00010869/202108

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Bempedoic acid- NILEMDO (CAP); bempedoic acid, ezetimibe - NUSTENDI (CAP) - PSUSA/00010841/202108

Applicant(s): Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Bictegravir, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - PSUSA/00010695/202108

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Botulinum toxin type A - NUCEIVA (CAP) - PSUSA/00010796/202107

Applicant: Evolus Pharma B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Bulevirtide - HEPCLUDEX (CAP) - PSUSA/00010873/202107

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Chlormethine - LEDAGA (CAP) - PSUSA/00010587/202108

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - PSUSA/00010916/202108

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Darolutamide - NUBEQA (CAP) - PSUSA/00010843/202107

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - PSUSA/00010701/202108

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Defatted powder of Arachis hypogaea L., semen (peanuts) - PALFORZIA (CAP) - PSUSA/00010902/202107

Applicant: Aimmune Therapeutics Ireland Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Desloratadine, pseudoephedrine - AERINAZE (CAP) - PSUSA/00000963/202107

Applicant: Organon N.V.

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Efavirenz, emtricitabine, tenofovir – ATRIPLA[13] - PSUSA/00001201/202107

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.19. Eravacycline - XERAVA (CAP) - PSUSA/00010718/202108

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Evinacumab - EVKEEZA (CAP) - PSUSA/00010945/202108

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/202108

Applicant: Holostem Terapie Avanzate s.r.l., ATMP[14]

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.22. Fedratinib - INREBIC (CAP) - PSUSA/00010909/202108

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/202108

Applicant: Norgine B.V.

[13] European Commission (EC) decision on the withdrawal of the marketing authorisation (MA) for Atripla dated 15 November 2021

[14] Advanced therapy medicinal product

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Fostemsavir - RUKOBIA (CAP) - PSUSA/00010911/202108

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Hydrocortisone[15] [16] - ALKINDI (CAP) - PSUSA/00010674/202108

Applicant: Diurnal Europe BV

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Icatibant - FIRAZYR (CAP) - PSUSA/00001714/202107

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Idelalisib - ZYDELIG (CAP) - PSUSA/00010303/202107

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Imlifidase - IDEFIRIX (CAP) - PSUSA/00010870/202108

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Centrally authorised product(s)
[16] Indication for adrenal insufficiency in paediatric patients only

6.1.29. Interferon beta-1b - BETAFERON (CAP); EXTAVIA (CAP) - PSUSA/00001759/202107

Applicant(s): Bayer AG (Betaferon), Novartis Europharm Limited (Extavia)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Lanadelumab - TAKHZYRO (CAP) - PSUSA/00010743/202108

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Lefamulin - XENLETA (CAP) - PSUSA/00010872/202108

Applicant: Nabriva Therapeutics Ireland DAC

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Lipegfilgrastim - LONQUEX (CAP) - PSUSA/00010111/202107

Applicant: Teva B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/202107

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Maraviroc - CELSENTRI (CAP) - PSUSA/00001934/202108

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Natalizumab - TYSABRI (CAP) - PSUSA/00002127/202108

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Palbociclib - IBRANCE (CAP) - PSUSA/00010544/202108

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Panobinostat - FARYDAK (CAP) - PSUSA/00010409/202108

Applicant: Secura Bio Limited

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Patisiran - ONPATTRO (CAP) - PSUSA/00010715/202108

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Pioglitazone - ACTOS (CAP), GLUSTIN[17]; pioglitazone, glimepiride – TANDEMACT (CAP); pioglitazone, metformin - COMPETACT (CAP); GLUBRAVA (CAP) - PSUSA/00002417/202107

Applicants: Cheplapharm Arzneimittel GmbH (Actos, Competact, Tandemact), Takeda Pharma A/S (Glubrava, Glustin), various

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[17] European Commission (EC) decision on the marketing authorisation (MA) cessation of Glustin dated 02 December 2021

6.1.40. Pretomanid - DOVPRELA (CAP) - PSUSA/00010863/202108

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Risdiplam - EVRYSDI (CAP) - PSUSA/00010925/202108

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Sacubitril, valsartan - ENTRESTO (CAP); NEPARVIS (CAP) - PSUSA/00010438/202107

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Smallpox vaccine (live, modified vaccinia Ankara virus) - IMVANEX (CAP) - PSUSA/00010119/202107

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Tezacaftor, ivacaftor - SYMKEVI (CAP) - PSUSA/00010730/202108

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Tisagenlecleucel - KYMRIAH (CAP) - PSUSA/00010702/202108

Applicant: Novartis Europharm Limited, ATMP[18]

[18] Advanced therapy medicinal product

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.46. Tocofersolan - VEDROP (CAP) - PSUSA/00002981/202107

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Upadacitinib - RINVOQ (CAP) - PSUSA/00010823/202108

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

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. Desloratadine - AERIUS (CAP); AZOMYR (CAP); DASSELTA (CAP); DESLORATADINE ACTAVIS (CAP); DESLORATADINE RATIOPHARM (CAP); DESLORATADINE TEVA (CAP); NEOCLARITYN (CAP); NAP - PSUSA/00000962/202107

Applicants: Actavis Group PTC ehf (Desloratadine Actavis), Krka, d.d., Novo mesto (Dasselta), Organon N.V. (Aerius, Azomyr, Neoclarityn), Ratiopharm GmbH (Desloratadine ratiopharm), Teva B.V. (Desloratadine Teva), various

PRAC Rapporteur: Laurence de Fays

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. Alprostadil[19] (NAP) - PSUSA/00010021/202107

Applicant(s): various

PRAC Lead: Sonja Hrabcik

[19] Indicated for patency of the ductus arteriosus only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amlodipine, rosuvastatin (NAP); amlodipine, perindopril, rosuvastatin (NAP) - PSUSA/00010434/202107

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Budesonide, salmeterol (NAP) - PSUSA/00010511/202107

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Cefuroxime sodium[20] (NAP) - PSUSA/00010206/202105

Applicant(s): various

PRAC Lead: Krõõt Aab

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Everolimus[21] (NAP) - PSUSA/00010269/202107

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Fluocinolone acetonide[22] (NAP) - PSUSA/00010224/202108

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[20] Intracameral use only
[21] Indicated for rejection of transplanted organs only
[22] Intravitreal implant(s) in applicator only

6.3.7. Fluticasone propionate, formoterol fumarate dihydrate (NAP) - PSUSA/00010339/202107

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Human plasma protease C1 inhibitor[23] (NAP) - PSUSA/00010163/202108

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Indium (^{111}In) chloride (NAP); indium (^{111}In) oxine (NAP) - PSUSA/00001734/202107

Applicant(s): various

PRAC Lead: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Leuprorelin[24] (NAP) - PSUSA/00010877/202107

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Lovastatin (NAP) - PSUSA/00010051/202107

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[23] Nationally authorised product(s) only
[24] Depot formulations only

6.3.12. Magnesium sulfate, sodium sulfate, potassium sulfate (NAP) - PSUSA/00010239/202108

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Montelukast (NAP) - PSUSA/00002087/202107

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Pilocarpine, timolol (NAP) - PSUSA/00002408/202107

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Tiapride (NAP) - PSUSA/00002944/202107

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Timolol[25] (NAP) - PSUSA/00010439/202107

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[25] Indicated for eye preparations only

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/LEG 057

Applicant: Upjohn EESV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Review of cases of abuse and dependence in patients without a history of substance disorders as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002511/202101) adopted in September 2021

Action: For adoption of advice to CHMP

6.4.2. Pregabalin - PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/LEG 009

Applicant: Upjohn EESV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Review of cases of abuse and dependence in patients without a history of substance disorders as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00002511/202101) adopted in September 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0025

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC concerning immunogenicity and loss of efficacy due to anti-emicizumab antibodies as requested in the conclusions of the latest periodic safety update report single assessment (PSUSA) procedure (PSUSA/00010668/202011) adopted in June 2021, together with a review of haemorrhagic cases as requested in the conclusions of the PSUSA procedure (PSUSA/00010668/202005) finalised in January 2021. The RMP (version 3.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[26]

6.6.1. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/MEA 014.8

Applicant: Janssen-Cilag International N.V.

[26] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Ninth expedited summary safety report (SSR) for COVID-19 Vaccine Janssen (COVID-19 vaccine (Ad26.COV2-S, recombinant)) during the coronavirus disease (COVID-19) pandemic

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. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/PSA/S/0083

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Substantial amendment to a protocol previously agreed in November 2013 for lomitapide observational worldwide evaluation registry to evaluate the occurrence and outcomes of pregnancy in females of reproductive potential treated with lomitapide

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

7.1.2. Valproate (NAP) - EMEA/H/N/PSP/J/0072.6

Applicant(s): Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0072.5 [progress report for a joint retrospective observational study to investigate the association between paternal exposure to valproate and the risk of congenital anomalies and neurodevelopmental disorders including autism in offspring, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in November 2021[28]

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

7.1.3. Voretigene neparvovec - LUXTURNA (CAP) - EMEA/H/C/PSA/S/0081.1

Applicant: Novartis Europharm Ltd, ATMP[29]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to PSA/S/0081 [substantial amendment to a protocol previously agreed in March 2021 (PSA/S/0066) for a post-authorisation multicentre, multinational, longitudinal, observational safety registry study to collect long-term safety information

[27] In accordance with Article 107n of Directive 2001/83/EC
[28] Held 25-28 October 2021
[29] Advanced therapy medicinal product

associated with voretigene neparvovec (vector and/or transgene), its subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products] as per the request for supplementary information (RSI) adopted in January 2022

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

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

7.2.1. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 002

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study PS0038: a non-interventional cohort study on the safety of bimekizumab in patients with plaque psoriasis comparing the risk of safety outcomes of interest in bimekizumab exposed patients compared to patients exposed to other biologics [final clinical study report (CSR) expected in December 2023] (from initial opinion/marketing authorisation(s))

Action: For adoption of advice to CHMP

7.2.2. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 003

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study PS0036: bimekizumab pregnancy exposure and outcome registry - an OTIS[31] autoimmune diseases in pregnancy study (from initial opinion/marketing authorisation(s))

Action: For adoption of advice to CHMP

7.2.3. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 004

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study PS0037: an observational cohort study to evaluate bimekizumab exposure during pregnancy and monitor the safety of bimekizumab use in pregnancy (from initial opinion/marketing authorisation(s))

Action: For adoption of advice to CHMP

7.2.4. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/MEA 051.1

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

[30] 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

[31] Organization of Teratology Information Specialists

Scope: MAH's response to MEA 051 [protocol for study 1160.307: a European non-interventional cohort study based on new data collection to measure the safety of dabigatran etexilate for the treatment of venous thromboembolism (VTE) and prevention of recurrent VTE in paediatric patients from birth to less than 2 years of age - final clinical study report (CSR) expected in Q2 2025 (from X/0122/G)] as per the request for supplementary information (RSI) adopted in October 2021[32]

Action: For adoption of advice to CHMP

7.2.5. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/MEA 011.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: MAH's response to MEA 011 [protocol for study AMY2009: a multicentre, prospective study of daratumumab-based therapy in newly diagnosed patients with light-chain (AL) amyloidosis (from variation II/0043)] as per the request for supplementary information (RSI) adopted in November 2021[33]

Action: For adoption of advice to CHMP

7.2.6. Drospirenone, estetrol - DROVELIS (CAP) - EMEA/H/C/005336/MEA 001.1

Applicant: Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.)

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 001 [protocol for an international active surveillance study (INAS-NEES): a prospective non-interventional comparative cohort observational study to characterize and compare the risks of estetrol/drospirenone with combined oral contraceptive-containing levonorgestrel (COC-LNG) in a study population that is representative of the actual users of these preparations. The main clinical outcome of interest is venous thromboembolism (VTE), specifically deep venous thrombosis (DVT) and pulmonary embolism (PE)] as per the request for supplementary information (RSI) adopted in November 2021[34]

Action: For adoption of advice to CHMP

7.2.7. Drospirenone, estetrol - LYDISILKA (CAP) - EMEA/H/C/005382/MEA 001.1

Applicant: Estetra SRL

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 001 [protocol for an international active surveillance study (INAS-NEES): a prospective non-interventional comparative cohort observational study to characterize and compare the risks of estetrol/drospirenone with combined oral contraceptive-containing levonorgestrel (COC-LNG) in a study population that is representative of the actual users of these preparations. The main clinical outcome of interest is venous thromboembolism (VTE), specifically deep venous thrombosis (DVT) and

[32] Held 27-30 September 2021
[33] Held 25-28 October 2021
[34] Held 25-28 October 2021

pulmonary embolism (PE) [final study report expected in December 2029] (from initial opinion/marketing authorisation (MA))] as per the request for supplementary information (RSI) adopted in November 2021[35]

Action: For adoption of advice to CHMP

7.2.8. Fenofibrate, simvastatin - CHOLIB (CAP) - EMEA/H/C/002559/MEA 002.7

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Maia Uusküla

Scope: Substantial amendment to a protocol previously agreed in September 2017 (MEA 002.6) for study NCEPPEUPASS15741 (listed as a category 3 study in the RMP): assessment of the clinical practice regarding concomitant use of fenofibrate and simvastatin both as free and fixed combination: a European PASS

Action: For adoption of advice to CHMP

7.2.9. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 003.2

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 003.1 [protocol for study GS-EU-417-9047: a non-interventional PASS of filgotinib in the treatment of patients with moderate to severe active rheumatoid arthritis within the Anti-Rheumatic Treatment in Sweden (ARTIS) register [final report expected in Q2 2030]] as per the request for supplementary information (RSI) adopted in December 2021

Action: For adoption of advice to CHMP

7.2.10. Rilpivirine - REKAMBYS (CAP) - EMEA/H/C/005060/MEA 004

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for an antiretroviral pregnancy registry: an observational, exposure-registration and follow-up study to detect major teratogenic effect in pregnancies exposed to the registry anti-retroviral drugs used to treat the human immunodeficiency virus (HIV)

Action: For adoption of advice to CHMP

7.2.11. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/MEA 005

Applicant: Amgen Europe B.V., ATMP[36]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Substantial amendment to a protocol previously agreed within the initial application/marketing authorisation in 2015 for study 20130193 (listed as category 3 study

[35] Held 25-28 October 2021
[36] Advanced therapy medicinal product

in the RMP): a post-marketing, prospective cohort study of patients treated with talimogene laherparepvec in clinical practice to characterize the risk of herpetic illness among patients, close contacts, and healthcare providers; and long term safety in treated patients

Action: For adoption of advice to CAT and CHMP

7.2.12. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 017.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 017 [protocol for study A3921352: an active surveillance, post-authorisation study to characterise the safety of tofacitinib in patients with moderately to severely active ulcerative colitis in the real-world setting using data from the united registries for clinical assessment and research (UR-CARE) in the European Union (EU)] as per the request for supplementary information (RSI) adopted in September 2021

Action: For adoption of advice to CHMP

7.2.13. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 017.2

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Substantial amendment to a protocol previously agreed in June 2021 for study C4591021 (previously known as vACcine Covid-19 monitoring readinESS/Vaccine monitoring Collaboration for Europe (ACCESS/VAC4EU)): an assessment of potential increased risk of adverse events of special interest (AESI), including myocarditis/pericarditis after being vaccinated with COVID-19 messenger ribonucleic acid (mRNA) vaccine estimating the time trend, in relation to DHPC letter dissemination, of the proportion of individuals who received real-world clinical assessments for myocarditis/pericarditis following Comirnaty (tozinameran) vaccination together with a statistical analysis plan (SAP)

Action: For adoption of advice to CHMP

7.2.14. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 037.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 037 [protocol for study C4591009: a non-interventional PASS in US to assess the occurrence of safety events of interest, including myocarditis and pericarditis (from variation II/0059 finalised in October 2021)] per the request for supplementary information (RSI) adopted in November 2021

Action: For adoption of advice to CHMP

7.2.15. Tralokinumab - ADTRALZA (CAP) - EMEA/H/C/005255/MEA 001

Applicant: LEO Pharma A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for a PASS of tralokinumab use in pregnancy (listed as a category 3 study in the RMP): an observational study based on electronic healthcare data (from initial opinion/marketing autorisation(s))

Action: For adoption of advice to CHMP

7.2.16. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 014

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Protocol for study P21-824: a study of growth and development in adolescents with atopic dermatitis who receive upadacitinib (version 1.0)

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[37]

7.3.1. Direct acting antivirals (DAAV): Dasabuvir - EXVIERA (CAP); elbasvir, grazoprevir - ZEPATIER (CAP); glecaprevir, pibrentasvir - MAVIRET (CAP); ledipasvir, sofosbuvir - HARVONI (CAP); ombitasvir, peritepreviir, ritonavir - VIEKIRAX (CAP); sofosbuvir - SOVALDI (CAP); sofosbuvir, velpatasvir - EPCLUSA (CAP); sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/PSR/J/0038

Applicant: Gilead Science International

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Final study report for a joint non-interventional PASS of early recurrence of hepatocellular carcinoma (HCC) in patients infected with chronic hepatitis C virus (HCV) after direct-acting antiviral (DAA) therapy as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in December 2016 (EMEA/H/A-20/1438)

Action: For adoption of recommendation to CHMP (or request for supplementary information (RSI))

7.4. Results of PASS non-imposed in the marketing authorisation(s)[38]

7.4.1. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0068

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.8 of the SmPC based on the final results from study OBS14697 (listed as a category 3 study in the RMP): a non-interventional, retrospective drug utilisation study (DUS) that was designed to assess in Europe the effectiveness of the dosing

[37] In accordance with Article 107p-q of Directive 2001/83/EC
[38] 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

recommendation and to describe patterns of alirocumab utilisation in real world clinical practice (in fulfilment of MEA 019.8). In addition, the MAH took the opportunity to implement editorial changes in the product information

Action: For adoption of PRAC Assessment Report

7.4.2. 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/0033, Orphan

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP[39]

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study STRIM-001 (listed as a category 3 study in the RMP): a cross-sectional study evaluating referring healthcare providers' and parents/carers' understanding of specific risks associated with Strimvelis treatment. The RMP (version 6.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0075

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report for study A8081062 (listed as a category 3 study in the RMP): a non-interventional, descriptive study of potential sight threatening event and severe visual loss following exposure to crizotinib (in fulfilment of MEA 024)

Action: For adoption of PRAC Assessment Report

7.4.4. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS2216/0052; glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/WS2216/0049; ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/WS2216/0064

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report for study B20-146 (listed as a category 3 study in the RMP): a non-imposed joint PASS to evaluate the risk of de novo hepatocellular carcinoma (HCC) in patients with compensated cirrhosis treated with direct-acting antivirals (DAA) for chronic hepatitis C (HCC de novo PASS)

Action: For adoption of PRAC Assessment Report

7.4.5. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/II/0033

Applicant: Merck Sharp & Dohme B.V.

[39] Advanced therapy medicinal product

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report for study B20-146 (listed as a category 3 study in the RMP): a non-imposed joint PASS to evaluate the risk of de novo hepatocellular carcinoma (HCC) in patients with compensated cirrhosis treated with direct-acting antivirals (DAA) for chronic hepatitis C (HCC de novo PASS)

Action: For adoption of PRAC Assessment Report

7.4.6. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0028

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final report for study BO40853 (listed as a category 3 study in the RMP): a survey to prescribers and patients/carers to evaluate awareness, knowledge and compliance to additional risk minimisation measures for Hemlibra (emicizumab). The RMP (version 4.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/II/0031, Orphan

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.2, 4.4, 4.9 and 5.1 of the SmPC based on the final study report from study SNT-IV-003 (PAROS) (listed as a category 2 study in the RMP and Annex II (SOB003)): a non-interventional study of clinical experience in patients prescribed Raxone (idebenone) for the treatment of Leber's hereditary optic neuropathy (LHON). Annex II and the RMP (version 1.14) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/II/0105

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final report from study CT-P13 4.2: an observational, prospective cohort study to evaluate safety and efficacy of Inflectra (infliximab) in patients with rheumatoid arthritis (study report excluding the joint analysis of patients in the PERSIST study) (in fulfilment of MEA 007.6)

Action: For adoption of PRAC Assessment Report

7.4.9. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0111

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final report from study CT-P13 4.2: an observational, prospective

cohort study to evaluate safety and efficacy of Remsima (infliximab) in patients with rheumatoid arthritis (study report excluding the joint analysis of patients in the PERSIST study)

Action: For adoption of PRAC Assessment Report

7.4.10. Ramucirumab - CYRAMZA (CAP) - EMEA/H/C/002829/II/0047

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study I4T-MC-JVDD (listed as a category 3 study in the RMP): safety and effectiveness of ramucirumab in patients with advanced gastric cancer in the European Union (EU) and North America - a prospective observational registry (in fulfilment of MEA 001.1). The RMP (version 10.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.11. Sapropterin - KUVAN (CAP) - EMEA/H/C/000943/II/0073

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final report from study BMN 162-501 (KAMPER) (formerly known as EMR700773-001) (listed as a category 3 study in the RMP): an observational drug registry to assess the long-term safety in subjects treated with Kuvan (sapropterin) (in fulfilment of MEA 020). The RMP (version 15.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.12. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS2222/0077; sofosbuvir, ledipasvir - HARVONI (CAP) - EMEA/H/C/003850/WS2222/0104; sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS2222/0064; sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/WS2222/0054

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study B20-146 (listed as a category 3 study in the RMP): a non-imposed joint PASS to evaluate the risk of de novo hepatocellular carcinoma (HCC) in patients with compensated cirrhosis treated with direct-acting antivirals (DAA) for chronic hepatitis C (HCC de novo PASS)

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/ANX 010.2

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Progress report for a drug utilisation study (DUS) to assess compliance with the therapeutic indication and effectiveness of measures to minimise the risk of cardiovascular and cerebrovascular adverse events in close temporal association with Lemtrada (alemtuzumab) infusion and immune-mediated adverse reactions, as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1483) finalised in 2019

Action: For adoption of advice to CHMP

7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.16

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Annual report (covering period from 04 July 2020 to 02 July 2021) on adverse events and/or lack of efficacy, immunological data, follow-up growth disturbances in children and data on urinary hexose tetrasaccharide (Hex4) from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status [final clinical study report expected in Q4 2021]

Action: For adoption of advice to CHMP

7.5.3. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 025.16

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Annual report (covering period from 04 July 2020 to 02 July 2021) on data on patients with renal or hepatic insufficiency from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status [final clinical study report expected in Q4 2021]

Action: For adoption of advice to CHMP

7.5.4. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/MEA 035.3

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second interim report for study 20180204: a registry study to evaluate the incidence and risk of hypocalcaemia in paediatric patients treated with cinacalcet with secondary hyperparathyroidism receiving maintenance dialysis within the International Pediatric Dialysis Network (IPDN) registry

Action: For adoption of advice to CHMP

7.5.5. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/ANX 038.13

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Eighth annual interim report for study CICL670E2422: an observational, multicentre cohort study to evaluate the long-term exposure and safety of deferasirox in the treatment of paediatric non-transfusion dependent thalassaemia patients over 10 years old for whom deferoxamine is contraindicated or inadequate] together with MAH's response to ANX 038.12 [seventh annual interim report for study CICL670E2422] as per the request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

7.5.6. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/MEA 002.5

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Fifth annual progress report for study 242-12-402 (listed as a category 3 study in the RMP): a multicentre EU-wide observational non-interventional post-authorisation study to assess the safety and drug usage of delamanid (OPC-67683) in routine medical practice in multidrug-resistant tuberculosis patients (Delamanid registry), together with MAH's response to MEA 002.3 [fourth annual progress report for study 242-12-402] as per the request for supplementary information (RSI) adopted in February 2021]

Action: For adoption of advice to CHMP

7.5.7. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/MEA 062.1

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Biennal interim report for study M11-001 (aHUS registry): an observational, non-interventional multicentre, multinational study to retrospectively and prospectively collect information on the long-term safety and effectiveness of eculizumab in patients with atypical hemolytic-uremic syndrome (aHUS) who have received or continue to receive eculizumab

Action: For adoption of advice to CHMP

7.5.8. Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/MEA 002.3

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: First interim report for study MK8835-062: a PASS to assess the risk of diabetic ketoacidosis among type 2 diabetes mellitus patients (T2DM) treated with ertugliflozin compared to patients treated with other antihyperglycemic agents

Action: For adoption of advice to CHMP

7.5.9. Ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/MEA 002.3

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: First interim report for study MK-8835-062: a PASS to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus (T2DM) patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents

Action: For adoption of advice to CHMP

7.5.10. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/MEA 002.3

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: First interim report for study MK-8835-062: a PASS to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus (T2DM) patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents

Action: For adoption of advice to CHMP

7.5.11. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 027.8

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fifth annual progress report of the ENEIDA registry (study MK-8259-042): a long-term, non-interventional observational study of patients with inflammatory bowel disease (IBD) in Spain to evaluate whether the use of golimumab is associated with a risk of colectomy for intractable disease, advanced neoplasia (colorectal cancer or high grade dysplasia), and hepatosplenic T-cell lymphoma (HSTCL) in patients with ulcerative colitis (UC) as compared with alternative therapies for similar severity of disease [final clinical study report (CSR) expected: March 2023]

Action: For adoption of advice to CHMP

7.5.12. Imatinib - GLIVEC (CAP) - EMEA/H/C/000406/ANX 191.10

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Eighth annual interim report for study CSTI571I2201: a European observational registry collecting efficacy and safety data in newly diagnosed paediatric Philadelphia positive (Ph+) acute lymphoblastic leukaemia (ALL) patients treated with chemotherapy + imatinib ± haematopoietic stem cell treatment (±HSCT)

Action: For adoption of advice to CHMP

7.5.13. Infliximab - REMICADE (CAP) - EMEA/H/C/000240/MEA 133.14

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourteenth annual paediatric inflammatory bowel disease (IBD) registry (DEVELOP): a multicentre, prospective registry of pediatric patients on long-term safety and efficacy of infliximab and other therapies, safety and efficacy of variable infliximab dosing intervals, episodic therapy, monotherapy (initiated de novo or following discontinuation of concomitant immunomodulators), combined infliximab and immunomodulator therapy (azathioprine/6-mercaptopurine (AZA/6-MP) or methotrexate (MTX))

Action: For adoption of advice to CHMP

7.5.14. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 007.2

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Interim report for study TEG4005: a pregnancy surveillance programme of infants and women exposed to Tegsedi (inotersen) during pregnancy

Action: For adoption of advice to CHMP

7.5.15. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/MEA 002.3

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: First annual interim report for study VX20-445-120: a five year-registry based study to assess real-world effects and utilisation patterns of elexacaftor/tezacaftor/ivacaftor combination therapy (ELX/TEZ/IVA) in patients with cystic fibrosis (CF)

Action: For adoption of advice to CHMP

7.5.16. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.9

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Fourth quarterly progress report for study A-LUT-T-E02-402 (SALUS): an international, non-interventional, post-authorisation long-term safety study of Lutathera (lutetium (^{177}Lu) oxodotreotide) in patients with unresectable or metastatic, well-differentiated, somatostatin receptor positive, gastro-enteropancreatic neuroendocrine tumours

Action: For adoption of advice to CHMP

7.5.17. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.12

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 006.11 [interim progress report for study D3820R00009 (EUPAS12669): an observational PASS of Moventig (naloxegol) among patients aged 18 years and older treated with opioids chronically] as per the request for supplementary information (RSI) adopted in November 2021

Action: For adoption of advice to CHMP

7.5.18. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.13

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Interim progress report for study D3820R00009 (EUPAS12669): an observational PASS of Moventig (naloxegol) among patients aged 18 years and older treated with opioids chronically

Action: For adoption of advice to CHMP

7.5.19. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/MEA 059.2

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study 20170701: an observational study to assess the effectiveness of the Neulasta (pegfilgrastim) patient alert card (PAC) and to measure medication errors related to the use of the On-Body injector (OBI) to assess respondent awareness of key safety messages and behavioural intent to carry out recommended actions as described in the PAC and to estimate the proportion of OBI administrations associated with medication error [final study report expected in March 2022]

Action: For adoption of advice to CHMP

7.5.20. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 003.3

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: First interim report for study 165-501: a multicentre, prospective global observational study to evaluate the long-term safety of subcutaneous injections of pegvaliase in patients with phenylketonuria

Action: For adoption of advice to CHMP

7.5.21. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 005.2

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: First interim report for study 165-504: a prospective global multicentre observational safety surveillance study to assess maternal, foetal and infant outcomes of

exposure to Palynziq (pegvaliase) during pregnancy and breastfeeding

Action: For adoption of advice to CHMP

7.5.22. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[40]) - EMEA/H/W/002300/MEA 003.6

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Fifth annual progress report for study EPI-MAL-003 (listed as a category 3 study in the RMP): a phase 4 prospective observational study to evaluate the safety, effectiveness and impact of Mosquirix (plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)) in young children in sub-Saharan Africa in order to estimate the incidence of potential adverse events of special interest (AESI) and other adverse events leading to hospitalisation or death, in children vaccinated with the vaccine [final study report expected Q2 2026]

Action: For adoption of advice to CHMP

7.5.23. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/MEA 002.4

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Annual interim report for study VX17-661-117 (study 117) (listed as a category 3 study in the RMP): an observational cohort study on utilisation patterns and real-world effects of tezacaftor and ivacaftor combination therapy (TEZ/IVA) in patients with cystic fibrosis (CF) [final report expected in December 2023]

Action: For adoption of advice to CHMP

7.5.24. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.4

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual progress report 2021 for study M-14745-40: a European psoriasis registry to collect long-term safety data for tildrakizumab and to further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine clinical practice

Action: For adoption of advice to CHMP

7.5.25. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.13

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

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

Scope: MAH's response to MEA 0044.12 [third interval safety registry for study CNTO1275PSO4056: an observational PASS of ustekinumab in the treatment of paediatric patients aged 12 years and older with moderate to severe plaque psoriasis (adolescent registry)] as per the request for supplementary information (RSI) adopted in November 2021

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/MEA 002.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: Interim report for study D8220C00008 (ASSURE): a phase 3b, multicentre, open-label, single-arm study of acalabrutinib (ACP-196) in subjects with chronic lymphocytic leukaemia to address missing information around moderate to severe cardiac impaired patients

Action: For adoption of advice to CHMP

7.6.2. Darvadstrocel - ALOFISEL (CAP) - EMEA/H/C/004258/MEA 007

Applicant: Takeda Pharma A/S, ATMP[41]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Interim report for study Cx601-0303 (ADMIRE CDII) to evaluate the long-term safety and efficacy of darvadstrocel including adverse events of special interest (related to MEA 002)

Action: For adoption of advice to CAT and CHMP

7.6.3. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038.4

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Second interim report for open-label extension phase study CFTY720D2311: a two-year, double-blind, randomized, multicentre, active-controlled core phase study to evaluate the safety and efficacy of fingolimod administered orally once daily versus interferon β-1a intramuscular (IM) once weekly in paediatric patients with multiple sclerosis with five-year fingolimod extension phase

Action: For adoption of advice to CHMP

[41] Advanced therapy medicinal product

7.6.4. Human C1-esterase inhibitor - CINRYZE (CAP) - EMEA/H/C/001207/MEA 021

Applicant: Shire Services BVBA

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Proposal for discontinuation of icatibant outcome survey (IOS) study: a prospective, international, observational open-ended disease registry designed to document over time the routine clinical outcomes of adult and paediatric patients with hereditary angioedema (HAE; HAE types I and II and HAE with normal C1-esterase inhibitor), angiotensin-converting enzyme inhibitor (ACE-I)-induced angioedema, non-histaminergic idiopathic angioedema, and acquired angioedema; and notification of change to the legal entity sponsoring the study

Action: For adoption of advice to CHMP

7.6.5. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 032.1

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: MAH's response to MEA 032 [submission of a critical analysis of the feasibility of using alternative data sources to complement the Transplantation Pregnancy Registry International (TPRI) study outcomes on pregnancy and breastfeeding] as per the request for supplementary information (RSI) adopted in October 2021

Action: For adoption of advice to CHMP

7.6.6. Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 024.1

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 024 [submission of a critical analysis of the feasibility of using alternative data sources to complement the Transplantation Pregnancy Registry International (TPRI) study outcomes on pregnancy and breastfeeding] as per the request for supplementary information (RSI) adopted in October 2021

Action: For adoption of advice to CHMP

7.6.7. Tralokinumab - ADTRALZA (CAP) - EMEA/H/C/005255/MEA 002

Applicant: LEO Pharma A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for study LP0162-1337 (ECZTEND) (listed as a category 3 study in the RMP): a phase 3 open label, single-arm, multicentre, long term extension trial to evaluate the safety and efficacy of tralokinumab in subjects with atopic dermatitis who participated in previous tralokinumab clinical trials (from initial opinion/marketing authorisation(s))

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/S/0042 (without RMP)

Applicant: Laboratoires CTRS

PRAC Rapporteur: Sofia Trantza

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0029 (with RMP)

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/S/0076 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

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. Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/R/0029 (without RMP)

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/R/0007 (with RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - EMEA/H/C/004750/R/0021 (without RMP)

Applicant: Novartis Gene Therapies EU Limited, ATMP[42]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.4. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/R/0031 (without RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.5. Selinexor - NEXPOVIO (CAP) - EMEA/H/C/005127/R/0005 (without RMP)

Applicant: Karyopharm Europe GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

[42] Advanced therapy medicinal product

8.3. Renewals of the marketing authorisation

8.3.1. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - EMEA/H/C/004391/R/0040 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Efavirenz, emtricitabine, tenofovir disoproxil - EFAVIRENZ/EMTRICITABINE/TENOFOVIR DISOPROXIL MYLAN (CAP) - EMEA/H/C/004240/R/0019 (without RMP)

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Efavirenz, emtricitabine, tenofovir disoproxil - EFAVIRENZ/EMTRICITABINE/TENOFOVIR DISOPROXIL ZENTIVA (CAP) - EMEA/H/C/004250/R/0025 (without RMP)

Applicant: Zentiva k.s.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/R/0032 (without RMP)

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Midostaurin - RYDAPT (CAP) - EMEA/H/C/004095/R/0023 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Tivozanib - FOTIVDA (CAP) - EMEA/H/C/004131/R/0021 (without RMP)

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Rugile Pilviniene

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 CHMP or EMA

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

11. Other safety issues for discussion requested by the Member States

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. Vote by proxy

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. EMA Emergency task force (ETF) - PRAC nominations

Action: For adoption

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.5. Cooperation with International Regulators

12.5.1. International Conference on Harmonisation (ICH) E2D(R1) - Post-approval safety data management: definitions and standards for expedited reporting

Action: For discussion

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

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

None

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

12.13.2. EudraVigilance – annual report 2021

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. Data analysis and real world interrogation network (DARWIN EU) – introduction of the coordination centre and next steps for real-world evidence (RWE)

Action: For discussion

12.21.2. Data protection notice – processing of scientific Committees (CxMP) members/alternates' contact details

Action: For discussion

12.21.3. Pharmacovigilance business team - activities and work plan

Action: For discussion

13. Any other business

14. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures

(Items 2 and 3 of the PRAC agenda)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, the EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

Signals assessment and prioritisation

(Item 4 of the PRAC agenda)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.
The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.
The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)

(Item 5 of the PRAC agenda)

The RMP describes what is known and not known about the side effects of a medicine and states how these risks will be prevented or minimised in patients. It also includes plans for studies and other activities to gain more knowledge about the safety of the medicine and risk factors for developing side effects.
RMPs are continually modified and updated throughout the lifetime of the medicine as new information becomes available.

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC agenda)

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.
PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC agenda)

A PASS is a study of an authorised medicinal product carried out to obtain further information on its safety, or to measure the effectiveness of risk management measures. The results of a PASS help regulatory agencies to evaluate the safety and benefit-risk profile of a medicine.

Product related pharmacovigilance inspections

(Item 9 of the PRAC agenda)

Inspections carried out by regulatory agencies to ensure that marketing authorisation holders comply with their pharmacovigilance obligations.

More detailed information on the above terms can be found on the EMA website: www.ema.europa.eu/