10 June 2024
EMA/PRAC/230613/2024
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 10-13 June 2024

Chair: Martin Huber

10 June 2024, 13:00 – 19:30, room 2C

11 June 2024, 08:30 – 19:30, room 2C

12 June 2024, 08:30 – 19:30, room 2C

13 June 2024, 08:30 – 16:00, room 2C

Organisational, regulatory and methodological matters (ORGAM)

27 June 2024, via teleconference

Health and safety information

In accordance with the Agency's health and safety policy, delegates are to be briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

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

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

Note on access to documents

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

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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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 10-13 June 2024. See June 2024 PRAC minutes (to be published post July 2024 PRAC meeting).

1.2. Agenda of the meeting on 10-13 June 2024

Action: For adoption

1.3. Minutes of the previous meeting on 13-16 May 2024

Action: For adoption

2. EU referral procedures for safety reasons: urgent EU procedures

2.1. Newly triggered procedures

2.1.1. Metamizole (NAP); metamizole, caffeine (NAP); metamizole, caffeine, codeine (NAP); metamizole, caffeine, codeine, paracetamol (NAP); metamizole, caffeine, codeine, paracetamol, phenobarbital (NAP); metamizole, caffeine, drotaverine (NAP); metamizole, caffeine, thiamine (NAP); metamizole, hyoscine (NAP); metamizole, pitofenone (NAP); metamizole, pitofenone, fenpipramide (NAP); metamizole, pitofenone, fenpiverinium (NAP); metamizole, triacetonamine (NAP) – EMEA/H/A-107i/1537

Applicant(s): various

PRAC Rapporteur: Julia Pallos; PRAC Co-rapporteur: Barbara Kovacic Bytyqi

Scope: Review of the benefit-risk balance following notification by Finland of a referral under Article 107i of Directive 2001/83/EC, based on pharmacovigilance data

Action: For adoption of a list of questions

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 and/or other sources

4.1.1. Roxadustat - EVRENZO (CAP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Anna Mareková

Scope: Signal of thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 20079 – New signal

Lead Member State(s): SK

[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

4.2. Signals follow-up and prioritisation

4.2.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/SDA/015.1; Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/SDA/013.1; Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/SDA/016.1; Idecabtagene vicleucel - ABECMA (CAP) - EMEA/H/C/004662/SDA/020.1; Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/SDA/019.1; Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/SDA/024.1;

Applicant(s): Bristol-Myers Squibb Pharma EEIG (Abecma, Breyanzi), Kite Pharma EU B.V. (Tecartus, Yescarta), Janssen-Cilag International NV (Carvykti), Novartis Europharm Limited (Kymriah), ATMP[3]

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of secondary malignancy of T-cell origin

Action: For adoption of PRAC recommendation

EPITT 20040 – Follow-up to April 2024

4.2.2. Medroxyprogesterone acetate (NAP)

Applicant: various

PRAC Rapporteur: Bianca Mulder

Scope: Signal of meningioma

Action: For adoption of PRAC recommendation

EPITT 20030 – Follow-up to February 2024

Lead Member State(s): NL

4.2.3. Valaciclovir (NAP)

Applicant: various

PRAC Rapporteur: Jana Lukačišinová

Scope: Signal of acute hepatitis

Action: For adoption of PRAC recommendation

EPITT 20047 – Follow-up to February 2024

Lead Member State(s): CZ

4.3. Variation procedure(s) resulting from signal evaluation

None

[3] Advanced therapy medicinal product

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Aflibercept - (CAP MAA) - EMEA/H/C/006150

Scope (pre D-180 phase): Treatment of age-related macular degeneration (AMD), visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO), due to diabetic macular oedema (DME) and due to myopic choroidal neovascularisation (myopic CNV)

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

5.1.2. Aflibercept - (CAP MAA) - EMEA/H/C/006056

Scope (pre D-180 phase): Treatment of age-related macular degeneration (AMD) and visual impairment

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

5.1.3. Bimatoprost - (CAP MAA) - EMEA/H/C/005916

Scope (pre D-180 phase): Indicated for the reduction of intraocular pressure (IOP) in adults with open angle glaucoma (OAG) or ocular hypertension (OHT) who are unsuitable for topical IOP-lowering medications

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

5.1.4. Liquid ethanolic extract 30 per cent (W/W) of Allium cepa fresh bulb and Citrus limon fresh fruit / Dry aqueous extract of paullinia cupana seed / Dry hydroethanolic extract of theobroma cacao seed -(CAP MAA) - EMEA/H/C/004155

Scope (pre D-180 phase): Treatment of alopecia areata in children and adolescents

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

5.1.5. Meningococcal group A, B, C, W and Y vaccine - (CAP MAA) - EMEA/H/C/006165

Scope (pre D-180 phase): Indicated for active immunisation to prevent invasive disease caused by Neisseria meningitidis groups A, B, C, W, and Y

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

5.1.6. Mirvetuximab soravtansine - (CAP MAA) - EMEA/H/C/005036, Orphan

Applicant: Immunogen Biopharma (Ireland) Limited

Scope (pre D-180 phase): Treatment of ovarian, fallopian tube, or primary peritoneal cancer

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

5.1.7. Temozolomide - (CAP MAA) - EMEA/H/C/006169, Orphan

Applicant: Orphelia Pharma

Scope (pre D-180 phase): Treatment of neuroblastoma

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

5.1.8. Ustekinumab - (CAP MAA) - EMEA/H/C/006585

Scope (pre D-180 phase): Treatment of active plaque psoriasis, paediatric plaque psoriasis, psoriatic arthritis (PsA) and Crohn's disease

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

5.1.9. Ustekinumab - (CAP MAA) - EMEA/H/C/006221

Scope (pre D-180 phase): Treatment of active plaque psoriasis, Crohn's disease, active ulcerative colitis and active psoriatic arthritis

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

5.1.10. Vilobelimab - (CAP MAA) - EMEA/H/C/006123

Scope (pre D-180 phase): Treatment of adult patients with SARS-CoV-2 induced septic acute respiratory distress syndrome (ARDS) receiving invasive mechanical ventilation (IMV) or extracorporeal membrane oxygenation (ECMO).

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. Cinacalcet - CINACALCET ACCORDPHARMA (CAP); NAP - EMEA/H/C/005236/WS2686/0011

Applicant(s): Accord Healthcare S.L.U., various

PRAC Rapporteur: Mari Thorn

Scope: To update the RMP to make updated in following safety concerns (important identified risks) after approval of the same changes in the reference product, Mimpara (in procedure EMEA/H/C/000570/IB/0069):
-Update of "Hypocalcemia" to "Hypocalcemia in the pediatric population"
-Removal of "QT prolongation and ventricular arrhythmias secondary to hypocalcaemia"
-Removal of "Convulsions/seizures"

Furthermore, the Marketing Authorisation Holder is taking the opportunity to consolidate into a single RMP the RMPs approved for Cinacalcet 30mg/60mg/90mg Film-coated tablets through CP (EMEA/H/C/005236) and DCP (FI/H/869/01-03/DC) procedures

Action: For adoption of PRAC Assessment Report

5.2.2. Dasatinib - SPRYCEL (CAP) - EMEA/H/C/000709/II/0090

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of an updated RMP version 18.0 in order to reflect the proposed revised commitments to assess the growth and development disorders and bone mineral metabolism disorders in paediatric subjects

Action: For adoption of PRAC Assessment Report

5.2.3. Human thrombin, Human fibrinogen - TACHOSIL (CAP) - EMEA/H/C/000505/II/0124

Applicant: Corza Medical GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of an updated RMP version 9.1 in order to reflect the extension of indication to include the paediatric population and to update the details of the planned non-interventional PASS: PASS-TachoSil Evaluation (PasTel)

Action: For adoption of PRAC Assessment Report

5.2.4. Mavacamten - CAMZYOS (CAP) - EMEA/H/C/005457/II/0008

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of an updated RMP version 3.0 in order to revise the number of patients planned to be enrolled in DISCOVER-HCM US-registry study CV027012 (MEA 005). In addition, the MAH took this opportunity to update protocol title for MAVEL-HCM study (CV027013) and include reference to study protocol in Annex 3 of the RMP, following the assessment of PAM procedure MEA 001

Action: For adoption of PRAC Assessment Report

5.2.5. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0063

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of an updated RMP version 32.0 in order to propose the removal of category 3 study A3921329 (A Long-Term, Observational Study within the CorEvitas [formerly Corrona] Inflammatory Bowel Disease (IBD) Registry to Characterize the Safety of Tofacitinib in Patients with Ulcerative Colitis in the Post-Approval Setting). In addition, the MAH took the opportunity to update the RMP with some other minor updates

Action: For adoption of PRAC Assessment Report

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

5.3.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0075/G, Orphan,

Applicant: Kite Pharma EU B.V., ATMP[4]

PRAC Rapporteur: Karin Erneholm

Scope: Grouped application comprising two type II variations as follows:
C.I.13 - Submission of the final report from study KTE-C19-101 (ZUMA-1) listed as a category 3 study in the RMP. This is a Phase 1/2 Multicenter Study Evaluating The Safety And Efficacy Of Kte-C19 In Subjects With Refractory Aggressive Non-Hodgkin Lymphoma.
C.I.13 - Submission of the final report from study KTE-C19-106 (ZUMA-6) listed as a category 3 study in the RMP. This is a Phase 1-2 Multi-Center Study Evaluating The Safety And Efficacy Of Kte-C19 In Combination With Atezolizumab In Subjects With Refractory Diffuse Large B-Cell Lymphoma (Dlbcl).
The RMP version 9.2 has also been submitted

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

5.3.2. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/II/0052

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include treatment of eosinophilic granulomatosis with polyangiitis (EGPA) for Fasenra, based on results from study D3253C00001 (Mandara); this was a randomised, double-blind, multicentre, parallel group, active-controlled, non-inferiority study that evaluated the efficacy and safety of benralizumab compared with mepolizumab in treatment of patients with EGPA on corticosteroid therapy with or without stable immunosuppressive therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 6.1 of the RMP has also been submitted. In addition, the MAH took this opportunity to introduce editorial changes. As part of the application, the MAH is requesting a 1-year extension of the market protection

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

5.3.3. Bulevirtide - HEPCLUDEX (CAP) - EMEA/H/C/004854/II/0031, Orphan

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of chronic hepatitis delta virus (HDV) infection in paediatric patients 3 years of age and older weighing at least 10 kg with compensated liver disease for Hepcludex, based on a modelling and simulation study and an extrapolation study to evaluate the use of Bulevirtide for the treatment of chronic hepatitis D infection in children from 3 to less than 18 years of age. As a consequence, sections 4.1,

[4] Advanced therapy medicinal product

4.2, 5.1 and 5.2 of the SmPC are updated. The package leaflet has been updated accordingly. Version 4.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the product information

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

5.3.4. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/WS2619/0066/G; Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/WS2619/0073/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Martin Huber

Scope: A grouped application consisting of two Type II variations, as follows:
C.I.4: Update of section 4.4 of the SmPC in order to amend an existing warning on diabetic ketoacidosis based on literature. The package leaflet is updated accordingly.
C.I.4: Update of sections 4.6 and 5.3 of the SmPC in order to update information on pregnancy based on literature. The RMP version 11.1 has also been submitted

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

5.3.5. Ceftazidime, avibactam - ZAVICEFTA (CAP) - EMEA/H/C/004027/II/0035

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to include treatment of paediatric patients from birth to less than 3-months of age in the following infections: complicated intra-abdominal infection (cIAI), complicated urinary tract infection (cUTI), including pyelonephritis, hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP) and in the treatment of infections due to aerobic Gram-negative organisms in patients with limited treatment options, for ZAVICEFTA, based on final results from study C3591024 and the population PK modelling/simulation analyses. Study C3591024 is a Phase 2a, 2-part, open-label, non-randomised, multicenter, single and multiple dose trial to evaluate pharmacokinetics, safety and tolerability of ceftazidime and avibactam in neonates and infants from birth to less than 3 months of age with suspected or confirmed infections due to gram-negative pathogens requiring intravenous antibiotic treatment. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 6.3 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 3.3 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.6. Cetuximab - ERBITUX (CAP) - EMEA/H/C/000558/II/0099

Applicant: Merck Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4 and 4.9 of the SmPC in order to introduce every two-weeks (Q2W) dosing regimen as an alternative to the already approved every week (Q1W) dosing regimen for the indications of metastatic colorectal cancer (CRC) and the

recurrent/metastatic squamous cell cancer of the head and neck (SCCHN) in combination with platinum-based chemotherapy, based on pharmacokinetic (PK)-TGI-OS modelling and simulations. The package leaflet is updated accordingly. The RMP version 19.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the product information

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

5.3.7. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/X/0080/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension application to introduce a new pharmaceutical form (granules in capsules for opening) associated with new strengths (20, 50 and 150 mg), grouped with a type II variation (C.I.6.a) to include the treatment of paediatric patients with relapsed or refractory, systemic ALK-positive ALCL or unresectable, recurrent, or refractory ALK-positive IMT to change the lower end of the age range from ≥6 years to ≥1 year for Xalkori following the assessment of II/0072 based on final results from study ADVL0912. 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 is updated in accordance. Version 9.1 of the RMP has also been submitted

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

5.3.8. Dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/WS2664/0066; Saxagliptin, dapagliflozin - QTERN (CAP) - EMEA/H/C/004057/WS2664/0043; Dapagliflozin, metformin - XIGDUO (CAP) - EMEA/H/C/002672/WS2664/0076

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.2, 4.4, 4.5, 4.8, 5.1 and 6.1 of the SmPC in order to align dapagliflozin related information in Fixed Dose Combination with Forxiga. The package leaflet is updated accordingly. The RMPs version 15.1 (Xigduo and Wbymect) and 9.1 (Qtern) has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the product information

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

5.3.9. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[5]) - EMEA/H/W/002168/II/0025/G

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser

Scope: A grouped application consisting of:
Type II (C.I.4): Update of section 4.6 of the SmPC in order to update information on

[5] 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)

breastfeeding based on final results from study MTN-043 (B-PROTECTED) listed as a category 3 study in the RMP (MEA/009). MTN-043 is a Phase 3b, randomised, open-label, safety, and drug detection study of dapivirine vaginal ring and oral truvada in breastfeeding mother-infant pairs. The package leaflet is updated accordingly. The RMP version 1.4 has also been submitted. In addition, the MAH took the opportunity to update Annex II of the product information
Type IB (C.I.11.z): Submission of an updated RMP version 1.4 in order to request a change on the due date for the MTN-034 (REACH) study

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

5.3.10. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0072, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include, in combination with bortezomib, lenalidomide and dexamethasone, the treatment of adult patients with newly diagnosed multiple myeloma, who are eligible for autologous stem cell transplant for Darzalex, based on the primary analysis results from the pivotal study 54767414MMY3014 (PERSEUS) and the results from study 54767414MMY2004 (GRIFFIN) and the D-VRd cohort of study 54767414MMY2040 (PLEIADES).
MMY3014 (PERSEUS) is a randomised, open-label, active-controlled, multicentre phase 3 study in adult subjects with newly diagnosed multiple myeloma, who are eligible for high dose therapy (as required for autologous stem cell transplant). The primary objective is to compare the efficacy of (subcutaneous) daratumumab in combination with bortezomib, lenalidomide and dexamethasone (D-VRd) versus bortezomib, lenalidomide and dexamethasone (VRd) in terms of progression free survival (PFS).
MMY2004 (GRIFFIN) is a randomised, open-label, active controlled, multicentre phase 2 study in adult subjects with newly diagnosed multiple myeloma, who are eligible for high dose therapy and autologous stem cell transplant. The primary objective is to compare the efficacy of daratumumab in combination with bortezomib, lenalidomide and dexamethasone (D-VRd) versus bortezomib, lenalidomide and dexamethasone (VRd), in terms of stringent complete response (sCR) rate.
MMY2040 (PLEIADES) is a randomised, open-label, multicentre phase 2 study to evaluate subcutaneous daratumumab in combination with standard multiple myeloma treatment regimens. The D-VRd cohort included adult subjects with newly diagnosed multiple myeloma, who were evaluated for clinical benefit in terms of very good partial response or better (VGPR) rate.
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 is updated in accordance. Version 10.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.11. Ebola vaccine (rDNA, replication-incompetent) - MVABEA (CAP) - EMEA/H/C/005343/II/0021

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy based on final results from study VAC52150EBL3010 listed as a category 3 study in the RMP as well as study VAC52150EBL3008 and two post-authorisation vaccination campaigns. Study VAC52150EBL3010 is a phase 3 open-label randomised clinical trial to evaluate the safety, reactogenicity and immunogenicity of a 2-dose Ebola vaccine regimen of Ad26.ZEBOV followed by MVA-BN-Filo in healthy pregnant women. The package leaflet is updated accordingly. The RMP version 3.3 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.12. Ebola vaccine (rDNA, replication-incompetent) - ZABDENO (CAP) - EMEA/H/C/005337/II/0019

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy based on final results from study VAC52150EBL3010 listed as a category 3 study in the RMP as well as study VAC52150EBL3008 and two post-authorisation vaccination campaigns. Study VAC52150EBL3010 is a phase 3 open-label randomised clinical trial to evaluate the safety, reactogenicity and immunogenicity of a 2-dose Ebola vaccine regimen of Ad26.ZEBOV followed by MVA-BN-Filo in healthy pregnant women. The package leaflet is updated accordingly. The RMP version 3.3 has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the product information

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

5.3.13. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0136

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Addition of a new strain (Spikevax JN.1, SARS-CoV-2 JN.1 mRNA) resulting in eight new monovalent presentations.

The Annex A, the SmPC, the Package Leaflet and Labelling are updated accordingly.
Editorial changes: In addition to the change described above, minor editorial updates to table footers throughout CTD sections including the addition of abbreviations have been included.
In addition, version 9.0 of the RMP has also been submitted.

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

5.3.14. Enalapril maleate - AQUMELDI (CAP) - EMEA/H/C/005731/X/0001/G

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Mari Thorn

Scope: Extension application to add a new strength of 1 mg orodispersible tablet grouped

with a type IB variation (C.I.z) to correct the SmPC to remove the recommended dose of epinephrine from Section 4.4

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

5.3.15. Etrasimod - VELSIPITY (CAP) - EMEA/H/C/006007/II/0001

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Mari Thorn

Scope: Update of section 4.4 to modify the macular oedema (MO) warning based on the evaluation of the cases of MO/cystoid MO reported in the etrasimod clinical studies and other S1P labels in the EU. The package leaflet and Annex II are updated in accordance. RMP version 1.1 has also been submitted. In addition, the MAH took this opportunity to introduce editorial changes to the product information

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

5.3.16. Faricimab - VABYSMO (CAP) - EMEA/H/C/005642/II/0005

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include treatment of adult patients with visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) for Vabysmo, based on results from the two phase 3 studies: GR41984 (BALATON) in patients with branch retinal vein occlusion (BRVO) and GR41986 (COMINO) in patients with central retinal vein occlusion (CRVO) or hemiretinal vein occlusion (HRVO). These are global, multicentre, randomised, double-masked, active comparator-controlled, parallel-group, 2-part studies evaluating the efficacy, safety, and PK of faricimab. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated. The package leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the product information

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

5.3.17. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0022/G, Orphan

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: A grouped application comprised of three Type II variations, as follows:
C.I.4: Update of sections 4.4 and 4.8 of the SmPC in order to modify the list of adverse drug reactions based on a revised safety ADR methodology for Dravet and Lennox-Gastaut syndromes, which includes pooled analyses encompassing studies ZX008-1503 and ZX008-1601 cohort B. The package leaflet is updated accordingly.
C.I.4: Update of section 5.1 of the SmPC in order to update clinical efficacy information for Dravet syndrome based on final results from study ZX008-1503 listed as a category 3 study in the RMP. This is an open-label extension trial to assess the long-term safety of ZX008 (fenfluramine hydrochloride) oral solution as an adjunctive therapy in children and young adults with Dravet syndrome.

C.I.4: Update of section 5.1 of the SmPC in order to update clinical efficacy information for Lennox-Gastaut syndrome based on final results from study ZX008-1601 Part 1 cohort B and interim results for study ZX008-1601 Part 2 cohort B. Study 1601 Part 1 was an international, randomised, double-blind, parallel-group, placebo-controlled study in subjects with LGS 2 to 35 years of age, while study 1601 Part 2 is a long-term, open-label, flexible-dose extension for subjects who completed study 1601 Part 1.
The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the product information, including to section 4.2 of the SmPC

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

5.3.18. Fenofibrate, pravastatin sodium - PRAVAFENIX (CAP) - EMEA/H/C/001243/II/0037

Applicant: Laboratoires SMB s.a.

PRAC Rapporteur: Nathalie Gault

Scope: Extension of indication to include treatment of mixed hyperlipidaemia in adult patients while on a treatment with pravastatin 40 mg monotherapy or on another moderate-intensity statin regimen for PRAVAFENIX, based on final results from the non-interventional PASS: POSE (Pravafenix Observational Study in Europe); this is a European, observational, three-year cohort comparative study on the safety of the fixed dose combination pravastatin 40 mg/fenofibrate 160 mg (Pravafenix) versus statin alone in real clinical practice. As a consequence, sections 4.1 and 4.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted

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

5.3.19. Inclisiran - LEQVIO (CAP) - EMEA/H/C/005333/II/0021

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final report from study ORION-8 - a long-term extension trial of the phase III lipid-lowering trials to assess the effect of long-term dosing of inclisiran given as subcutaneous injections in subjects with high cardiovascular risk and elevated LDL-C, listed as a category 3 study in the RMP. The RMP version 3.0 has also been submitted

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

5.3.20. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/II/0126

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Submission of the final report from study VX15-770-126 (study 126) listed as a category 3 study in the RMP; this is a phase 3, 2-arm, multicenter open-label study to evaluate the safety and pharmacodynamics of long-term ivacaftor treatment in subjects with cystic fibrosis who are less than 24 months of age at treatment initiation and have an approved ivacaftor-responsive mutation. The RMP version 16.0 has also been submitted

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

5.3.21. Macitentan - OPSUMIT (CAP) - EMEA/H/C/002697/X/0051/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension application to introduce a new pharmaceutical form associated with new strengths (1 and 2.5 mg dispersible tablet) grouped with an extension of indication (C.I.6.a) to include, as monotherapy or in combination, the long-term treatment of pulmonary arterial hypertension (PAH) in paediatric patients aged 1 month to less than 18 years of age of WHO Functional Class (FC) I to III for OPSUMIT, based on interim results from AC-055-312 study (TOMORROW). This is a multicentre, open-label, randomised study with single-arm extension period to assess the pharmacokinetics, safety, and efficacy of macitentan versus standard of care in children with pulmonary arterial hypertension. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 4.9, 5.1 and 5.2 of the SmPC for film-coated tablets are updated. The package leaflet and Labelling are updated in accordance. Version 14.1 of the RMP has also been submitted

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

5.3.22. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/II/0024/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped application comprising two variations as follows:
Type II (C.I.4) – Update of sections 4.4 and 4.8 the SmPC in order to add a new warning on liver injury, to add liver injury to the list of adverse drug reactions (ADRs) with frequency rare based on the cumulative review of the MAH safety database, clinical trials and literature search. The RMP version 8.0 also been submitted.
Type IA (A.6) – To change the ATC code from L04AA38 to L04AE02

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

5.3.23. Pegzilarginase - LOARGYS (CAP) - EMEA/H/C/005484/II/0002/G, Orphan

Applicant: Immedica Pharma AB

PRAC Rapporteur: Martin Huber

Scope: Grouped application comprising two type II variations as follows:
C.I.4 – Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study CAEB1102-300A (SOB 003), listed as a specific obligation in Annex II. Study 300A was a Phase 3, randomised, double blind, placebo-controlled study of the efficacy and safety of pegzilarginase in adults, adolescents and children with arginase 1 deficiency (ARG1 D).
C.I.4 – Update of section 4.8 of the SmPC in order to update efficacy and safety information based on final results from study CAEB1102-102A (SOB 004), listed as a specific obligation in Annex II.
Study 102A was an open label extension study to evaluate the long-term safety, tolerability, and efficacy of pegzilarginase in adults, adolescents and children with arginase 1 deficiency (ARG1 D).
The package leaflet and Annex II are updated accordingly. The RMP version 1.1 has also

been submitted. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template version 10.4 and to introduce minor editorial changes

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

5.3.24. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0153

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication for KEYTRUDA in combination with carboplatin and paclitaxel to include first-line treatment of primary advanced or recurrent endometrial carcinoma in adults, based on final results from study KEYNOTE-868. This is a randomised Phase 3, placebo-controlled, double-blind study of pembrolizumab vs placebo in combination with chemotherapy (paclitaxel plus carboplatin) for newly diagnosed Stage III/Stage IVA, Stage IVB, or recurrent endometrial cancer.
As a consequence, sections 4.1 and 5.1 of the SmPC are updated. Version 46.1 of the RMP has also been submitted

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

5.3.25. Pirtobrutinib - JAYPIRCA (CAP) - EMEA/H/C/005863/II/0002

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adult patients with chronic lymphocytic leukemia (CLL) who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor for JAYPIRCA, based on interim results from study LOXO-BTK-20020 (BRUIN CLL-321); this is a phase 3 open-label, randomised study of LOXO-305 versus investigator's choice of idelalisib plus rituximab or bendamustine plus rituximab in BTK inhibitor pretreated CLL/SLL.
As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.
As part of the application the MAH is requesting a 1-year extension of the market protection

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

5.3.26. Ranibizmab - BYOOVIZ (CAP) - EMEA/H/C/005545/II/0016/G

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 1. Type II (B.II.e.1.b.2) The updated RMP version 3.1 has also been submitted to introduce changes and to update the MedDRA Search Terms version and applicant's overall search terms strategy for the purpose of safety surveillance.

2. Type IB (B.II.b.3.z)

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

5.3.27. Sapropterin - KUVAN (CAP) - EMEA/H/C/000943/II/0078

Applicant: BioMarin International Limited

PRAC Rapporteur: Eamon O'Murchu

Scope: Submission of the final report from study KOGNITO, listed as a category 3 study in the RMP. This is a phase IV open-label, single-cohort study of the long-term neurocognitive outcomes in 4- to 5-year-old children with phenylketonuria treated with sapropterin dihydrochloride (Kuvan) for 7 years. The RMP version 16.0 has also been submitted

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

5.3.28. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/II/0028

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on interim results from study LIBRETTO-431 (JZJC) listed as a specific obligation in the Annex II (SOB/002); this is a randomised Phase 3 study comparing selpercatinib to platinum-based and pemetrexed therapy with or without pembrolizumab in patients with locally advanced or metastatic, RET-fusion-positive NSCLC. The package leaflet is updated accordingly. The RMP version 6.1 has also been submitted. In addition, the MAH took the opportunity to update Annex II

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

5.3.29. Setmelanotide - IMCIVREE (CAP) - EMEA/H/C/005089/II/0018, Orphan

Applicant: Rhythm Pharmaceuticals Netherlands B.V.,

PRAC Rapporteur: Anna Mareková

Scope: Extension of indication to include the population of children aged 2 years and above for the treatment of pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin Type 1 (PCSK1) deficiency or biallelic leptin receptor (LEPR) deficiency and Bardet-Biedl Syndrome (BBS) for IMCIVREE, based on the final results from study RM-493-033 "A Phase 3 multicentre, one-year, open-label study of setmelanotide in paediatric patients aged 2 to <6 years of age with rare genetic causes of obesity"; this is an open label study to evaluate the weight-related parameters along with the safety and tolerability of setmelanotide in patients aged 2 to <6 years. 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 is updated in accordance. Version 2.1 of the RMP has also been submitted. In addition, the MAH took this opportunity to introduce editorial changes to the product information

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

5.3.30. Sodium phenylbutyrate - PHEBURANE (CAP) - EMEA/H/C/002500/X/0037

Applicant: Eurocept International B.V.

PRAC Rapporteur: Eamon O'Murchu

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (500 mg film-coated tablets). The RMP (version 1.1) is updated in accordance

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

5.3.31. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/II/0055

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Type II (B.IV.1.c)

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

5.3.32. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0121

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report from study ZUMA-8 (PAM). This is a phase 1 multicenter study evaluating the safety and tolerability of KTE-X19 in adult subjects with Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma. The RMP version 29.0 has also been submitted

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

5.3.33. Turoctocog alfa pegol - ESPEROCT (CAP) - EMEA/H/C/004883/II/0023

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include children below 12 years of age for treatment and prophylaxis of bleeding with haemophilia A for Esperoct, including previously untreated patients (PUPs) based on the final results from studies 3776, 4410, 3908, 3859, 3885, 3860, 4033 and 4595. As a consequence, section 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. Furthermore, the product information is brought in line with the latest QRD template version 10.4

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

5.3.34. Ustekinumab - UZPRUVO (CAP) - EMEA/H/C/006101/X/0001

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (130 mg concentrate for solution for infusion) and a new route of administration (intravenous use). The RMP version 1.1 is updated in accordance

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. Amivantamab - RYBREVANT (CAP) - PSUSA/00010977/202311

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Buprenorphine[6] - SIXMO (CAP) - PSUSA/00010778/202311

Applicant: L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Capmatinib - TABRECTA (CAP) - PSUSA/00011022/202311

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Cefiderocol - FETCROJA (CAP) - PSUSA/00010849/202311

Applicant: Shionogi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA (CAP) - PSUSA/00010449/202311

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

[6] Implant

Action: For adoption of recommendation to CHMP

6.1.6. Darbepoetin alfa - ARANESP (CAP) - PSUSA/00000932/202310

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Defibrotide - DEFITELIO (CAP) - PSUSA/00010086/202310

Applicant: Gentium S.r.l.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Dinutuximab beta - QARZIBA (CAP) - PSUSA/00010597/202311

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Diphtheria, tetanus, pertussis antigens (pertussis toxoid, filamentous haemagglutinin, pertactin) (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated), haemophilus type b conjugate vaccines (adsorbed) - INFANRIX HEXA (CAP) - PSUSA/00001122/202310

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Drospirenone, estetrol - DROVELIS (CAP); LYDISILKA (CAP) - PSUSA/00010938/202311

Applicant: Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.) (Drovelis), Estetra SRL (Lydisilka)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Emicizumab - HEMLIBRA (CAP) - PSUSA/00010668/202311

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Empagliflozin, linagliptin - GLYXAMBI (CAP) - PSUSA/00010539/202311

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Etranacogene dezaparvovec - HEMGENIX (CAP) - PSUSA/00011037/202311

Applicant: CSL Behring GmbH, ATMP[7]

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.14. Fosamprenavir - TELZIR (CAP) - PSUSA/00001470/202310

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Givosiran - GIVLAARI (CAP) - PSUSA/00010839/202311

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Glasdegib - DAURISMO (CAP) - PSUSA/00010859/202311

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Bianca Mulder

[7] Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Granisetron[8] - SANCUSO (CAP) - PSUSA/00010101/202310

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Hepatitis B surface antigen, CpG 1018 adjuvant - HEPLISAV B (CAP) - PSUSA/00010919/202311

Applicant: Dynavax GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Ibrutinib - IMBRUVICA (CAP) - PSUSA/00010301/202311

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/202311

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Insulin human - ACTRAPID (Art 58[9]) - EMEA/H/W/005779/PSUV/0006

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUR procedure

[8] Transdermal patch only

[9] 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)

Action: For adoption of recommendation to CHMP

6.1.22. Insulin human - INSULATARD (Art 58[9]) - EMEA/H/W/005780/PSUV/0005

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.23. Ivosidenib - TIBSOVO (CAP) - PSUSA/00011048/202311

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Ixazomib - NINLARO (CAP) - PSUSA/00010535/202311

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Larotrectinib - VITRAKVI (CAP) - PSUSA/00010799/202311

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Linzagolix choline - YSELTY (CAP) - PSUSA/00010998/202311

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Lonafarnib - ZOKINVY (CAP) - PSUSA/00011005/202311

Applicant: EigerBio Europe Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Lumasiran - OXLUMO (CAP) - PSUSA/00010884/202311

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Lurasidone - LATUDA (CAP) - PSUSA/00010114/202310

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

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Macitentan - OPSUMIT (CAP) - PSUSA/00010115/202310

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Maribavir - LIVTENCITY (CAP) - PSUSA/00011024/202311

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Nelarabine - ATRIANCE (CAP) - PSUSA/00002132/202310

Applicant: Sandoz Pharmaceuticals d.d.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Obeticholic acid - OCALIVA (CAP) - PSUSA/00010555/202311

Applicant: Advanz Pharma Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Obinutuzumab - GAZYVARO (CAP) - PSUSA/00010279/202310

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - PSUSA/00010501/202311

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Pasireotide - SIGNIFOR (CAP) - PSUSA/00009253/202310

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Patiromer - VELTASSA (CAP) - PSUSA/00010618/202310

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Pegcetacoplan - ASPAVELI (CAP) - PSUSA/00010974/202311

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Pegunigalsidase alfa - ELFABRIO (CAP) - PSUSA/00011049/202311

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Piflufolastat (^{18}F) - PYLCLARI (CAP) - PSUSA/00000097/202311

Applicant: Curium Pet France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Prucalopride - RESOLOR (CAP) - PSUSA/00002568/202310

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Relugolix, estradiol, norethisterone acetate - RYEQO (CAP) - PSUSA/00010942/202311

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Respiratory syncytial virus vaccine (bivalent, recombinant) - ABRYSVO (CAP) - PSUSA/00000102/202311

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Rituximab - BLITZIMA (CAP); MABTHERA (CAP); RIXATHON (CAP); RIXIMYO (CAP); RUXIENCE (CAP); TRUXIMA (CAP) - PSUSA/00002652/202311

Applicant: Roche Registration GmbH (MabThera), Sandoz GmbH (Rixathon, Riximyo), Pfizer Europe MA EEIG (Ruxience), Celltrion Healthcare Hungary Kft. (Blitzima, Truxima)

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/202311

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Coronavirus (COVID-19) vaccine (B.1.351 variant, prefusion Spike delta TM protein, recombinant) - VIDPREVTYN BETA (CAP)[10] - PSUSA/00011035/202311

Applicant: Sanofi Pasteur

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.47. Satralizumab - ENSPRYNG (CAP) - PSUSA/00010944/202311

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Selpercatinib - RETSEVMO (CAP) - PSUSA/00010917/202311

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Setmelanotide - IMCIVREE (CAP) - PSUSA/00010941/202311

Applicant: Rhythm Pharmaceuticals Netherlands B.V.,

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[10] Markteing Authorisation was withdrawn – Comission Implementing Decision date 11 March 2024:

6.1.50. Sirolimus[11] - HYFTOR (CAP) - PSUSA/00000025/202311

Applicant: Plusultra pharma GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Sotorasib - LUMYKRAS (CAP) - PSUSA/00010970/202311

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Stiripentol - DIACOMIT (CAP) - PSUSA/00002789/202311

Applicant: BIOCODEX

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Tirzepatide - MOUNJARO (CAP) - PSUSA/00011019/202311

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Tixagevimab, cilgavimab - EVUSHELD (CAP) - PSUSA/00010992/202311

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/202311

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

[11] Indicated for treatment of angiofibroma associated with tuberous sclerosis complex only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Turoctocog alfa - NOVOEIGHT (CAP) - PSUSA/00010138/202310

Applicant: Novo Nordisk

A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.57. Vestronidase alfa - MEPSEVII (CAP) - PSUSA/00010709/202311

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Zanubrutinib - BRUKINSA (CAP) - PSUSA/00010960/202311

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Bianca Mulder

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. Insulin human - ACTRAPID (CAP), INSUMAN (CAP); insulin human, insulin isophane[12] - ACTRAPHANE (CAP), INSULATARD (CAP), MIXTARD (CAP), PROTAPHANE (CAP); NAP - PSUSA/00001753/202310

Applicant(s): Novo Nordisk A/S (Actraphane, Actrapid, Insulatard, Mixtard, Protaphane), Sanofi-Aventis Deutschland GmbH (Insuman), various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Subcutaneous and intravenous uses only

6.2.2. Methotrexate - JYLAMVO (CAP); NORDIMET (CAP); NAP - PSUSA/00002014/202310

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

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Ascorbic acid, chlorphenamine maleate, paracetamol (NAP) - PSUSA/00000696/202311

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Atorvastatin (NAP) - PSUSA/00010347/202310

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Bromocriptine (NAP) - PSUSA/00000438/202310

Applicant(s): various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Ceftazidime (NAP) - PSUSA/00000608/202310

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Citric acid, potassium salts, potassium citrate (NAP) - PSUSA/00000783/202311

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Clevidipine (NAP) - PSUSA/00010288/202311

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Drospirenone (NAP) - PSUSA/00010853/202311

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Etifoxine (NAP) - PSUSA/00001321/202310

Applicant(s): various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Flutamide (NAP) - PSUSA/00001453/202310

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Hydrochlorothiazide, nebivolol (NAP) - PSUSA/00001658/202311

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Hydroxyzine, hydroxyzine combination (NAP) - PSUSA/00001696/202311

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Ketotifen[13] (NAP) - PSUSA/00001813/202310

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Methacholine (NAP) - PSUSA/00010891/202310

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Minoxidil[14] (NAP) - PSUSA/00002067/202310

Applicant(s): various

PRAC Lead: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Nimodipine (NAP) - PSUSA/00002166/202311

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[13] Oral formulation(s) only
[14] Topical formulation only

6.3.16. Tetrabenazine (NAP) - PSUSA/00002911/202310

Applicant(s): various

PRAC Lead: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Human C1-esterase inhibitor - CINRYZE (CAP) - EMEA/H/C/001207/LEG 022

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to questions raised during procedure PSUSA/00010104/202306 (cumulative review):
Periodic Safety Update Report (16 June 2021 to 15 June 2023)
Issue to be addressed as a post authorisation measure: The case related to "Creutzfeldt-Jakob disease" needs to be further assessed. The MAH is therefore requested to submit within 1 month a comprehensive presentation of this case (incl. CJD subtype, patient details, batch number, follow-up information, medical reports, etc.), a causality assessment and a justified evaluation of any potential implication(s) on the benefit-risk balance of Cinryze

Action: For adoption of advice to CHMP

6.4.2. Delafloxacin - QUOFENIX (CAP) - EMEA/H/C/004860/LEG 004

Applicant: A. Menarini Industrie Farmaceutiche Riunite s.r.l.

PRAC Rapporteur: Petar Mas

Scope: From Art 31 referral
MAHs is requested to provide a cumulative review on spontaneously reported cases of prolonged, potentially irreversible, serious suspected adverse drug reactions to fluoroquinolones in the remit of the PSUR, however data will be assessed in the remit of a separate follow-up procedure.

The MAH has submitted all relevant data in the PSUR, no further submission is deemed necessary, this procedure is linked to the PSUR submission

Action: For adoption of advice to CHMP

6.4.3. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/002789/LEG 006

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: ***5-year Cumulative Safety Review***(from 1 January 2017 - 31 December 2022)

following the outcome of the Art 31 referral procedure : A cumulative review of all these cases of long-lasting, disabling and potentially irreversible ADRs with a particular focus on risk factors should be performed in 5 years by the MAHs and should be submitted as part of the PSURs for MAHs required submitting a PSUR as per EURD list

Action: For adoption of advice to CHMP

6.4.4. Piperaquine tetraphosphate, Artenimol - EURARTESIM (CAP) - EMEA/H/C/001199/LEG 018.2

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to LEG 018.1 [the issue of autoimmune haemolytic anaemia] RSI as adopted in February 2024

Action: For adoption of advice to CHMP

6.4.5. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/LEG 017.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: From II-0031
Interim Report for period covering 05 June 2023 - 04 December 2023
The MAH shall provide targeted tumour lysis syndrome (TLS) assessment reports on a biannual basis (submitted annually within the PSUR, and 6 months after the PSUR submission in a separate report) through 2023, and annually thereafter, as per the RMP v8.0.

These biannual assessment reports ensure close monitoring of the important identified risk of TLS, and the evaluation of the impact of newly implemented risk minimisation measures for TLS, on adherence to both already existing and updated recommendation added to the SmPC, the impact of the DHPC distributed to haematologists, and the patient card

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

None

6.5.1. Atazanavir - REYATAZ (CAP) - EMEA/H/C/000494/II/0140

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Nathalie Gault

Scope: Update of section 4.4 of the SmPC in order to clarify and update the warning regarding dyslipidaemia in relation to other comparators, following PRAC's recommendation in the outcome of procedure PSUSA/00000258/202106. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

Action: For adoption of PRAC Assessment Report

6.5.2. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/II/0090/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped application comprising two variations as follows:
Type II (C.I.3.b) - Update of sections 4.3 and 4.4 of the SmPC in order to add history of progressive multifocal leukoencephalopathy (PML) as a new contraindication and to amend an existing warning on PML and to update the educational material to improve the general readability of these documents and better address key messages and recommendations for healthcare professionals following the assessment of procedure PSUSA/00001393/202302. The package leaflet and Annex II are updated accordingly. The RMP version 20.0 has also been submitted.
Type IA (A.6) - To change the ATC Code of Fingolimod from L04AA27 to L04AE01

Action: For adoption of PRAC Assessment Report

6.5.3. Meningococcal Group A, C, W and Y conjugate vaccine - MENQUADFI (CAP) - EMEA/H/C/005084/II/0031

Applicant: Sanofi Pasteur

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 4.8 of the SmPC in order to add 'hypersensitivity including anaphylaxis' to the list of adverse drug reactions (ADRs) with frequency not known, based on a cumulative review of cases of hypersensitivity/allergic reaction (including anaphylaxis) following the request by PRAC in the Assessment Report for PSUSA/00010044/202304. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[15]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[16]

7.1.1. Exagamglogene autotemcel - CASGEVY (CAP) - EMEA/H/C/PSA/S/0113

Applicant: Vertex Pharmaceuticals (Ireland) Limited, ATMP

[15] 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
[16] In accordance with Article 107n of Directive 2001/83/EC

PRAC Rapporteur: Bianca Mulder

Scope: Substantial amendment to a protocol for a long-term registry-based study of patients with transfusion-dependent β-thalassemia (TDT) or sickle cell disease (SCD) treated with exagamglogene autotemcel (exa-cel)

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

7.1.2. Voretigene neparvovec - LUXTURNA (CAP) - EMEA/H/C/PSA/S/0114

Applicant: Novartis Europharm Ltd, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Substantial amendment to a post-authorisation observational study to collect long-term safety information (i.e., for 5 years after treatment) 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

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

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

7.2.1. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/ANX 011.2

Applicant: Kite Pharma EU B.V., ATMP[18]

PRAC Rapporteur: Bianca Mulder

Scope: **REVISED PROTOCOL combining STUDY No. KTE-EU-472-6036 & KT-EU-474-6644**
From Initial MAA
ANX 002: Study No. KTE-EU-472-6036:
KT-EU-472-6036: Long-term, non-interventional study of recipients of Tecartus for treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)

From II-008-G
ANX 011: KT-EU-474-6644: Long-term, non-interventional study of the treatment by Tecartus of adult patients with relapsed or refractory (r/r) B-cell precursor acute lymphoblastic leukemia (ALL)

MAH Response to ANX 011.1 as adopted in December 2023:
Joint protocol combining studies KTE-EU-472-6036 & KT-EU-474-6644 as follows:
KT-EU-472-6036: Long-term, non-interventional study of recipients of Tecartus for treatment of adult patients with relapsed or refractory (r/r) mantle cell lymphoma (MCL) or adult patients with r/r B-cell precursor acute lymphoblastic leukemia (ALL)

Action: For adoption of advice to CAT and CHMP

[17] 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
[18] Advanced therapy medicinal product

7.2.2. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/LEG 016.6

Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: ***Protocol Study***
Draft Study Title: Post-hoc analysis of the SPICE III (academic) trial dataset to address the risk of increased mortality among patients ≤65y sedated with dexmedetomidine. (category 3 study)

Action: For adoption of advice to CHMP

7.2.3. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/MEA 007.1

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: From MEA 002.1
**REVISED PROTOCOL (ver. 0.5) for PASS (non-imposed/non-interventional/Cat. 3) Evaluation of long-term risk of malignancies in patients with myasthenia gravis (MG) treated with efgartigimod compared to MG patients on any other MG therapy and who do not have malignancy history in the lookback period.

MAH Response to MEA 007 as adopted in January 2024:
A revised protocol for the non-imposed non-interventional PASS should be submitted by 02.04.2024 taking into account the comments included in section 4 overall conclusion of EMEA/H/C/005849/MEA/007 procedure

Action: For adoption of advice to CHMP

7.2.4. Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/MEA 036.7

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: **PASS Protocol Study no.: CA184557**
Title: Long-term Follow-up of Nivolumab and Ipilimumab (as Monotherapy and as Combination Therapy)-treated Pediatric Patients Enrolled in the Dutch Melanoma Treatment Registry (DMTR).

MAH Response to MEA 036.6 as adopted in January 2024:
1. The MAH is requested to provide an update on whether they are aware of any other registry that has the infrastructure and resources to collect long-term follow-up of paediatric melanoma patients in the capacity of DMTR.
2. The MAH is requested to provide an update on the patient enrolment for patients treated with ipilimumab monotherapy and discuss the impact of the current landscape on the patient enrolment for the added treatment options.
3. The MAH amended al mention of the grade 3 and 4 AEs to grade 3 and 4 treatment related AEs. No further justification is provided. It remains unclear if the amendment concerns a change in the DMTR protocol. The MAH is requested to provide a proper justification for this amendment and clarify if the DMTR collects all reported AEs or

only treatment related AEs

Action: For adoption of advice to CHMP

7.2.5. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001.11

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: ***REVISED PROTOCOL for PASS Study TEG4001*** (Version 4.1)
A Prospective, Non-interventional, Long-term, Multinational Cohort Safety Study of Patients with Hereditary Transthyretin Amyloidosis with Polyneuropathy (hATTR-PN).

Action: For adoption of advice to CHMP

7.2.6. Linzagolix choline - YSELTY (CAP) - EMEA/H/C/005442/MEA 002.3

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: From Initial MAA:
REVISED PROTOCOL (ver. 4) for PASS YSELTY (NI/NI/RMP/Cat. 3)
A multinational PASS on real-world treatment in patients receiving YSELTY® (linzagolix choline) for moderate to severe symptoms of uterine fibroids, to evaluate routinely collected data on bone mineral density and to assess safety during long term (>12 months) use for linzagolix 200mg (with ABT) and 100mg (with and without ABT) dosing regimen

Action: For adoption of advice to CHMP

7.2.7. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/MEA 057.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: ***PASS Study no.: CA184557***
Title: Long-term Follow-up of Nivolumab and Ipilimumab (as Monotherapy and as Combination Therapy)-treated Pediatric Patients Enrolled in the Dutch Melanoma Treatment Registry (DMTR).

MAH Response to MEA 057 as adopted in January 2024:
A revised protocol for the non-imposed non-interventional PASS should be submitted by 25 March 2024 taking into account the comments below:
As it is not acceptable, that long-term safety data in pediatric patients < 12 years of age will be collected as a separate off-label use cohort, the MAH is asked to make the changes in the protocol accordingly

Action: For adoption of advice to CHMP

7.2.8. Omaveloxolone - SKYCLARYS (CAP) - EMEA/H/C/006084/MEA 002

Applicant: Reata Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: From initial MAA
PROTOCOL (ver. 3) for PASS 296FA401 (408-C-2301)
An observational, multinational, post-marketing registry of omaveloxolone-treated patients with Friedreich's ataxia

Action: For adoption of advice to CHMP

7.2.9. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 005.9

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: From Initial MAA:
REVISED PROTOCOL (Version 5) for Study 165-504
A prospective global pregnancy observational safety surveillance study. A global multicentre study to assess maternal, fetal and infant outcomes of exposure to Palynziq (pegvaliase-pqpz) during pregnancy.

MAH Response to MEA 005.7 as adopted in February 2024:
1. Adequately justify the purpose of the change in enrolment method.
2. Clarify if HCP initiated enrolment or enrolment via HCP has been in use to enrol subjects at any time point since the start of data collection.
3. Discuss how the change in enrolment method may impact on the number of subjects enrolled.
4. Discuss the limitations of the proposed enrolment method and how the MAH proposes to address these limitations.
5. Add detail to the protocol on how potential subjects are being encouraged to participate in the study and are being made aware of the existence of the study.
6. Add a description of any mechanisms and procedures to ensure data quality and integrity of data obtained and recorded by the co-ordinating centres and/or the MAH.
7. Update the milestones in appendix 3 of the protocol

Action: For adoption of advice to CHMP

7.2.10. Piflufolastat (18F) - PYLCLARI (CAP) - EMEA/H/C/005520/MEA 002

Applicant: Curium Pet France

PRAC Rapporteur: Kimmo Jaakkola

Scope: From initial MAA
PROTOCOL PASS NO. CURF18PSM0002 (NI/NI/RMP/Cat. 3)
A observational study to evaluation the effectiveness of the self-administered educational training programme to the nuclear medicine physicians who will have to interpret PET findings with Pylclari

Action: For adoption of advice to CHMP

7.2.11. Respiratory syncytial virus vaccine (bivalent, recombinant) - ABRYSVO (CAP) - EMEA/H/C/006027/MEA 003

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: From initial MAA
PROTOCOL FOR PASS NO. C3671026 (NINI/RMP/Cat. 3)
A post-authorisation safety study (PASS) of ABRYSVO (respiratory syncytial virus stabilised prefusion F subunit vaccine) in pregnant women and their offspring in a real world setting in Europe and UK

Action: For adoption of advice to CHMP

7.2.12. Respiratory syncytial virus vaccine (bivalent, recombinant) - ABRYSVO (CAP) - EMEA/H/C/006027/MEA 004

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: From initial MAA
PROTOCOL PASS NO. C3671038 (NINI/RMP/Cat. 3)
A PASS of ABRYSVO in immunocompromised, or renally or hepatically impaired older adults aged 60 years and older in a real world setting in Europe and UK

Action: For adoption of advice to CHMP

7.2.13. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 009.2

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: From X/0020/G:
REVISED PROTOCOL FOR PASS No. P23-653 (non-imposed/non-interventional) Pregnancy Exposure and Outcomes for Women with Crohn's Disease Treated with Risankizumab.
A comparative cohort study to describe risankizumab exposure in pregnant patients with Crohn's disease, and compare pregnancy and infant outcomes to pregnant patients with Crohn's disease who were treated with alternative therapies (e.g., biologics). In addition, descriptive analyses of pregnancy outcomes in patients with Crohn's disease without exposure to any treatments under investigation will also be conducted

MAH Response to MEA 009.1 as adopted in December 2023:
A revised protocol for the non-imposed non-interventional PASS should be submitted by 6 February 2024 taking into account the comments included in the AR section 4

Action: For adoption of advice to CHMP

7.2.14. Ritlecitinib - LITFULO (CAP) - EMEA/H/C/006025/MEA 001

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adam Przybylkowski

Scope: From intial MAA:
DRAFT PROTOCOL FOR PASS B7981101 (Cat. 3/RMP/NINI)
Active Surveillance Study to Monitor the Real-World Safety of Ritlecitinib Among Patients with Alopecia Areata in Europe

Action: For adoption of advice to CHMP

7.2.15. Ritlecitinib - LITFULO (CAP) - EMEA/H/C/006025/MEA 002

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adam Przybylkowski

Scope: From intial MAA:
DRAFT PROTOCOL FOR PASS B7981092 (Cat. 3/RMP/NINI)
Prospective Active Surveillance Study to Monitor the Real-World Safety of Ritlecitinib Among Adolescents with Alopecia Areata

Action: For adoption of advice to CHMP

7.2.16. Ritlecitinib - LITFULO (CAP) - EMEA/H/C/006025/MEA 003

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adam Przybylkowski

Scope: From intial MAA:
Study B7981102 - A Drug Utilization Study to Evaluate Indicators of Adherence to the Risk Minimization Measures for Ritlecitinib Using Electronic Healthcare Data in Denmark, France, and Sweden
Protocol Study B7981102

Action: For adoption of advice to CHMP

7.2.17. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/MEA 002.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: MAH's responses to MEA 002.1 [8B-MC-B011] RSI as adopted in November 2023:
A revised protocol for the non-imposed non-interventional PASS should be submitted within 4 months of CHMP opinion taking into account the comments raised in the AR. The review of the revised protocol will follow a 74-day timeline

Action: For adoption of advice to CHMP

7.2.18. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/MEA 005.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: MAH's responses to MEA 005.1 [(IBF-MC-B014 (formerly IBF-MC-B013)] RSI

adopted in November 2023:
A revised protocol for the non-imposed non-interventional PASS should be submitted within 4 months of CHMP opinion taking into account the comments raised in the AR. The review of the revised protocol will follow a 74-day timeline

Action: For adoption of advice to CHMP

7.2.19. Ublituximab - BRIUMVI (CAP) - EMEA/H/C/005914/MEA 001.2

Applicant: Neuraxpharm Pharmaceuticals S.L.

PRAC Rapporteur: Liana Martirosyan

Scope: ***Revised PASS Protocol / Study TG1101-RMS402 (ENLIGHTEN) (cat. 3)***
Final protocol submission of the Study entitled "Evaluating Long-Term Safety of BRIUMVI in Patients with Relapsing Multiple Sclerosis (RMS) in a Real-World Setting from Registry Data"

Action: For adoption of advice to CHMP

7.2.20. Ublituximab - BRIUMVI (CAP) - EMEA/H/C/005914/MEA 002.1

Applicant: Neuraxpharm Pharmaceuticals S.L.

PRAC Rapporteur: Liana Martirosyan

Scope: From initial MAA
PASS No TG1101-RMS403, NI/NI, cat. 3
Final protocol submission of the BRIUMVI Pregnancy Registry: A Prospective Registry Study of Pregnancy and Infant Outcomes in Patients Treated with BRIUMVI

Action: For adoption of advice to CHMP

7.2.21. Ublituximab - BRIUMVI (CAP) - EMEA/H/C/005914/MEA 003.1

Applicant: Neuraxpharm Pharmaceuticals S.L.

PRAC Rapporteur: Liana Martirosyan

Scope: From initial MAA
PASS No TG1101-RMS404, NI/NI, cat. 3
Final protocol submission of the Post-Authorisation Study to Characterize the Safety of Briumvi Use in Pregnant Patients with Multiple Sclerosis Using Data from a US Administrative Healthcare Claims Database

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[19]

None

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[20]

7.4.1. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0047

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from non-interventional Study I4V-MC-B012 listed as a category 3 study in the RMP. This is a post-marketing safety surveillance of baricitinib in three European registries. The RMP version 23.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.2. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/II/0206/G

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application comprised of 3 Type II variations as follows:

C.I.13: Submission of the final report from study C4591012 listed as a category 3 study in the RMP. This is a non-interventional Post-Emergency Use Authorisation active safety surveillance study among individuals in the Veteran's Affairs health system receiving Pfizer-BioNTech Coronavirus Disease 2019 (COVID-19) vaccine. The RMP version 11.2 has also been submitted.

C.I.11.b: Submission of an updated RMP version 11.2 in order to implement changes to an agreed post-authorisation study (C4591052 protocol amendments 1 & 2) in the RMP, where there is an impact on the description of the study.

C.I.11.b: Submission of an updated RMP version 11.2 in order to implement changes to an agreed post-authorisation study (C4591021 protocol amendment 4) in the RMP, where there is an impact on the description of the study.

In addition, the MAH took the opportunity to update the milestones for the two studies C4591022 and C4591051 in the RMP

Action: For adoption of PRAC Assessment Report

7.4.3. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0131

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of the final report from study mRNA-1273-919 - An Observational Study to Assess Maternal and Infant Outcomes Following Exposure to Spikevax During Pregnancy, listed as a category 3 study in the RMP

[20] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

Action: For adoption of PRAC Assessment Report

7.4.4. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0100

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report from the postmarketing observational study 20090522, listed as a category 3 study in the RMP. This is a denosumab global safety assessment among women with postmenopausal osteoporosis (PMO), men with osteoporosis, and men and women who receive Prolia with glucocorticoid exposure in multiple observational databases

Action: For adoption of PRAC Assessment Report

7.4.5. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/WS2587/0085; Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/WS2587/0015

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study 109MS401, a multicenter, global, observational study to collect information on safety and to document the drug utilization of Tecfidera (Dimethyl Fumarate) when used in routine medical practice in the treatment of Multiple Sclerosis (ESTEEM), listed as a category 3 study in the RMP (MEA007.6). The RMPs version 16.1 for Tecfidera and version 2.1 for Vumerity, have also been submitted

Action: For adoption of PRAC Assessment Report

7.4.6. Empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS2571/0055; Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS2571/0082; Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS2571/0076

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study 1245-0201. This is an observational post-authorisation safety study (PASS) to assess the risk of acute pancreatitis in type 2 diabetes mellitus (T2DM) patients newly initiating empagliflozin compared to other oral non-incretin/non-sodium glucose co-transporter-2 inhibitors (SGLT2i)-containing glucose lowering drugs. The RMP versions 22.0, 15.0 and 10.0 have also been submitted for Jardiance, Synjardy and Glyxambi, respectively

Action: For adoption of PRAC Assessment Report

7.4.7. Inotuzumab ozogamicin - BESPONSA (CAP) - EMEA/H/C/004119/II/0028, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report from study B1931028; this is a non-interventional

post-authorisation safety study (PASS) of inotuzumab ozogamicin to characterize complications post-hematopoietic stem cell transplantation (HSCT) following inotuzumab ozogamicin treatment in adult and pediatric patients with B-cell precursor acute lymphoblastic leukemia (ALL). The RMP version 3.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.8. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0045

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final report from study 67896049PAH0002 (EXTRACT) and interim report for study AC-065A401 (EXPOSURE), listed as a category 3 study in the RMP. EXTRACT is a Retrospective Medical Chart Review of Patients with PAH newly treated with either Uptravi (selexipag) or any other PAH-specific therapy. EXPOSURE is an observational cohort study of PAH patients newly treated with either Uptravi (selexipag) or any other PAH-specific therapy, in clinical practice

Action: For adoption of PRAC Assessment Report

7.4.9. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/II/0091/G, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: A grouped application comprised of two Type II Variations, as follows:

C.I.4: Update of the Annex II based on final results from study B3461001 (THAOS) listed as a category 3 study in the RMP. This is a global, multi-center, longitudinal, observational survey of patients with documented transthyretin gene mutations or wild-type transthyretin amyloidosis.

C.I.13: Submission of the final report from study B3461042 listed as a category 3 study in the RMP. This is a post-marketing safety surveillance study in Japanese patients with AATR-PN.

The RMP version 10.0 has also been submitted. In addition, the MAH took the opportunity to provide B3461028 Clinical Study Report (CSR) Errata

Action: For adoption of PRAC Assessment Report

7.4.10. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0062

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the final report from study A3921203 (Tofacitinib Pregnancy Exposure Registry OTIS Autoimmune Diseases in Pregnancy Project) listed as a category 3 study in the RMP; this is a prospective, observational cohort study of pregnancy outcomes in women with a disease for which tofacitinib had an approved indication

Action: For adoption of PRAC Assessment Report

7.4.11. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0100

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy based on the final synoptic report from study CNTO1275PSO4037 (OTIS); this is a pregnancy exposure registry for Stelara. The package leaflet is updated accordingly. The RMP version 26.2 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.12. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0104

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final report from study RRA-20745 listed as a category 3 study in the RMP. This is an observational post-authorisation safety study (PASS) to describe the safety of ustekinumab and other Crohn's disease treatments in a cohort of patients with Crohn's disease. The RMP version 27.2 has also been submitted

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. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050.6

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: From II/0058:
PASS to assess the long-term safety of ATRA+ATO in newly diagnosed low to intermediate risk APL patients in a real-world clinical practice setting
Study Title: A post-authorisation long term safety cohort study in acute promyelocytic leukaemia (APL) patients treated with Trisenox
*** FORTH ANNUAL INTERIM REPORT***/ PASS C18477-ONC-50025

Action: For adoption of advice to CHMP

7.5.2. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 005.2

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: From Initial MAA:
Study PS0014:

A multicenter, open-label study to assess the long-term safety, tolerability, and efficacy of bimekizumab in adult study participants with moderate-to-severe chronic plaque PSO. Assess the safety and efficacy of long-term use of bimekizumab.

MAH Response to MEA 005.1 as adopted in March 2024:
There are two outstanding issues requiring further discussion. Both issues are related to the uncertainties regarding the effect of ADA and nAb status on bimekizumab efficacy

Action: For adoption of advice to CHMP

7.5.3. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/ANX 002.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: From initial MAA:
SECOND INTERIM REPORT FOR PASS NO. 215161 (Cat. 1)
The MAH will conduct a real-world five-year Drug Utilisation Study (DUS). This observational cohort study will aim to better understand the patient population receiving cabotegravir long acting injection and/or rilpivirine long acting injection containing regimens in routine clinical practice. The study will assess usage patterns, adherence, and post marketing clinical effectiveness of these regimens and monitor for resistance among virologic failures for whom data on resistance testing are available.

Action: For adoption of advice to CHMP

7.5.4. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/MEA 004.4

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: ***Second annual interim report of a category 3***
Non-interventional study aiming to monitor for hepatotoxicity and discontinuation of the regimen due to liver-related adverse events (AEs) following initiation of CAB+RPV including the month of oral lead-in, followed by injectable long-acting CAB+RPV. The MAH is requested to submit annual interim reports and a final report as agreed in the pharmacovigilance plan

Action: For adoption of advice to CHMP

7.5.5. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/ANX 003.2

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: MAH Response to ANX 003.1 [PASS Study 68284528MMY4004] RSI as adopted in January 2024.
Title: An Observational Post-authorisation Safety Study to Evaluate the Safety of Multiple Myeloma Patients Treated with Ciltacabtagene Autoleucel

Action: For adoption of advice to CAT and CHMP

7.5.6. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.15

Applicant: Hexal AG

PRAC Rapporteur: Bianca Mulder

Scope: ***Thirteenth Interim Report / SMART Study no. EP06-501***
Title: Non-interventional, prospective, long-term observational study to assess the safety and effectiveness of Zarzio/Filgrastim HEXAL administered to healthy unrelated stem cell donors for peripheral blood progenitor cell mobilization. The primary objective of this non-interventional study (NIS) is to evaluate the occurrence of adverse events (AEs) suspected to be drug-related

Action: For adoption of advice to CHMP

7.5.7. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.15

Applicant: Sandoz GmbH

PRAC Rapporteur: Bianca Mulder

Scope: **13th Interim Report / SMART Study no. EP06-501**
Title: Non-interventional, prospective, long-term observational study to assess the safety and effectiveness of Zarzio/Filgrastim HEXAL administered to healthy unrelated stem cell donors for peripheral blood progenitor cell mobilization. The primary objective of this non-interventional study (NIS) is to evaluate the occurrence of adverse events (AEs) suspected to be drug-related

Action: For adoption of advice to CHMP

7.5.8. Mercaptamine - CYSTADROPS (CAP) - EMEA/H/C/003769/MEA 001.5

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: From Initial MAA:
THIRD INTERIM REPORT for PASS No. CYT-DS-001 (Categ. 3)
Open-label longitudinal Post Authorisation safety Study to assess safety of Cystadrops in paediatric and adult cystinosis patients in long term use

Action: For adoption of advice to CHMP

7.5.9. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 003.3

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: ***ALITHIOS Study COMB157G2399***
An open-label, single arm, multi-center extension study evaluating long-term safety, tolerability and effectiveness of ofatumumab in subjects with relapsing multiple sclerosis (Categ. 3)
THIRD INTERIM ANNUAL REPORT

Action: For adoption of advice to CHMP

7.5.10. Rilpivirine - REKAMBYS (CAP) - EMEA/H/C/005060/ANX 002.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Martirosyan

Scope: ***Second annual interim report of a category 1 imposed study***
Imposed study aiming to assess usage patterns, adherence, post marketing clinical effectiveness and to monitor for resistance among virologic failure. The MAH is requested to submit annual interim reports and a final report to fulfil its obligations as agreed in the pharmacovigilance plan.

Action: For adoption of advice to CHMP

7.5.11. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/MEA 002.7

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Monica Martinez Redondo

Scope: From initial MAA
FOURTH INTERMIM REPORT FOR PASS "Safety surveillance program using existing European Rheumatoid Arthritis Registries"
This study is conducted in 4 countries: Germany (OBS15180), Spain (OBS16829), Sweden (OBS15220) and UK (OBS16828)

Action: For adoption of advice to CHMP

7.5.12. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 017.9

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Interim study report for study C4591021 (formerly named ACCESS/VAC4EU) - Assessment of potential increased risk of adverse events of special interest (AESI), including myocarditis/pericarditis after being vaccinated with COVID-19 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 vaccination
Fifth Interim Report / Study C4591021 (former ACCESS/VAC4EU)

Action: For adoption of advice to CHMP

7.5.13. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 005.4

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: From initial MAA
ANNUAL PROGRESS REPORT for PASS P20-199
Drug utilisation study of upadacitinib (Rinvoq) in Europe to evaluate the effectiveness of additional risk minimisation measures among patients with Rheumatoid Arthritis

Action: For adoption of advice to CHMP

7.5.14. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.18

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: FROM II 0042 & II-0073
SIXTH ANNUAL REPORT FOR PASS No. CNTO1275PSO4056 (Cat. 3)
Adolescent Registry: An Observational PASS of Ustekinumab in the Treatment of Pediatric Patients Aged 12 Years and Older With Moderate to Severe Plaque Psoriasis

Action: For adoption of advice to CHMP

7.5.15. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.11

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: **6TH PROGRESS REPORT for Registry Study Cohort No P16-562 (RMP)
Prospective observational study to assess the long-term safety profile of venetoclax in a Swedish cohort of Chronic Lymphocytic Leukaemia (CLL) patient

Action: For adoption of advice to CHMP

7.5.16. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 015.2

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: From II/0031
FIRST ANNUAL UPDATE REPORT for PASS NO. P22-907 (NI/NI/RMP/Cat. 3)
Cross-sectional Study Evaluating the Effectiveness of Venetoclax Risk-Minimisation Measures Among Haematologists in Europe

Action: For adoption of advice to CHMP

7.5.17. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 016.2

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: From II/0031
FIRST ANNUAL UPDATE REPORT for PASS NO. P22-905 (NI/NI/RMP/Cat. 3)
Cross-sectional Study Evaluating the Effectiveness of the Venetoclax Patient Card Among Adult Patients in Europe

Action: For adoption of advice to CHMP

7.5.18. Voretigene neparvovec - LUXTURNA (CAP) - EMEA/H/C/004451/ANX 011.1

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: **FOURTH INTERIM ANALYSIS for PASS CLTW888A12401 (PERCEIVE)**
A Post-Authorisation, Multicenter, Multinational, Longitudinal, Observational Safety Registry Study for Patients Treated with Voretigene Neparvovec
The objective of this post-authorisation observational study is to collect long-term safety information (i.e. for 5 years after treatment) 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

Action: For adoption of advice to CAT and CHMP

7.6. Others

None

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Clofarabine - EVOLTRA (CAP) - EMEA/H/C/000613/S/0081 (with RMP)

Applicant: Sanofi B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/003922/S/0035 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

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. Pirtobrutinib - JAYPIRCA (CAP) - EMEA/H/C/005863/R/0004 (with RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Valoctocogene roxaparvovec - ROCTAVIAN (CAP) - EMEA/H/C/005830/R/0011 (with RMP)

Applicant: BioMarin International Limited, ATMP[21]

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Clopidogrel, acetylsalicylic acid - CLOPIDOGREL/ACETYLSALICYLIC ACID VIATRIS (CAP) - EMEA/H/C/004996/R/0012 (with RMP)

Applicant: Viatris Limited

PRAC Rapporteur: Carla Torre

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Delafloxacin - QUOFENIX (CAP) - EMEA/H/C/004860/R/0026 (without RMP)

Applicant: A. Menarini Industrie Farmaceutiche Riunite s.r.l.

PRAC Rapporteur: Petar Mas

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Esketamine - SPRAVATO (CAP) - EMEA/H/C/004535/R/0023 (with RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

[21] Advanced therapy medicinal product

Action: For adoption of advice to CHMP

8.3.4. Glucagon - BAQSIMI (CAP) - EMEA/H/C/003848/R/0015 (without RMP)

Applicant: Amphastar France Pharmaceuticals

PRAC Rapporteur: Eamon O'Murchu

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Netarsudil - RHOKIINSA (CAP) - EMEA/H/C/004583/R/0022 (with RMP)

Applicant: Santen Oy

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Pegfilgrastim - CEGFILA (CAP) - EMEA/H/C/005312/R/0020 (with RMP)

Applicant: Mundipharma Corporation (Ireland) Limited

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/R/0025 (without RMP)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Fluoroquinolones for systemic and inhalation use: ciprofloxacin (NAP); levofloxacin (NAP); lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP) - CZ/H/PSUFU/A31/1452/202210

Applicant: various

PRAC Lead: Eva Jirsová

Scope: PRAC consultation on a PSUR follow-up procedure regarding risk minimisation measures following submission of cumulative reviews of spontaneously reported cases of prolonged, potentially irreversible, serious suspected adverse drug reactions, in accordance to the outcome of the referral procedure under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1452) concluded in 2019, at the request of Czech Republic

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. Vote by proxy

None

12.1.3. Scientific Committee Meetings – alternating face-to-face and virtual meetings schedule for 2025

Action: For adoption

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. Real World Evidence European Specialised Expert Community (ESEC)– update

Action: For discussion

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

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

12.10.5. Periodic safety update reports single assessment (PSUSA) – review of 'other considerations' section in the assessment report – proposed approach post pilot phase

PRAC lead: Sabine Straus, Martin Huber

Action: For discussion

12.11. Signal management

None

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.15.3. Good pharmacovigilance practices (GVP) module VIII on 'Post-authorisation safety studies (PASS)' Revision 4 - update

Action: For discussion

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

12.20.1. Good pharmacovigilance practice (GVP) module XVI on 'Risk minimisation measures: selection of tools and effectiveness indicators' – revision 3 on principles and methods to evaluate the effectiveness of risk minimisation measures (RMM)

PRAC lead: Sabine Straus

Action: For discussion

12.21. Others

12.21.1. Real World Evidence and Data analysis and real-world interrogation network (DARWIN EU®) – quarterly update

Action: For discussion

13. Any other business

Next meeting on: 08-11 July 2024

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: Referral procedures: human medicines | European Medicines Agency (europa.eu)

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.

For a list of acronyms and abbreviations, see:
List of abbreviations used in EMA human medicines scientific committees and CMDh documents, and in Pharmacovigilance Risk Assessment Committee (PRAC)

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