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SCIENCE MEDICINES HEALTH

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Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 08-11 July 2024

Chair: Sabine Straus – Vice-Chair: Martin Huber

08 July 2024, 13:00 – 19:30, room 1C

09 July 2024, 08:30 – 19:30, room 1C

10 July 2024, 08:30 – 19:30, room 1C

11 July 2024, 08:30 – 16:00, room 1C

Organisational, regulatory and methodological matters (ORGAM)

25 July 2024, 09:00 – 12:00, 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](#)).



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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 08-11 July 2024. See July month 2024 PRAC minutes (to be published post September 2024 PRAC meeting).

1.2. Agenda of the meeting on 08-11 July 2024

Action: For adoption

1.3. Minutes of the previous meeting on 10-13 June 2024

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

2.2.1. 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, fempipramide (NAP); metamizole, pitofenone, fempiverinium (NAP); metamizole, triacetoneamine (NAP) – EMEA/H/A-107i/1537

Applicant(s): various

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

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 for experts

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 procedures¹

None

3.5. Others

None

4. Signals assessment and prioritisation

4.1. New signals detected from EU spontaneous reporting systems and/or other sources

4.1.1. Angiotensin II receptor blockers: azilsartan - EDARBI (CAP), NAP; irbesartan - APROVEL (CAP); IFIRMASTA (CAP); IRBESARTAN TEVA (CAP); IRBESARTAN ZENTIVA (CAP); KARVEA (CAP), NAP; irbesartan, hydrochlorothiazide - COAPROVEL (CAP); IFIRMACOMBI (CAP); IRBESARTAN HYDROCHLOROTHIAZIDE ZENTIVA (CAP); IRBESARTAN/HYDROCHLOROTHIAZIDE TEVA (CAP); KARVEZIDE (CAP), NAP; telmisartan - KINZALMONO (CAP), MICARDIS (CAP), PRITOR (CAP), TELMISARTAN ACTAVIS (CAP), TELMISARTAN TEVA PHARMA (CAP), TOLURA (CAP), NAP; telmisartan, amlodipine - TWYNSTA (CAP), NAP; telmisartan, hydrochlorothiazide - ACTELSAR HCT (CAP), KINZALKOMB (CAP), MICARDISPLUS (CAP), PRITORPLUS (CAP), TOLUCOMBI (CAP), NAP; valsartan, sacubitril - ENTRESTO (CAP), NEPARVIS (CAP); valsartan, amlodipine - COPALIA (CAP), DAFIRO (CAP), EXFORGE (CAP), NAP; valsartan, amlodipine, hydrochlorothiazide -

¹ Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

COPALIA HCT (CAP), DAFIRO HCT (CAP), EXFORGE HCT (CAP), NAP; other fixed-dose combinations containing angiotensin II receptor blockers (NAP)

Applicant(s): Actavis Group PTC ehf. (Actelsar HCT, Telmisartan Actavis), Bayer AG (Kinzalkomb, Kinzalmono, Pritor, PritorPlus), Boehringer Ingelheim International (Micardis, MicardisPlus, Twynsta), KRKA, d.d., Novo mesto (Ifirmacombi, Ifirmasta, Tolucombi, Tolura), Novartis Europharm Limited (Copalia, Copalia HCT, Dafiro, Entresto, Exforge, Exforge HCT, Neparvis), Sanofi Winthrop Industrie (Aprovel, CoAprovel, Karvea, Karvezide), Takeda Pharma A/S (Edarbi), Teva B.V. (Irbesartan Teva, Irbesartan/Hydrochlorothiazide Teva), Teva Pharmaceuticals Europe B.V.(Telmisartan Teva Pharma), Zentiva, k.s. (Irbesartan Hydrochlorothiazide Zentiva, Irbesartan Zentiva), various

PRAC Rapporteur: To be appointed

Scope: Signal of intestinal angioedema

Action: For adoption of PRAC recommendation

EPITT 20104 – New signal

Lead Member State(s): DE

4.1.2. Atezolizumab – TECENTRIQ (CAP); Avelumab – BAVENCIO (CAP); Cemiplimab – LIBTAYO (CAP); Dostarlimab – JEMPERLI (CAP); Durvalumab -IMFINZI (CAP); Ipilimumab – YERVOY (CAP); Nivolumab - OPDIVO (CAP), OPDUALAG (CAP); Pembrolizumab – KEYTRUDA (CAP); Retifanlimab - ZYNYZ (CAP); Tislelizumab – TEVIMBRA (CAP); Tremelimumab - IMJUDO (CAP)

Applicant(s): AstraZeneca AB (Imfinzi, Imjudo), Beigene Ireland Limited (Tevimbra), Bristol-Myers Squibb Pharma EEIG (Yervoy, Opdivo, Opdualag), GlaxoSmithKline (Ireland) Incyte Biosciences Distribution B.V. (Zynyz), Limited (Jemperli), Merck Europe B.V. (Bavencio), Merck Sharp & Dohme B.V. (Keytruda), Regeneron Ireland Designated Activity (Libtayo), Roche Registration GmbH (Tecentriq)

PRAC Rapporteur: To be appointed

Scope: Signal of thrombotic microangiopathy

Action: For adoption of PRAC recommendation

EPITT 20090 – New signal

Lead Member State(s): DE, DK, NL, NO, PT

4.1.3. Azathioprine – JAYEMPI (CAP); NAP

Applicant(s): Nova Laboratories Ireland Limited, various

PRAC Rapporteur: Karin Erneholm

Scope: Signal of non-cirrhotic portal hypertension/Portosinusoidal vascular disease

Action: For adoption of PRAC recommendation

EPITT 20091 – New signal

Lead Member State(s): DK

4.1.4. Paracetamol (NAP); fixed dose combinations containing paracetamol (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of high anion gap metabolic acidosis (HAGMA) due to pyroglutamate acidosis

Action: For adoption of PRAC recommendation

EPITT 20105 – New signal

Lead Member State(s): BE

4.1.5. Esketamine – SPRAVATO (CAP)

Applicant(s): Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Signal of bradycardia

Action: For adoption of PRAC recommendation

EPITT 20103 – New signal

Lead Member State(s): FI

4.1.6. Montelukast (NAP)

Applicants: various

PRAC Rapporteur: To be appointed

Scope: Signal of persistent neuropsychiatric events

Action: For adoption of PRAC recommendation

EPITT 20100 – New signal

Lead Member State(s): FI

4.1.7. Nitric oxide – INOMAX (CAP); NAP

Applicant(s): Linde Healthcare AB, various

PRAC Rapporteur: Jo Robays

Scope: Signal of pulmonary oedema in patients with veno-occlusive disease

Action: For adoption of PRAC recommendation

EPITT 20086 – New signal

Lead Member State(s): BE

4.1.8. Risperidone² (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of medication errors associated with accidental overdoses in children and adolescents treated with risperidone 1 mg/mL oral solution

Action: For adoption of PRAC recommendation

EPITT 20085 – New signal

Lead Member State(s): DE

4.1.9. Rosuvastatin (NAP)

Applicant: various

PRAC Rapporteur: To be appointed

Scope: Signal of tubulointerstitial nephritis

Action: For adoption of PRAC recommendation

EPITT 20084 – New signal

Lead Member State(s): NL

4.1.10. Semaglutide - OZEMPIC, RYBELSUS, WEGOVY (CAP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Signal of tubulointerstitial nephritis

Action: For adoption of PRAC recommendation

EPITT 20092 – New signal

Lead Member State(s): SE

4.1.11. Semaglutide - OZEMPIC, RYBELSUS, WEGOVY (CAP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Signal of appendicitis

Action: For adoption of PRAC recommendation

EPITT 20095 – New signal

Lead Member State(s): SE

² Oral solution only

4.2. Signals follow-up and prioritisation

4.2.1. Acetazolamide (NAP)

Applicant: various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of pulmonary oedemas

Action: For adoption of PRAC recommendation

EPITT 20050 – Follow-up to March 2024

4.2.2. Bumetanide (NAP)

Applicant: various

PRAC Rapporteur: Mari Thorn

Scope: Signal of toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS)

Action: For adoption of PRAC recommendation

EPITT 20033 – Follow-up to March 2024

4.2.3. Ceftriaxone (NAP)

Applicant: various

PRAC Rapporteur: Zane Neikena

Scope: Signal of precipitation when administered with calcium-containing solutions in infants between 29 days and 1 year

Action: For adoption of PRAC recommendation

EPITT 1964 – Follow-up to February 2024

4.2.4. Dupilumab – DUPIXENT (CAP) – EMEA/H/C/004390/SDA/014

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 20054 – Follow-up to March 2024

4.2.5. Glofitamab – COLUMVI (CAP) - EMEA/H/C/005751/SDA/006

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Signal of immune effector cell-associated neurotoxicity syndrome

Action: For adoption of PRAC recommendation

EPITT 20058 – Follow-up to March 2024

- 4.2.6. Glucagon-like peptide-1 (GLP-1) receptor agonists: dulaglutide – TRULICITY (CAP) - EMEA/H/C/002825/SDA/015.1; exenatide – BYDUREON (CAP) - EMEA/H/C/002020/SDA/031.1, BYETTA (CAP) - EMEA/H/C/000698/SDA/051.1; insulin degludec, liraglutide – XULTOPHY (CAP) - EMEA/H/C/002647/SDA/003.1; liraglutide – SAXENDA (CAP) - EMEA/H/C/003780/SDA/021.1, VICTOZA (CAP) - EMEA/H/C/001026/SDA/041.1; insulin glargine, lixisenatide – SULIQUA (CAP) - EMEA/H/C/004243/SDA/010.1; lixisenatide - LYXUMIA (CAP) - EMEA/H/C/002445/SDA/018.1; semaglutide – OZEMPIC (CAP) - EMEA/H/C/004174/SDA/009.1, RYBELSUS (CAP) - EMEA/H/C/004953/SDA/014.1, WEGOVY (CAP) - EMEA/H/C/005422/SDA/008.1; tirzepatide – MOUNJARO (CAP) - EMEA/H/C/005620/SDA/006.1
-

Applicant: AstraZeneca AB (Bydureon, Byetta), Eli Lilly Nederland B.V. (Trulicity, Mounjaro), Novo Nordisk A/S (Ozempic, Rybelsus, Saxenda, Victoza, Wegovy, Xultophy), Sanofi Winthrop Industrie (Lyxumia, Suliqua)

PRAC Rapporteur: Mari Thorn

Scope: Signal of aspiration and pneumonia aspiration

Action: For adoption of PRAC recommendation

EPITT 19974 – Follow-up to March 2024

- 4.2.7. Human Papillomavirus 9-valent Vaccine (Recombinant, adsorbed) - GARDASIL 9 (CAP) - EMEA/H/C/003852/SDA/013; human papillomavirus vaccine [types 6, 11, 16, 18] (Recombinant, adsorbed) - GARDASIL (CAP) - EMEA/H/C/003852/SDA/090
-

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of granuloma

Action: For adoption of PRAC recommendation

EPITT 20046 – Follow-up to March 2024

4.3. Variation procedure(s) resulting from signal evaluation

- 4.3.1. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0028
-

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 4.8 of the SmPC in order to add 'scleritis' to the list of adverse drug reactions (ADRs) with frequency 'not known', following the recommendation by PRAC in the outcome for the signal assessment of Scleritis. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Apremilast (CAP MAA) - EMEA/H/C/006193

Scope (pre D-180 phase): Treatment of psoriatic arthritis, psoriasis, Behçet's disease

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

5.1.2. Eplontersen (CAP MAA) - EMEA/H/C/006295, Orphan

Applicant: AstraZeneca AB

Scope (pre D-180 phase): Indicated for the treatment of adult patients with polyneuropathy associated with hereditary transthyretin-mediated amyloidosis (ATTRv).

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

5.1.3. Levetiracetam (CAP MAA) - EMEA/H/C/006186

Scope (pre D-180 phase): Treatment of partial onset seizures

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

5.1.4. Marstacimab (CAP MAA) - EMEA/H/C/006240, Orphan

Applicant: Pfizer Europe Ma EEIG

Scope (pre D-180 phase): Indicated for routine prophylaxis of bleeding episodes in patients with haemophilia A or haemophilia B

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

5.1.5. Mozafancogene autotemcel (CAP MAA) - EMEA/H/C/005537, PRIME, Orphan

Applicant: Rocket Pharmaceuticals B.V., ATMP

Scope (pre D-120 phase): Treatment of paediatric patients with Fanconi Anaemia Type A

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

5.1.6. Obecabtagene autoleucel (CAP MAA) - EMEA/H/C/005907, PRIME, Orphan

Applicant: Autolus GmbH, ATMP

Scope (pre D-120 phase): Treatment of patients with relapsed or refractory B cell precursor acute lymphoblastic leukaemia (ALL)

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

5.1.7. [Odevixibat \(CAP MAA\) - EMEA/H/C/006462](#)

Scope (pre D-180 phase): Treatment of cholestatic pruritus in Alagille syndrome (ALGS)

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

5.1.8. [Pomalidomide \(CAP MAA\) - EMEA/H/C/006302](#)

Scope (pre D-180 phase): In combination with dexamethasone is indicated in the treatment of adult patients with relapsed and refractory multiple myeloma (MM)

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

5.1.9. [Ranibizumab \(CAP MAA\) - EMEA/H/C/006528](#)

Scope: Treatment of neovascular (wet) age-related macular degeneration (AMD), visual impairment due to diabetic macular oedema (DME), proliferative diabetic retinopathy (PDR), visual impairment due to macular oedema secondary to retinal vein occlusion (branch RVO or central RVO) and visual impairment due to choroidal neovascularisation (CNV)

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

5.1.10. [Sargramostim \(CAP MAA\) - EMEA/H/C/006411](#)

Scope (pre D-120 phase, accelerated assessment): Treatment for exposure to myelosuppressive doses of radiation

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

5.1.11. [Ustekinumab \(CAP MAA\) - EMEA/H/C/006448](#)

Scope: Treatment of Crohn's disease, Ulcerative colitis, Plaque psoriasis, Paediatric plaque psoriasis and Psoriatic arthritis (PsA)

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

5.1.12. [Vorasidenib \(CAP MAA\) - EMEA/H/C/006284, Orphan](#)

Applicant: Les Laboratoires Servier

Scope (pre D-180 phase): Treatment of predominantly non-enhancing astrocytoma or oligodendroglioma with a IDH1 R132 mutation or IDH2 R172 mutation

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. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/II/0024

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an updated RMP version 8.0 in order to remove the PASS
CBYL719C2404 (Cat. 3) RMP commitment (MEA 002)

Action: For adoption of PRAC Assessment Report

5.2.2. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/II/0044/G

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Grouped application comprising four variations as follows:

Type II (C.I.11.b): To update Annex II and the RMP version 7.1 for Bavencio to change the classification of "safety in patients with autoimmune disease" to the important identified risk "other immune mediated adverse reactions" along with removal of the patient information brochure from the educational material, following the PRAC assessment report PSUSA/00010635/202303.

Type IA (A.6): To change ATC level name from Other antineoplastic agents, monoclonal antibodies to Antineoplastic agents, monoclonal antibodies, PD-1/PDL-1 (Programmed cell death protein 1/death ligand 1) inhibitors in Section 5.1 of the Summary of Product Characteristics (SmPC). The ATC code remains unchanged.

Type IA (C.I.z): To update the statement for "infusion-related reactions" in section 4.4 of the SmPC and to align terminology with the RMP for the term "immune-related" versus "immune-mediated".

Type IAIN (C.I.12): To remove from the product information the black symbol and explanatory statements for medicinal products subject to additional monitoring.

In addition, the MAH took this opportunity to introduce editorial changes and to bring the PI in line with the latest QRD template version 10.3

Action: For adoption of PRAC Assessment Report

5.2.3. Epoetin beta - NEORECORMON (CAP) - EMEA/H/C/000116/II/0126

Applicant: Roche Registration GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 4.0 in order to align with GVP Module V (Rev. 2)

Action: For adoption of PRAC Assessment Report

5.2.4. Larotrectinib - VITRAKVI (CAP) - EMEA/H/C/004919/II/0036

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Submission of an updated RMP version 2.1 in order to adjust the sample size for the non-interventional PASS ON-TRK as well as to update epidemiological, clinical trial and post-marketing data

Action: For adoption of PRAC Assessment Report

5.2.5. [Voxelotor - OXBRYTA \(CAP\) - EMEA/H/C/004869/II/0011, Orphan](#)

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Jo Robays

Scope: Submission of an updated RMP version 1.2 in order to include the current data for the main existing treatment options and to extend the submission deadline for Study GBT440-0122 (C5341029) and for Study GBT440-034 (C5341022)

Action: For adoption of PRAC Assessment Report

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

5.3.1. [Apremilast - OTEZLA \(CAP\) - EMEA/H/C/003746/II/0044/G](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Monica Martinez Redondo

Scope: A grouped application of a Type II Variation with two Type IA Variations, as follows:

Type II (C.I.6.a): Extension of indication to include the treatment of moderate to severe chronic plaque psoriasis in children and adolescents from the age of 6 years who have a contraindication, have an inadequate response, or are intolerant to at least one other systemic therapy or phototherapy for OTEZLA, based on final results from study CC-10004-PPSO-003 as well as results from studies CC-10004-PPSO-001 and CC-10004-PPSO-004. CC-10004-PPSO-003 is a phase 3, multi-center, randomised, double-blind, placebo-controlled study to assess the efficacy and safety of apremilast (CC-10004) in paediatric subjects from 6 through 17 years of age with moderate to severe plaque psoriasis. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 15.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial and formatting changes to the PI and to update the list of local representatives in the package leaflet.

2 Type IA (B.II.e.5.a.1)

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

5.3.2. [Encorafenib - BRAFTOVI \(CAP\) - EMEA/H/C/004580/WS2538/0034;](#) [Binimetinib - MEKTOVI \(CAP\) - EMEA/H/C/004579/WS2538/0030](#)

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to include binimetinib in combination with encorafenib for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) with a BRAF V600 mutation for MEKTOVI and BRAFTOVI based on results from study PHAROS (Study ARRAY-818-202) at the primary completion date; this is a Phase II, open-label, multicentre, non-comparative study (interventional). As a consequence, sections 4.1, 4.4, 4.8, 5.1, 5.2, 9 and 10 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection for MEKTOVI

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

5.3.3. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/X/0058/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Extension application to introduce a new pharmaceutical form (hard capsules) associated with two new strengths (50 mg and 100 mg) grouped with an extension of indication (C.I.6.a) to include treatment of paediatric patients greater than or equal to 1 year of age with newly-diagnosed (ND) chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML) for BOSULIF, based on interim results from study ITCC-054/AAML1921 (BCHILD); this is a phase 1/2, multicenter, international, single-arm, open-label study of bosutinib in pediatric patients with newly diagnosed chronic phase or resistant/intolerant Ph+ chronic myeloid leukemia. 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 accordingly. Version 7.0 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

5.3.4. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0111, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication for ADCETRIS to include treatment for adult patients with previously untreated CD30+ Stage IIB with risk factors, Stage III or Stage IV HL in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone (BrECADD), based on final results from phase 3 study HD21 (NCT02661503). This study is titled Treatment Optimization Trial in the First-Line Treatment of Advanced-Stage Hodgkin Lymphoma; Comparison of 4-6 Cycles of Escalated BEACOPP With 4-6 Cycles of BrECADD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 20.0 of the RMP has also been submitted.

In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the package leaflet and to implement editorial changes to the SmPC

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

5.3.5. [Canakinumab - ILARIS \(CAP\) - EMEA/H/C/001109/II/0085](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: 1. Type II (B.II.e.1.b.2)

The updated RMP version 14.0 has also been submitted to introduce changes related to the addition of the PFS presentation

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

5.3.6. [COVID-19 Vaccine Janssen \(Ad26.COVID.S\) - JCOVDEN \(CAP\) - EMEA/H/C/005737/II/0076](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.5, 4.8 and 5.1 of the SmPC in order to update information regarding the co-administration of JCOVDEN with influenza vaccine based on the final report from study VAC31518COV3005 listed as a category 3 study in the RMP; this is a randomised, double-blind, Phase 3 study to evaluate safety, reactogenicity, and immunogenicity of co-administration of Ad26.COVID.S and influenza vaccines in healthy adults 18 years of age and older. The package leaflet is updated accordingly. Version 8.1 of the RMP has also been submitted

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

5.3.7. [Dapivirine - DAPIVIRINE VAGINAL RING 25 MG \(Art 58³\) - 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 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, randomized, 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 PI.

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

³ 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)

5.3.8. Darvadstrocel - ALOFISEL (CAP) - EMEA/H/C/004258/II/0051/G, Orphan

Applicant: Takeda Pharma A/S, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: A grouped application comprised of 4 Type II Variations, as follows:

(C.I.4): Update of sections 4.8 and 5.1 of the SmPC in order to update the safety information, based on pooled safety data from the two phase 3 controlled studies (ADMIRE-CD & ADMIRE-CD II) and to update efficacy information based on final results from study ADMIRE-CD II, listed as an obligation in the Annex II. ADMIRE-CD II (Cx601-0303) is a Phase III randomised double blind, placebo controlled study to assess efficacy and safety of Cx601, adult allogeneic expanded adipose-derived stem cells (eASC) for the treatment of complex perianal fistula(s) in patients with Crohn's disease. The Annex II is updated accordingly. In addition, the MAH took the opportunity to introduce minor changes to the PI, including to section 4.2 of the SmPC and to the package leaflet.

3 x (C.I.13): Submission of interim results from studies Darvadstrocel-3003 and Alofisel-5003 (INSPIRE) and final results from study Darvadstrocel-3002 to support the benefit-risk assessment of darvadstrocel based on all new available clinical data

The RMP version 8.0 has also been submitted

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

5.3.9. Dengue tetravalent vaccine⁴ (live, attenuated) - DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (Art 58⁵) - EMEA/H/W/005362/WS2695/0015; Dengue tetravalent vaccine (live, attenuated) - QDENG A (CAP) - EMEA/H/C/005155/WS2695/0016

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Update of section 4.4 and 4.8 of the SmPC in order to add anaphylactic reaction to the list of adverse drug reactions (ADRs) with frequency not known, based on post-authorisation experience. The package leaflet is updated accordingly. The RMP version 1.2 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4 and to introduce minor editorial changes to the PI

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

5.3.10. Dengue tetravalent vaccine⁶ (live, attenuated) - DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (Art 58⁷) - EMEA/H/W/005362/WS2593/0012;

⁴ Dengue virus, serotype 2, expressing Dengue virus, serotype 1, surface proteins, live, attenuated, Dengue virus, serotype 2, expressing Dengue virus, serotype 3, surface proteins, live, attenuated, Dengue virus, serotype 2, expressing Dengue virus, serotype 4, surface proteins, live, attenuated, Dengue virus, serotype 2, live, attenuated

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)

⁶ Dengue virus, serotype 2, expressing Dengue virus, serotype 1, surface proteins, live, attenuated, Dengue virus, serotype 2, expressing Dengue virus, serotype 3, surface proteins, live, attenuated, Dengue virus, serotype 2, expressing Dengue virus, serotype 4, surface proteins, live, attenuated, Dengue virus, serotype 2, live, attenuated

⁷ 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)

Dengue tetravalent vaccine (live, attenuated) - QDENG A (CAP) - EMEA/H/C/005155/WS2593/0013

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Update of section 4.5 of the SmPC in order to add co-administration information with HPV vaccine based on final results from study DEN-308 listed as a category 3 study in the RMP (MEA003/MEA004); this is a Phase 3, open-label, randomised trial to investigate the immunogenicity and safety of the co-administration of a subcutaneous dengue tetravalent vaccine (live, attenuated) (TDV) and an intramuscular recombinant 9-valent human papillomavirus (9vHPV) vaccine in subjects aged ≥ 9 to < 15 years in an endemic country for dengue; the package leaflet is updated accordingly. The RMP version 1.1 has also been submitted. In addition, the MAH took this opportunity to introduce editorial changes and to update the text on PSUR submissions in Annex II for Dengue tetravalent vaccine

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

5.3.11. Eliglustat - CERDELGA (CAP) - EMEA/H/C/003724/X/0036/G, Orphan

Applicant: Sanofi B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension application to introduce a new strength (21 mg capsule, hard) grouped with an extension of indication (C.I.6.a) to include treatment of paediatric patients with GD1 who are 6 years and older with a minimum body weight of 15 kg, who have been previously treated with enzyme replacement therapy (ERT), and who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs) for Cerdelga, based on interim results from study EFC13738 (Open label, two cohort (with and without imiglucerase), multicenter study to evaluate pharmacokinetics, safety, and efficacy of eliglustat in pediatric patients with Gaucher disease type 1 and type 3). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. The RMP version 8.0 has also been submitted. In addition, the MAH took this opportunity to introduce editorial changes to the PI

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

5.3.12. Enfortumab vedotin - PADCEV (CAP) - EMEA/H/C/005392/II/0013

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include in combination with pembrolizumab, the first-line treatment of adult patients with locally advanced or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy for PADCEV, based on the final results from study KEYNOTE-A39/EV-302: "An open label, randomised, controlled phase 3 study of enfortumab vedotin in combination with pembrolizumab versus chemotherapy alone in previously untreated locally advanced (LA) or metastatic urothelial cancer (mUC)"; As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 3.0 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

5.3.13. [Etrasimod - VELSIPITY \(CAP\) - EMEA/H/C/006007/II/0002/G](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Mari Thorn

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

C.I.4: Update of sections 4.2, 4.3 and 5.2 of the SmPC in order to amend recommendation regarding administration to patients with severe hepatic impairment and remove contraindication for severe hepatic impairment, based on in vitro studies to further characterise the drug-drug interaction (DDI) potential of metabolites M3 and M6. The Annex II and package leaflet are updated accordingly. The RMP version 1.2 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.

C.I.13: Submission of the final report from study 24GR036 (hERG Channel Automated Patch-Clamp Test); this is an assessment of the effects of PF-08034694, PF-08034742, PF-08039030, and PF-08039032 on the Kv11.1 (hERG) potassium current

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

5.3.14. [Evinacumab - EVKEEZA \(CAP\) - EMEA/H/C/005449/II/0015](#)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication for EVKEEZA to include the treatment of paediatric patients with homozygous familial hypercholesterolaemia aged 6 months to less than 5 years, based on the results of population PK and population PK/PD model-based extrapolation reports (R1500-PM-23202-SR-01V2 and R1500-PM-23089-SR-01V2). As a consequence, sections 4.1, 4.2, 4.8, 5.1, and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement minor changes to sections 4.2, 4.4, and 4.7 of the SmPC, along with editorial changes to the SmPC

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

5.3.15. [Naloxone - NYXOID \(CAP\) - EMEA/H/C/004325/II/0019](#)

Applicant: Mundipharma Corporation (Ireland) Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the interim report from the PAES MR903-9501 listed as an obligation in the Annex II, supported by Real World Evidence from literature and European Take-Home Naloxone programs (THN) demonstrating the effectiveness of Nyxoid in a real-world setting. Study MR903-9501 is a non-interventional multi-national, prospective, mixed methods

study of the effectiveness of naloxone (including intranasal Nyxoid) administration by lay people in reversing opioid overdose. The Annex II and the RMP version 3.0 are updated accordingly. In addition, the MAH took the opportunity to introduce minor administrative changes to the package leaflet

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

5.3.16. [Nivolumab - OPDIVO \(CAP\) - EMEA/H/C/003985/WS2672/0141;](#) [Ipilimumab - YERVOY \(CAP\) - EMEA/H/C/002213/WS2672/0111](#)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: A Worksharing application for OPDIVO and YERVOY, as follows:

Extension of indication to include OPDIVO in combination with ipilimumab in the first-line treatment of adult patients with mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) unresectable or metastatic colorectal cancer, based on interim results from study CA2098HW; this is a phase 3 randomised clinical trial of nivolumab alone, nivolumab in combination with ipilimumab, or investigator's choice chemotherapy in participants with microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 37.0 of the RMP has also been submitted.

Extension of indication to include YERVOY in combination with nivolumab in the first-line treatment of adult patients with mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) unresectable or metastatic colorectal cancer, based on interim results from study CA2098HW; this is a phase 3 randomised clinical trial of nivolumab alone, nivolumab in combination with ipilimumab, or investigator's choice chemotherapy in participants with microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 41.0 of the RMP has also been submitted

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

5.3.17. [Isatuximab - SARCLISA \(CAP\) - EMEA/H/C/004977/II/0030](#)

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Monica Martinez Redondo

Scope: Extension of indication to include in combination with bortezomib, lenalidomide, and dexamethasone the treatment of adult patients with newly diagnosed active multiple myeloma who are not eligible for autologous stem cell transplant (ASCT) or with no intent for ASCT as initial therapy for Sarclisa, based on results from EFC12522 (IMROZ) pivotal phase III study and the supportive TCD13983 phase 1b/2 study. EFC12522 is an ongoing prospective, multicenter, international, randomised, open-label, 2-arm parallelgroup study to assess the clinical benefit of VRd (control group) versus IVRd (active group) for the treatment of participants with NDMM who are not eligible for ASCT. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.7, 4.8, 5.1 and 5.2 of the SmPC are updated. The package

leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted

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

5.3.18. [Letemovir - PREVYMIS \(CAP\) - EMEA/H/C/004536/X/0037/G, Orphan](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Extension applications to introduce a new pharmaceutical form (granules in sachet) associated with new strengths (20 and 120 mg) grouped with a type II variation (C.I.6.a) to include treatment of paediatric patients from birth up to 18 years old based on the final results from studies P030 and P031.

Study P030 was a Phase 2b, open-label, single-arm study to evaluate PK, efficacy, safety, and tolerability of letemovir (LET) when used for CMV prophylaxis in pediatric participants from birth to <18 years of age who are at risk of developing clinically significant CMV infection (CS-CMV) following an allogeneic hematopoietic stem cell transplant (HSCT).

Study P031 was an open-label, single-dose, four-period, seven-treatment, crossover study designed to evaluate the bioavailability of 2 pediatric formulations of MK-8228 (Formulations A and B) administered alone or in soft food (applesauce and vanilla pudding) compared to a currently marketed tablet formulation.

As a consequence, sections 4.1, 4.2, 4.5, 4.8, 4.9, 5.1 and 5.2 of the SmPC are updated.

The package leaflet is updated in accordance. Version 5.1 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 and to introduce editorial changes

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

5.3.19. [Levetiracetam - KEPRA \(CAP\) - EMEA/H/C/000277/WS2529/0200](#)

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Jo Robays

Scope: Type II - B.IV.1.a.3 An updated RMP version 10.0 and a DHPC are proposed. In addition, the Applicant has taken the opportunity to include the change in the local representatives of the Marketing Authorisation Holder in Estonia, Latvia, and Lithuania.

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

5.3.20. [Meningococcal group A, C, W135 and Y conjugate vaccine - MENVEO \(CAP\) - EMEA/H/C/001095/X/0119](#)

Applicant: GSK Vaccines S.r.l

PRAC Rapporteur: Liana Martirosyan

Scope: Extension application to introduce a new pharmaceutical form (solution for injection). The RMP (version 11.0) is updated in accordance

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

5.3.21. Mycophenolate mofetil - CELLCEPT (CAP) - EMEA/H/C/000082/II/0170/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Karin Erneholm

Scope: C.I.6.a: Extension of indication to include paediatric patients (3 months to 18 years of age) for hepatic and cardiac transplants and to extend the indication for renal transplants for paediatric patients starting from 3 months, based on pharmacokinetic data, published literature and the Roche Global Safety Database. As a consequence, sections 4.1, 4.2, 4.8 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly.

Type IB (C.I.z): To update section 4.2 of the SmPC for the CellCept 500 mg tablets formulation in order to be in line with the other three CellCept formulations. For alignment with the current QRD guidance, the package leaflet was updated to cross reference section 2 in section 6 for sodium content.

In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and bring the PI in line with the latest QRD template version 10.3

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

5.3.22. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/X/0057/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Extension application to add a new strength of 25 mg hard capsules, grouped with an extension of indication (C.I.6.a) to include treatment of fibrosing Interstitial Lung Diseases (ILDs) in children and adolescents from 6 to 17 years of age for Ofev, following the assessment of procedure X/0052/G, based on final results from study 1199-0337 (A Double Blind, Randomised, Placebo-controlled Trial to Evaluate the Dose-exposure and Safety of Nintedanib Per os on Top of Standard of Care for 24 Weeks, Followed by Open Label Treatment With Nintedanib of Variable Duration, in Children and Adolescents (6 to 17 Year-old) With Clinically Significant Fibrosing Interstitial Lung Disease), which is supplemented by the currently ongoing prospective Phase III extension trial 1199-0378 (An Open-label Trial of the Long-term Safety and Tolerability of Nintedanib Per os, on Top of Standard of Care, Over at Least 2 Years, in Children and Adolescents With Clinically Significant Fibrosing Interstitial Lung Disease). The main objective of the study 1199-0337 was to evaluate dose-exposure and safety of nintedanib in children and adolescents with fibrosing Interstitial Lung Disease (ILD). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 12.0 of the RMP has also been submitted

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

5.3.23. Nirmatrelvir, Ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/II/0057/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of:

C.I.4: Update of sections 4.2, 4.4, 4.8 and 5.2 of the SmPC in order to provide a new dosing recommendation in patients with severe renal impairment based on final results from study C4671028; this is a Phase 1, Open-Label, Non-Randomised Study to Investigate the Safety and PK Following Multiple Oral Doses of PF-07321332 (Nirmatrelvir)/Ritonavir in Adult Participants With COVID-19 and Severe Renal Impairment Either on Hemodialysis or Not on Hemodialysis. The package leaflet and Labelling are updated accordingly. The updated RMP version 3.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC.

B.II.e.5.a.2

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

5.3.24. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/II/0041

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.6 and 5.3 of the SmPC in order to amend the recommendations for breast-feeding during ocrelizumab therapy, based on newly available clinical data. The package leaflet is updated accordingly. The RMP version 10.0 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

5.3.25. Opicapone - ONGENTYS (CAP) - EMEA/H/C/002790/WS2702/0066; Opicapone - ONTILYV (CAP) - EMEA/H/C/005782/WS2702/0021

Applicant: Bial - Portela & C^a, S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 4.8 of the SmPC in order to add 'fall' and 'fatigue' to the list of adverse drug reactions (ADRs) with frequency uncommon based on the cumulative review of literature. The package leaflet is updated accordingly. The Ongentys RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet, to bring the PI in line with the latest QRD template version 10.4 and to introduce minor editorial changes to the product information

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

5.3.26. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/II/0056

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adult patients with locally advanced, unresectable (stage III) NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations and whose disease has not progressed during or following platinum-based chemoradiation therapy for TAGRISSO as monotherapy, based on results from study D5160C00048 (LAURA); this is a Phase III, randomised, double-blind, placebo-controlled, multicentre international study of osimertinib as maintenance therapy in patients

with locally advanced unresectable EGFR mutation-positive non-small cell lung cancer (stage III) whose disease has not progressed following definitive platinum-based chemoradiation therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 17.0 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

5.3.27. 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

5.3.28. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0150

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include in combination with enfortumab vedotin, the first-line treatment of locally advanced or metastatic urothelial carcinoma in adults, based on the final results from KEYNOTE-A39/EV-302: "An open label, randomised, controlled phase 3 study of enfortumab vedotin in combination with pembrolizumab versus chemotherapy alone in previously untreated locally advanced (LA) or metastatic urothelial cancer (mUC)"; As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 45.1 of the RMP has also been submitted

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

5.3.29. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0154

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include in combination with pemetrexed and platinum chemotherapy the first-line treatment of adults and adolescents aged 12 years and older with unresectable advanced or metastatic malignant pleural mesothelioma for Keytruda, based on final results from study KEYNOTE-483; this is a multicenter, open-label, Phase 2/3 randomised study to evaluate the efficacy and safety of pembrolizumab in combination with pemetrexed/platinum chemotherapy in participants with unresectable advanced or metastatic malignant pleural mesothelioma (MPM). As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 47.1 of

the RMP has also been submitted

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

5.3.30. Pemigatinib - PEMAZYRE (CAP) - EMEA/H/C/005266/II/0015, Orphan

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adults with myeloid/lymphoid neoplasms (MLNs) with Fibroblast Growth Factor Receptor1 (FGFR1) rearrangement for PEMAZYRE, based on final results from study INCB 54828-203 (FIGHT-203); this is a phase 2, open-label, monotherapy, multicenter study to evaluate the efficacy and safety of INCB054828 in subjects with myeloid/lymphoid neoplasms with FGFR1 rearrangement. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet 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 PI. 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

5.3.31. Respiratory syncytial virus, glycoprotein F, recombinant, stabilised in the pre-fusion conformation, adjuvanted with AS01E - AREXVY (CAP) - EMEA/H/C/006054/II/0008

Applicant: GlaxoSmithkline Biologicals S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include treatment of adults 50-59 years of age who are at increased risk for RSV disease for AREXVY, based on results from study 219238 (RSV OA=ADJ-018); this is a phase 3, observer-blind, placebo-controlled, randomised, multi-country, multi-center, non-inferiority study with 2 cohorts to evaluate immunogenicity, reactogenicity and safety of a single dose of RSVPreF3 OA in adults 50-59 years of age. As a consequence, sections 4.1, 4.6, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI, to bring it in line with the latest QRD template version 10.3, and to update the list of local representatives in the package leaflet. 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

5.3.32. Rilpivirine - EDURANT (CAP) - EMEA/H/C/002264/X/0042/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (2.5 mg dispersible tablets). The new presentation is indicated, in combination with other antiretroviral medicinal products, for the treatment of HIV-1 infection in patients ≥ 2 to < 18 years of age and weighing at least 10 kg to less than 25 kg. The PI and RMP have been updated in accordance.

Type II variation (C.I.6.a) to modify the approved therapeutic indication of the already authorised 25 mg film-coated tablets presentation to include, in combination with other antiretroviral medicinal products, treatment of human immunodeficiency virus type 1 (HIV-1) infection in antiretroviral treatment-naïve and virologically suppressed (HIV-1 RNA less than 50 copies per ml) paediatric patients from 2 to less than 12 years weighing at least 25 kg, based on final results from study studies TMC278-TiDP38-C213 Cohort 2. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. The updated RMP version 10.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to Annex II and 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

5.3.33. [Selpercatinib - RETSEVMO \(CAP\) - EMEA/H/C/005375/II/0032](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC in order to add urinary tract infections, stomatitis, calcium decreased, albumin decreased, sodium decreased and potassium decreased to the list of adverse drug reactions (ADRs) with frequency Very common and to update efficacy, safety and pk information based on results from study LIBRETTO-531 (JZJB) listed as a specific obligation in the Annex II; This study is a Phase 3 confirmatory study comparing selpercatinib to physicians choice of cabozantinib or vandetanib in patients with progressive advanced, kinase inhibitor naïve RET-mutant medullary thyroid cancer (MTC). The package leaflet and Annex II are updated accordingly. The RMP version 9.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI

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

5.3.34. [Selpercatinib - RETSEVMO \(CAP\) - EMEA/H/C/005375/X/0031](#)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new pharmaceutical form (film-coated tablets) associated with new strengths (40 mg, 80 mg, 120 mg and 160 mg). The RMP (version 7.1) is updated in accordance

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

5.3.35. [Semaglutide - RYBELSUS \(CAP\) - EMEA/H/C/004953/II/0041](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Update of section 4.6 of the SmPC in order to update information on breast-feeding based on final results from study NN9924-4669. This was an open-label, single-armed, multiple-dose, multi-centre study evaluating the semaglutide and SNAC concentrations in

breastmilk from healthy lactating women dosed once daily with oral semaglutide for 10 days (3 mg for 5 days followed by 7 mg for 5 days). The primary endpoints were evaluated during a 24 hours pharmacokinetic (PK) sampling period after the 10th dose. The package leaflet is updated accordingly. The RMP version 9.0 has also been submitted

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

5.3.36. [Smallpox and monkeypox vaccine \(live modified vaccinia virus Ankara\) - IMVANEX \(CAP\) - EMEA/H/C/002596/II/0100](#)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 5.1 of the SmPC in order to add vaccine effectiveness data, and the removal of the two open specific obligations (POX-MVA-039 (SOB02) and SEMVAc (SOB03)), based on the IMVANEX vaccine effectiveness data in real-world use during the 2022 monkeypox outbreak. Consequently, the MAH proposes a switch from exceptional marketing authorisation to full marketing authorisation. The Annex II and package leaflet are updated accordingly. The RMP version 10.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI

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

5.3.37. [Teclistamab - TECVAYLI \(CAP\) - EMEA/H/C/005865/II/0009](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jana Lukacisinova

Scope: Update of section 4.4 of the SmPC in order to update the warning on Progressive Multifocal Leukoencephalopathy (PML) based on a cumulative safety review. The package leaflet is updated accordingly. The RMP version 4.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor updates to the PI and 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

5.3.38. [Velaglucerase alfa - VPRIV \(CAP\) - EMEA/H/C/001249/II/0063](#)

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.2 of the SmPC in order to add information to support at-home self-administration of VPRIV by a trained patient and/or a caregiver based on post-marketing data and literature. The package leaflet and Annex IID are updated accordingly. The updated RMP version 13.0 has also been submitted

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

5.3.39. Zoonotic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - EMEA/H/C/002094/II/0086

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of individuals 6 months of age and older for AFLUNOV, based on final results from study V87_30. This is a Phase 2, Randomised, Observer-Blind, Multicenter Study to Evaluate the Immunogenicity and Safety of Several Doses of Antigen and MF59 Adjuvant Content in a Monovalent H5N1 Pandemic Influenza Vaccine in Healthy Pediatric Subjects 6 Months to < 9 Years of Age.

As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated accordingly. Version 5.3 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes to the SmPC

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. Angiotensin II - GIAPREZA (CAP) - PSUSA/00010785/202312

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Artesunate - ARTESUNATE AMIVAS (CAP) - PSUSA/00010958/202312

Applicant: Amivas Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Atidarsagene autotemcel - LIBMELDY (CAP) - PSUSA/00010899/202312

Applicant: Orchard Therapeutics (Netherlands) B.V., ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.4. Berotralstat - ORLADEYO (CAP) - PSUSA/00010930/202312

Applicant: BioCryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Budesonide⁸ - KINPEYGO (CAP) - PSUSA/00011007/202312

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. COVID-19 Vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA⁹ - PSUSA/00010912/202312

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.7. Dalbavancin - XYDALBA (CAP) - PSUSA/00010350/202311

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Efgartigimod alfa - VYVGART (CAP) - PSUSA/00011014/202312

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Elacestrant - ORSERDU (CAP) - PSUSA/00000120/202312

Applicant: Stemline Therapeutics B.V.

⁸ For centrally authorised products indicated for primary immunoglobulin A nephropathy only

⁹ Withdrawn Marketing Authorisation in the European Union – Commission Decision dated 27 March 2024

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. [Eladocagene exuparvovec - UPSTAZA \(CAP\) - PSUSA/00011004/202312](#)

Applicant: PTC Therapeutics International Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.11. [Elasomeran \(Spikevax\), elasomeran, imelasomeran \(Spikevax bivalent Original/Omicron BA.1\), elasomeran, davesomeran \(Spikevax bivalent Original/Omicron BA.4-5\), andusomeran \(Spikevax XBB.1.5\) - SPIKEVAX \(CAP\) - PSUSA/00010897/202312 \(with RMP\)](#)

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. [Enfortumab vedotin - PADCEV \(CAP\) - PSUSA/00010989/202312](#)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. [Entrectinib - ROZLYTREK \(CAP\) - PSUSA/00010874/202312](#)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. [Eribulin - HALAVEN \(CAP\) - PSUSA/00001254/202311](#)

Applicant: Eisai GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. [Follitropin delta - REKOVELLE \(CAP\) - PSUSA/00010554/202311](#)

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. [Formoterol fumarate dihydrate, glycopyrronium bromide, budesonide - RILTRAVA AEROSPHERE \(CAP\); TRIXEO AEROSPHERE \(CAP\) - PSUSA/00010908/202312](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. [Inclisiran - LEQVIO \(CAP\) - PSUSA/00010904/202312](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. [Inebilizumab - UPLIZNA \(CAP\) - PSUSA/00010996/202312](#)

Applicant: Horizon Therapeutics Ireland DAC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. [Inotuzumab ozogamicin - BESPONSA \(CAP\) - PSUSA/00010659/202312](#)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. [Levodopa - INBRIJA \(CAP\) - PSUSA/00107800/202312](#)

Applicant: Acorda Therapeutics Ireland Limited

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Lonococog alfa - AFSTYLA (CAP) - PSUSA/00010559/202401

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Mosunetuzumab - LUNSUMIO (CAP) - PSUSA/00010999/202312

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - PSUSA/00010984/202312

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Octreotide¹⁰ - MYCAPSSA (CAP) - PSUSA/00011036/202312

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Olaparib - LYNPARZA (CAP) - PSUSA/00010322/202312

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁰ For centrally authorised products only

6.1.26. Osimertinib - TAGRISSO (CAP) - PSUSA/00010472/202311

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - PREVENAR 20 (CAP) - PSUSA/00010981/202312

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Ponatinib - ICLUSIG (CAP) - PSUSA/00010128/202312

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Prasterone¹¹ - INTRAROSA (CAP) - PSUSA/00010672/202311

Applicant: Endoceutics S.A.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Quizartinib - VANFLYTA (CAP) - PSUSA/00000176/202312

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Raloxifene - EVISTA (CAP); OPTRUMA (CAP) - PSUSA/00002603/202312

Applicant: Substipharm (Evista), Eli Lilly Nederland B.V. (Optruma)

PRAC Rapporteur: Kirsti Villikka

¹¹ Pessary, vaginal use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Ravulizumab - ULTOMIRIS (CAP) - PSUSA/00010787/202312

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Ritlecitinib - LITFULO (CAP) - PSUSA/00000133/202312

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Rotavirus vaccine pentavalent (live, oral) - ROTATEQ (CAP) - PSUSA/00002666/202311

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Roxadustat - EVRENZO (CAP) - PSUSA/00010955/202312

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Rucaparib - RUBRACA (CAP) - PSUSA/00010694/202312

Applicant: Pharmaand GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. [Coronavirus \(COVID-19\) vaccine \(recombinant, adjuvanted\) - NUVAXOVID \(CAP\) - PSUSA/00010972/202312](#)

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. [Tabelecleucel - EBVALLO \(CAP\) - PSUSA/00011028/202312](#)

Applicant: Pierre Fabre Medicament, ATMP

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.39. [Tagraxofusp - ELZONRIS \(CAP\) - PSUSA/00010896/202312](#)

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. [Tezepelumab - TEZSPIRE \(CAP\) - PSUSA/00011015/202312](#)

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. [Tirbanibulin - KLISYRI \(CAP\) - PSUSA/00010943/202312](#)

Applicant: Almirall, S.A.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. [Tislelizumab - TEVIMBRA \(CAP\) - PSUSA/00000136/202312](#)

Applicant: Beigene Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. [Tozinameran \(COMIRNATY\), tozinameran, riltozinameran \(COMIRNATY Original/Omicron BA.1\), tozinameran, famtozinameran \(COMIRNATY Original/Omicron BA.4-5\), raxtozinameran \(COMIRNATY Omicron XBB.1.5\) - COMIRNATY \(CAP\) - PSUSA/00010898/202312](#)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. [Tralokinumab - ADTRALZA \(CAP\) - PSUSA/00010937/202312](#)

Applicant: LEO Pharma A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. [Trastuzumab deruxtecan - ENHERTU \(CAP\) - PSUSA/00010894/202312](#)

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. [Ublituximab - BRIUMVI \(CAP\) - PSUSA/00000045/202312](#)

Applicant: Neuraxpharm Pharmaceuticals S.L.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. [Ustekinumab - STELARA \(CAP\) - PSUSA/00003085/202312](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Vadadustat - VAFSEO (CAP) - PSUSA/00011050/202312

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.49. Vonicog alfa - VEYVONDI (CAP) - PSUSA/00010714/202312

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Mari Thorn

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. Erlotinib - TARCEVA (CAP); NAP - PSUSA/00001255/202311

Applicants: Roche Registration GmbH (Tarceva), various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Human hepatitis B immunoglobulin - ZUTECTRA (CAP); NAP - PSUSA/00001631/202311

Applicants: Biotest Pharma GmbH (Zutectra), various

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Riluzole - RILUTEK (CAP); RILUZOLE ZENTIVA (CAP); NAP - PSUSA/00002645/202312

Applicants: Sanofi Winthrop Industrie (Rilutek), Zentiva, k.s. (Riluzole Zentiva), various

PRAC Rapporteur: Karin Erneholm

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. Atomoxetine (NAP) - PSUSA/00000262/202311

Applicant(s): various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Carbimazole (NAP) - PSUSA/00000550/202312

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Cefpodoxim (NAP) - PSUSA/00000604/202312

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Ciprofloxacin hydrochloride, hydrocortisone (NAP) - PSUSA/00000774/202311

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Codeine, ibuprofen (NAP) - PSUSA/00000850/202312

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Danaparoid (NAP) - PSUSA/00000923/202312

Applicant(s): various

PRAC Lead: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. [Diphtheria, tetanus, pertussis \(acellular, component\), poliomyelitis \(inactivated\), haemophilus type b conjugate vaccine \(adsorbed\) \(NAP\) - PSUSA/00001124/202311](#)

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. [Dydrogesterone, estradiol \(NAP\) - PSUSA/00001276/202312](#)

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. [Ethanol extracts of: Iberis amara L., planta tota recens, Angelica archangelica L., radix, Matricaria recutita L., flos, Carum carvi L., fructus, Silybum marianum \(L.\) Gaertn., fructus, Melissa officinalis L., folium, Mentha piperita L., folium, Chelidonium majus L., herba, Glycyrrhiza glabra L., radix \(NAP\) - PSUSA/00010800/202311](#)

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. [Flupentixol \(NAP\) - PSUSA/00001444/202311](#)

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. [Flupentixol, melitracene \(NAP\) - PSUSA/00001445/202311](#)

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Glatiramer (NAP) - PSUSA/00001529/202311

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Hydroxycarbamide¹² (NAP) - PSUSA/00009182/202312

Applicant(s): various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Imidapril (NAP) - PSUSA/00001726/202312

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Ketoconazole (NAP) - PSUSA/00001808/202312

Applicant(s): various

PRAC Lead: Guðrún Þengilsdóttir

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Ketoprofen, sucralfate (NAP) - PSUSA/00002797/202312

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

¹² Except for centrally authorised product

6.3.17. Lisinopril, torasemide (NAP) - PSUSA/00010685/202312

Applicant(s): various

PRAC Lead: Jana Lukačšínová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Methylprednisolone (NAP) - PSUSA/00002026/202311

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Nabilone (NAP) - PSUSA/00002100/202312

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Neomycin sulfate, nystatin, triamcinolone acetonide (NAP) - PSUSA/00002140/202312

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Salicylic acid¹³ (NAP) - PSUSA/00002680/202312

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Sulfasalazine (NAP) - PSUSA/00002816/202312

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

¹³ Topical use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Tafluprost, timolol (NAP) - PSUSA/00010324/202312

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. Terazosin (NAP) - PSUSA/00002895/202311

Applicant(s): various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. Tinzaparin (NAP) - PSUSA/00002967/202312

Applicant(s): various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

None

6.5.1. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0054, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Lukacisinova

Scope: To update sections 4.2, 4.4, 4.8 of the SmPC to include Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS); and to update section D of Annex II to remove educational materials for physicians, pharmacists and nurses and to include ICANS within neurologic events in educational material for patient/caregivers and patient alert card following the outcome of PSUR procedure EMEA/H/C/PSUSA/00010460/202212. The package leaflet is updated accordingly. The RMP version 17.0 has also been submitted

Action: For adoption of PRAC Assessment Report

6.5.2. Naltrexone hydrochloride, Bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0063

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: To update sections 4.3, 4.4 and 4.5 of the SmPC to update and streamline the relevant wording on opioids following the assessment of PSUSA/00010366/202209 procedure. The package leaflet is updated accordingly. The RMP version 12.9 has also been submitted.

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews¹⁴

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)¹⁵

7.1.1. Valproate - EMEA/H/N/PSP/J/0094.4

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Progress report & substantial amendment: Characterization of neurodevelopmental disorders in children exposed in utero to valproate and/or other antiepileptic drugs with long-term followup: retrospective study of multiple European data sources

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

7.1.2. Topiramate - EMEA/H/N/PSP/J/0106

Applicant: Janssen (on behalf of a consortium)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Drug evaluation study (DUS) to evaluate the effectiveness of the implemented risk minimisation measures, particularly focusing on preventing pregnancies and further characterising the prescribing patterns for topiramate in the target populations for pregnancy prevention

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

¹⁴ 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

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

7.1.3. Topiramate - EMEA/H/N/PSP/J/0107

Applicant: Janssen (on behalf of a consortium)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: PASS survey among healthcare professionals and patients to assess their knowledge and behaviour regarding the risks of topiramate use during pregnancy, the measures implemented to prevent pregnancy, and the receipt/use of educational materials as part of the pregnancy prevention program

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)¹⁶

7.2.1. Agalsidase beta - FABRAZYME (CAP) - EMEA/H/C/000370/MEA 065.1

Applicant: Sanofi B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: MAH's responses to MEA 065 [***EPIDEMIOLOGY STUDY PROTOCOL*** / Study no.: EPM0086] RSI as adopted in February 2024.

Fabrazyme (agalsidase beta) home infusion educational materials effectiveness evaluation: a survey of nurses administering home infusions

Action: For adoption of advice to CHMP

7.2.2. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 004.4

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: MAH response to MEA 004.3 [***Protocol Study No. PS0037***] RSI and protocol amendment (Version 2.0, amendment #3) as adopted in April 2024.

An observational cohort study to evaluate bimekizumab exposure during pregnancy. To monitor the safety of bimekizumab use in pregnancy

Action: For adoption of advice to CHMP

7.2.3. Cabotegravir - APRETUDE (CAP) - EMEA/H/C/005756/MEA 003.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's responses to MEA 003 [***Draft Protocol***CAB LA PrEP Cohort] RSI and an updated revised study protocol draft as adopted in March 2024.

CAB LA PrEP Cohort: Prospective Cohort Study to Assess Adherence and Effectiveness of, and Monitor for Hepatotoxicity and Resistance to Cabotegravir for Pre-Exposure Prophylaxis in Europe

¹⁶ 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

Action: For adoption of advice to CHMP

7.2.4. Darbepoetin alfa - ARANESP (CAP) - EMEA/H/C/000332/MEA 092.6

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH Response to MEA 092.5 RSI and REVISED PASS PROTOCOL / STUDY 20190404 as adopted in March 2024.

Title: Use of Erythropoiesis Stimulating Agents (ESAs) in Subjects Receiving Myelosuppressive Chemotherapy in Europe

Action: For adoption of advice to CHMP

7.2.5. Mirikizumab - OMVOH (CAP) - EMEA/H/C/005122/MEA 001.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Hrabcik

Scope: MAH response to questions on MEA 001 [Protocol / I6T-MC-B003] and an Updated Protocol / I6T-MC-B003 as adopted in February 2024.

Observational Study of Pregnancy and Infant Outcomes Among Women Exposed to Mirikizumab During Pregnancy in US-based Administrative Claims Data

Action: For adoption of advice to CHMP

7.2.6. Mirikizumab - OMVOH (CAP) - EMEA/H/C/005122/MEA 002.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Hrabcik

Scope: MAH's response to questions on MEA 002 [Protocol / I6T-MC-B004] and an updated revised protocol I6T-MC-B004 as adopted in February 2024.

Observational Secondary Database Study to Assess the Long-Term Safety of Mirikizumab in Routine Clinical Practice Using US Administrative Claims Data

Action: For adoption of advice to CHMP

7.2.7. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58¹⁷) - EMEA/H/W/002300/MEA 003.10

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: **Protocol Amendment (version 3) / EPI-MALARIA-003 study protocol**

The EPI-MAL-003 study is a Phase IV prospective observational study to evaluate the safety, effectiveness and impact of the RTS,S/AS01E vaccine in young children in sub-Saharan Africa

¹⁷ 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 advice to CHMP

7.2.8. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 001.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: MAH's response to MEA 001.2 [Rimegepant Pregnancy Registry study C4951005 (formerly no BHV3000-402) **UPDATED PROTOCOL / ANNUAL INTERIM REPORT**], revised protocol (v4.0) and SAP (v3.0) as adopted in September 2023.

A Prospective, Registry-based, Observational Study to Assess Maternal, Fetal and Infant Outcomes Following Exposure to Rimegepant: The Migraine Observational Nurtec Pregnancy Registry (MONITOR)

Action: For adoption of advice to CHMP

7.2.9. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 003.6

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault

Scope: ***Protocol Amendment*** / study AC-065A403 (version 5):

A PASS to evaluate risk minimisation measures for mEDication errors with Uptravi (selexipag) during the titration phase in patients with pulmonary arterial hypertension (PAH) in Clinical prAcTicE (EDUCATE)

Action: For adoption of advice to CHMP

7.2.10. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.9

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH response to MEA 003.8 and revised protocol [***FOURTH Annual Interim Results*** / Study No.: M-14745-40] as adopted in March 2024.

Title: Tildrakizumab Post-Authorisation SafetyStudy (PASS) in European Psoriasis Registries. To collect long-term safety data in particular relating to event of special interest (important potential risks and pregnancy related outcomes) for tildrakizumab. (Malignancies, MACEs, Serious infections, SIBH, Hypersensitivity, IBD, Safety in pregnant and lactating women)

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)¹⁸

None

¹⁸ In accordance with Article 107p-q of Directive 2001/83/EC

7.4. Results of PASS non-imposed in the marketing authorisation(s)¹⁹

7.4.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0218

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report for study P10-023 listed as a category 3 study in the RMP. This is a 10-year, post marketing, observational registry to assess long term safety of Humira (adalimumab) in adult patients with chronic plaque psoriasis (Ps)

Action: For adoption of PRAC Assessment Report

7.4.2. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS2705/0050; Edoxaban - ROTEAS (CAP) - EMEA/H/C/004339/WS2705/0036

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Nathalie Gault

Scope: Submission of a Summary of Changes for the DSE-EDO-05-14-EU clinical study report, as an erratum detailing the updates.
DSE-EDO-05-14-EU is a non-interventional PASS on Edoxaban treatment in routine clinical practice for patients with acute venous thromboembolism in Europe (ETNA-VTE-Europe) which was listed as a category 3 study in the RMP (MEA 007)

Action: For adoption of PRAC Assessment Report

7.4.3. Elasmomeran - 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

Action: For adoption of PRAC Assessment Report

7.4.4. Epoetin alfa - ABSEAMED (CAP) - EMEA/H/C/000727/WS2615/0108; Epoetin alfa - BINOCRIT (CAP) - EMEA/H/C/000725/WS2615/0108; Epoetin alfa - EPOETIN ALFA HEXAL (CAP) - EMEA/H/C/000726/WS2615/0108

Applicant: Sandoz GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report from Non-Interventional Post authorisation Safety Study, NI-PASS HX575-507 listed as a category 3 study in the RMP. The non-interventional study (NIS PASS) study HX575-507 was conducted to address a post-approval requirement (MEA 13.5) to evaluate the safety profile of HX575 administered s.c. in patients with CKD-

¹⁹ 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

induced anemia under real-life conditions, in order to increase confidence on the safe use of s.c. HX575. The RMP version 19.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.5. [Vonicog alfa - VEYVONDI \(CAP\) - EMEA/H/C/004454/II/0033](#)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report from study TAK-577-4005 listed as a category 3 PASS in the RMP. This is a non-interventional retrospective cohort study that evaluated the safety of VEYVONDI in real-world clinical practice. The RMP version 5.0 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. [Avapritinib - AYVAKYT \(CAP\) - EMEA/H/C/005208/SOB 009.3](#)

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: MAH's responses to SOB 009.2 [Study BLU-285-1406] RSI as adopted in March 2024.

Study BLU-285-1406 is a multinational, open-label, observational post-authorisation safety study that will evaluate the long-term safety and efficacy of avapritinib for the first-line treatment or following ≤ 4 months of imatinib treatment in at least 50 patients with PDGFRA D842V-mutated GIST

Action: For adoption of advice to CHMP

7.5.2. [Burosumab - CRYSVITA \(CAP\) - EMEA/H/C/004275/MEA 004.4](#)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: ***Second interim study report*** [Study No EUPAS32190]

Non-interventional PASS of Burosumab in the Treatment of Children >1 year of age, Adolescents and Adults with X-linked Hypophosphataemia (protocol number 2019-36-EU-CRY)

Action: For adoption of advice to CHMP

7.5.3. [Covid-19 Vaccine \(recombinant, adjuvanted\) - NUVAXOVID \(CAP\) - EMEA/H/C/005808/MEA 004.6](#)

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to MEA 004.5 [Protocol, study no. 2019nCoV-402] RSI as adopted in January 2024.

UK PASS Using the Clinical Practice Research Datalink (CPRD): A surveillance study to characterise the safety profile of Nuvaxovid in adults aged 18 years and older in the real-world setting using the UK CPRD

Action: For adoption of advice to CHMP

7.5.4. Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/MEA 002.3

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: ***Annual Progress Report / Study 272MS403***

Title: An observational study utilising data from big MS data registries to evaluate the long-term safety of Vumerity and Tecfidera

Action: For adoption of advice to CHMP

7.5.5. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/MEA 011.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Carla Torre

Scope: From EMEA/H/C/004077/II/0043:

Interim study result / Study AMY2009

Study AMY2009 is a multicenter, multicohort, open-label, Phase 2 study in participants with newly diagnosed systemic AL amyloidosis. The primary objective of the study is to further characterize cardiac adverse events in patients with newly diagnosed AL amyloidosis treated with subcutaneous daratumumab-based therapy in terms of the incidence, severity, clinical presentation, management, and outcome

Action: For adoption of advice to CHMP

7.5.6. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/MEA 062.3

Applicant: Alexion Europe SAS

PRAC Rapporteur: Monica Martinez Redondo

Scope: MAH's response to MEA 062.2 [***aHUS Registry Biennial Interim Report*** /Protocol M11-001] RSI as adopted in March 2024.

Title: An Observational, non-interventional multicenter, multinational study of patients with atypical hemolytic-uremic syndrome

Action: For adoption of advice to CHMP

7.5.7. Esketamine - SPRAVATO (CAP) - EMEA/H/C/004535/MEA 003.2

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's responses to MEA 003.1 [***Interim Study / Study no.: PCSNSP002812***] RSI as adopted in March 2024.

Survey to Assess the Effectiveness of SPRAVATO Educational Materials for Additional Risk Minimization Measures in the European Union

Action: For adoption of advice to CHMP

7.5.8. [Lisocabtagene maraleucel, Lisocabtagene maraleucel - BREYANZI \(CAP\) - EMEA/H/C/004731/MEA 007.1](#)

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to MEA 007 [LTFU study (GC LTFU 001)] RSI as adopted in January 2024.

Long-term follow-up of safety and efficacy for all paediatric and adult subjects exposed do a GM T cell therapy in Bristol-Myers Squibb sponsored, or Bristol Myers Squibb alliance partner sponsored, clinical trials in accordance with Health Authorities' guidance for long-term (up to 15 years) follow-up of subjects treated with gene therapy products

Action: For adoption of advice to CAT and CHMP

7.5.9. [Mexiletine - NAMUSCLA \(CAP\) - EMEA/H/C/004584/MEA 001.4](#)

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Registry study to determine the long-term safety and tolerability of Namuscla for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorder. (Cat. 3 study in the RMP)

SECOND INTERIM STUDY REPORT, Study LUP/MEX/2018/001

Action: For adoption of advice to CHMP

7.5.10. [Nonacog beta pegol - REFIXIA \(CAP\) - EMEA/H/C/004178/ANX 001.1](#)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: MAH response to ANX 001 [***Fifth Progress Report (yearly) for PASS NN7999-4031/Paradigm 8***] RSI as adopted in 21 March 2024.

A Non-Interventional PASS in male haemophilia B patients receiving Nonacog Beta Pegol (N9-GP) prophylaxis treatment

Action: For adoption of advice to CHMP

7.5.11. [Ofatumumab - KESIMPTA \(CAP\) - EMEA/H/C/005410/MEA 002.5](#)

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: MAH Response to MEA 002.4 [Study COMB157G2407 / PRIM] RSI as adopted in March 2024:

Provision of the answers to the outstanding concerns raised in the assessment report of EMEA/H/C/005410/MEA/002.4 pertaining to second interim report for the Pregnancy outcomes Intensive Monitoring (PRIM), study (COMB157G2407) report for Kesimpta (ofatumumab)

Action: For adoption of advice to CHMP

7.5.12. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 002.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: MAH response to MEA 002.2 [Rimegepant Pregnancy Outcomes study C4951006 (formerly BHV3000-403)**UPDATED PROTOCOL / ANNUAL INTERIM REPORT / UPDATED SAP**], revised protocol (v6.0) and revised SAP (v2.0) as adopted in September 2023. Retrospective Cohort Study of Pregnancy Outcomes in Women Exposed to Rimegepant During Pregnancy

Action: For adoption of advice to CHMP

7.5.13. Somatrogen - NGENLA (CAP) - EMEA/H/C/005633/MEA 001.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: From Initial MAA:

Statistical Analysis Plan PASS C0311023

An Active Surveillance PASS to Monitor the Real-World Long-term Safety of Somatrogen Among Paediatric Patients in Europe to estimate the incidence rates of neoplasms, diabetes mellitus type 2, and the clinical endpoints related to immunogenicity, and medication errors in paediatric patients treated with somatrogen, and paediatric patients treated with once daily somatropin, in the course of routine clinical care

Action: For adoption of advice to CHMP

7.5.14. Sutimlimab - ENJAYMO (CAP) - EMEA/H/C/005776/MEA 003.1

Applicant: Sanofi B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: From initial MAA:

Study OBS16454 (RMP category 3) PASS (non-imposed)

Title: Sutimlimab Cold Agglutinin Disease Real World Evidence Registry (CADENCE).

**ANNUAL INTERIM REPORT*

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Dengue tetravalent vaccine (live, attenuated) - DENGIVAXIA (CAP) - EMEA/H/C/004171/MEA 014

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: From Initial MAA:

Non-Feasibility Assessment PASS DNG00043 (Cat. 3)

Cross-sectional survey to evaluate vaccinator's knowledge and understanding of the restricted indication to only individuals previously infected will be used to measure the effectiveness of risk minimization measures (HCP guide) in Europe

Action: For adoption of advice to CHMP

7.6.2. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 037.6

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: From II/0059:

Study Protocol C4591009

A non-interventional PASS in US to assess the occurrence of safety events of interest, including myocarditis and pericarditis, among individuals in the general US population and in subcohorts of interest within selected data sources participating in the US Sentinel System.

Monitoring report, Study C4591009

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Amifampridine - FIRDAPSE (CAP) - EMEA/H/C/001032/S/0077 (without RMP)

Applicant: SERB SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/004061/S/0024 (without RMP)

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0116 (without RMP)

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Martirosyan

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0056 (without RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Zanamivir - DECTOVA (CAP) - EMEA/H/C/004102/S/0018 (without RMP)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

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. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/R/0019 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Adalimumab - AMSPARITY (CAP) - EMEA/H/C/004879/R/0008 (with RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Arsenic trioxide - ARSENIC TRIOXIDE ACCORD (CAP) - EMEA/H/C/005175/R/0009 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Bortezomib - BORTEZOMIB FRESENIUS KABI (CAP) - EMEA/H/C/005074/R/0010 (without RMP)

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/R/0030 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. [Deferasirox - DEFERASIROX ACCORD \(CAP\) - EMEA/H/C/005156/R/0011 \(without RMP\)](#)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. [Fostamatinib - TAVLESSE \(CAP\) - EMEA/H/C/005012/R/0018 \(with RMP\)](#)

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. [Imipenem, Cilastatin, Relebactam - RECARBRIO \(CAP\) - EMEA/H/C/004808/R/0029 \(without RMP\)](#)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. [Osilodrostat - ISTURISA \(CAP\) - EMEA/H/C/004821/R/0022 \(without RMP\)](#)

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. [Ospemifene - SENSHIO \(CAP\) - EMEA/H/C/002780/R/0048 \(without RMP\)](#)

Applicant: Shionogi B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. [Siponimod - MAYZENT \(CAP\) - EMEA/H/C/004712/R/0029 \(without RMP\)](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Solriamfetol - SUNOSI (CAP) - EMEA/H/C/004893/R/0023 (with RMP)

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Julia Pallos

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/R/0051 (without RMP)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

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. Oral retinoids (acitretin, alitretinoin, isotretinoin) (NAP) - PT/H/xxxx/WS/069

Applicant(s): various

PRAC Lead: Ana Sofia Martins

Scope: PRAC consultation on a worksharing procedure to assess the protocol of a category 3 qualitative study among healthcare professionals (HCPs) and patients to investigate barriers and reasons why certain measures parts of the oral retinoid therapy Pregnancy Prevention Programme (PPP) are not always followed in clinical practice and the preferred ways of HCPs and patients to receive information on the PPP, submitted following PRAC conclusions on the assessment of the final results of the category 1 PASS (EMA/H/N/PSR/J/0040)

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. Election of PRAC Chairperson

Action: For adoption

12.1.2. PRAC membership

Action: For information

12.1.3. Vote by proxy

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

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

Action: For discussion

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Health threats and EMA Emergency Task Force (ETF) activities - update

Action: For discussion

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. Marketing authorisation applications (MAA) forecast for 2024 – planning update dated Q2 2024

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

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

12.11.1. Signal management – feedback from Signal Management Review Technical (SMART) Working Group

PRAC lead: Martin Huber

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.15.3. Good pharmacovigilance practices (GVP) module VIII on 'Post-authorisation safety studies (PASS)' 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) – mid-year update 2024

PRAC lead: Sabine Straus

Action: For discussion

12.21. Others

12.21.1. IRIS - update on transfer of procedures to IRIS by the end of 2024

Action: For information

12.21.2. PRAC drafting group on the risks of dependence and addiction of opioids – update

PRAC lead: Liana Martirosyan

Action: For discussion

12.21.3. PRAC Assessors trainings - update

PRAC Lead(s): Martin Huber, Sabine Straus

Action: For discussion

13. Any other business

None

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 \(europa.eu\)](https://www.europeanmedicinesagency.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/