28 October 2024
EMA/PRAC/457736/2024
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 28-31 October 2024

Chair: Ulla Wändel Liminga – Vice-Chair: Liana Martirosyan

28 October 2024, 10:30 – 19:30, via teleconference

29 October 2024, 08:30 – 19:30, via teleconference

30 October 2024, 08:30 – 19:30, via teleconference

31 October 2024, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

14 November 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 28-31 October 2024. See November month 2024 PRAC minutes (to be published post December 2024 PRAC meeting).

1.2. Agenda of the meeting on 28-31 October 2024

Action: For adoption

1.3. Minutes of the previous meeting on 30 September-03 October 2024

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

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

4.1.1. Avelumab – BAVENCIO (CAP); atezolizumab – TECENTRIQ(CAP); cemiplimab - LIBTAYO(CAP); dostarlimab – JEMPERLI(CAP); durvalumab – IMFINZI(CAP); ipilimumab – YERVOY(CAP); nivolumab - OPDIVO, OPDUALAG (CAP); pembrolizumab – KEYTRUDA (CAP); retifanlimab – ZYNYZ (CAP); tislelizumab – TEVIMBRA (CAP); toripalimab – LOQTORZI (CAP); tremelimumab – IMJUDO (CAP); durvalumab – IMFINZI (CAP)

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

PRAC Rapporteur: David Olsen

Scope: Signal of scleroderma, systemic scleroderma, morphea

Action: For adoption of PRAC recommendation

EPITT 20119 – New signal

Lead Member State(s): NO

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

4.1.2. Domperidone (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of hypertension in patients with a phaeochromocytoma

Action: For adoption of PRAC recommendation

EPITT 20106– New signal

Lead Member State(s): BE

4.1.3. Ixekizumab – TALTZ (CAP)

Applicant: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of demyelinating disorders

Action: For adoption of PRAC recommendation

EPITT 20124 – New signal

Lead Member State(s): DE

4.1.4. Tegafur, gimeracil, oteracil – TEYSUNO (CAP)

Applicant: Nordic Group B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Signal of hyperammonaemia

Action: For adoption of PRAC recommendation

EPITT 20115 – New signal

Lead Member State(s): NL

4.2. Signals follow-up and prioritisation

4.2.1. Angiotensin II receptor blockers: amlodipine, valsartan - COPALIA (CAP) - EMEA/H/C/000774/SDA/021; amlodipine, valsartan - DAFIRO (CAP) - EMEA/H/C/000776/SDA/020; amlodipine, valsartan - EXFORGE (CAP) - EMEA/H/C/000716/SDA/020; amlodipine, valsartan, hydrochlorothiazide - COPALIA HCT (CAP) - EMEA/H/C/001159/SDA/010; amlodipine, valsartan, hydrochlorothiazide - EXFORGE HCT (CAP) - EMEA/H/C/001068/SDA/010; azilsartan medoxomil - EDARBI (CAP) - EMEA/H/C/002293/SDA/013; irbesartan - APROVEL (CAP) - EMEA/H/C/000141/SDA/023; irbesartan - IFIRMASTA (CAP) - EMEA/H/C/000962/SDA/015; irbesartan - IRBESARTAN TEVA (CAP) - EMEA/H/C/001093/SDA/006; irbesartan - IRBESARTAN ZENTIVA (CAP) - EMEA/H/C/000785/SDA/014; irbesartan - KARVEA (CAP) - EMEA/H/C/000142/SDA/023; irbesartan, hydrochlorothiazide - COAPROVEL (CAP) -

EMEA/H/C/000222/SDA/011; irbesartan, hydrochlorothiazide – IFIRMACOMBI (CAP) – EMEA/H/C/002302/SDA/004; irbesartan, hydrochlorothiazide - IRBESARTAN HYDROCHLOROTHIAZIDE ZENTIVA (CAP) - EMEA/H/C/000783/SDA/012; irbesartan, hydrochlorothiazide - IRBESARTAN/HYDROCHLOROTHIAZIDE TEVA (CAP) - EMEA/H/C/001112/SDA/009; irbesartan, hydrochlorothiazide - KARVEZIDE (CAP) - EMEA/H/C/000221/SDA/011; telmisartan, sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/SDA/012; telmisartan - KINZALMONO (CAP) - EMEA/H/C/000211/SDA/031; telmisartan - MICARDIS (CAP) - EMEA/H/C/000209/SDA/032;telmisartan - PRITOR (CAP) - EMEA/H/C/000210/SDA/025; telmisartan - TELMISARTAN ACTAVIS (CAP) - EMEA/H/C/001168/SDA/007; telmisartan - TOLURA (CAP) - EMEA/H/C/001196/SDA/009; telmisartan, amlodipine - TWYNSTA (CAP) - EMEA/H/C/001224/SDA/013; telmisartan, hydrochlorothiazide - ACTELSAR HCT (CAP) - EMEA/H/C/002676/SDA/002; telmisartan, hydrochlorothiazide - KINZALKOMB (CAP) - EMEA/H/C/000415/SDA/031; telmisartan, hydrochlorothiazide - MICARDISPLUS (CAP) - EMEA/H/C/000413/SDA/030; telmisartan, hydrochlorothiazide - PRITORPLUS (CAP) - EMEA/H/C/000414/SDA/031; telmisartan, hydrochlorothiazide – TOLUCOMBI (CAP) – EMEA/H/C/002549/SDA/002; sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/SDA/010; other relevant 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 HCT, Neparvis), Sanofi Winthrop Industrie (Aprovel, Coaprovel, Karvea, Karvezide), Takeda Pharma A/S (Edarbi), Teva B.V. (Irbesartan Teva, Irbesartan/Hydrochlorothiazide Teva), Zentiva, k.s. (Irbesartan Hydrochlorothiazide Zentiva, Irbesartan Zentiva), various

PRAC Rapporteur: Martin Huber

Scope: Signal of intestinal angioedema

Action: For adoption of PRAC recommendation

EPITT 20104 – Follow-up to Month July 2024

4.2.2. Eptinezumab - VYEPTI (CAP) - EMEA/H/C/005287/SDA/008; erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/SDA/007; fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/SDA/010; galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/SDA/007

Applicant(s): H. Lundbeck A/S (Vyepti), Novartis Europharm Limited (Aimovig), TEVA GmbH (Ajovy), Eli Lilly Nederland B.V. (Emgality)

PRAC Rapporteur: Terhi Lehtinen

Scope: Signal of insomnia

Action: For adoption of PRAC recommendation

EPITT 20077 – Follow-up to Month May 2024

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

Applicant: various

PRAC Rapporteur: Jean-Michel Dogné

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

Action: For adoption of PRAC recommendation

EPITT 20105 – Follow-up to Month July 2024

4.3. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Aflibercept (CAP MAA) - EMEA/H/C/006339

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

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

5.1.2. Aflibercept (CAP MAA) - EMEA/H/C/006551

Scope (pre D-180 phase): Treatment of age-related macular degeneration (AMD) and visual impairment, treatment of age-related macular degeneration (AMD), visual impairment and retinopathy of prematurity (ROP)

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

5.1.3. Datopotamab (CAP MAA) - EMEA/H/C/006547

Scope (pre D-180 phase): Treatment of adult patients with inoperable or metastatic HR-positive / HER2-negative breast cancer with disease progression following chemotherapy in the metastatic setting

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

5.1.4. Datopotamab (CAP MAA) - EMEA/H/C/006081

Scope (pre D-180 phase): Treatment of adult patients with locally advanced or metastatic non squamous non-small cell lung cancer (NSCLC)

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

5.1.5. Denosumab (CAP MAA) - EMEA/H/C/006398

Scope (pre D-180 phase): Prevention of skeletal related events with advanced malignancies

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

5.1.6. Denosumab (CAP MAA) - EMEA/H/C/006157

Scope (pre D-180 phase): Prevention of skeletal related events with advanced malignancies

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

5.1.7. Denosumab (CAP MAA) - EMEA/H/C/006399

Scope (pre D-180 phase): Treatment of osteoporosis and bone loss

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

5.1.8. Denosumab (CAP MAA) - EMEA/H/C/006156

Scope (pre D-180 phase): Treatment of osteoporosis and bone loss

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

5.1.9. Pegfilgrastim (CAP MAA) - EMEA/H/C/006407

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

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

5.1.10. Tocilizumab (CAP MAA) - EMEA/H/C/006196

Scope (pre D-180 phase): Treatment of rheumatoid arthritis (RA)

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

5.1.11. Ustekinumab (CAP MAA) - EMEA/H/C/006444

Scope (pre D-180 phase): For the treatment of Crohn’s disease and ulcerative colitis

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. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0053, Orphan

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 9.12 to include changes made to the pharmacokinetic study CUV052 including the inclusion of adolescent patients in the protocol. CUV052 is an interventional study to evaluate the pharmacokinetics of afamelanotide in patients with Erythropoietic Protoporphyria (EPP).

Action: For adoption of PRAC Assessment Report

5.2.2. Alendronic acid, colecalciferol - ADROVANCE (CAP) - EMEA/H/C/000759/WS2696/0055; Alendronic acid, colecalciferol - FOSAVANCE (CAP) - EMEA/H/C/000619/WS2696/0058; Alendronic acid, colecalciferol - VANTAVO (CAP) - EMEA/H/C/001180/WS2696/0045

Applicant: Organon N.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of an updated RMP version 8.0 following the assessment outcome from procedure WS/2467 to reclassify the risk of atypical femoral fracture from "important potential risk" to "important identified risk" and to extend the risk of "atypical femoral fracture" to "atypical fractures of long bones".

Action: For adoption of PRAC Assessment Report

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

Applicant: Corza Medical GmbH

PRAC Rapporteur: Gabriele Maurer

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

Action: For adoption of PRAC Assessment Report

5.2.4. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/II/0055, Orphan

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of an updated RMP version 8.0 in order to remove the category 3 PASS 3000-04-002/ GSK 214708; this is an integrated meta-analysis of MDS/AML and other SPM incidence in patients with ovarian cancer who have been treated with niraparib.

Action: For adoption of PRAC Assessment Report

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

5.3.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0052, Orphan

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.2 of the SmPC in order to update the posology recommendations by removing the current recommendation of a maximum of four implants per year, based on a literature review and analysis of safety data. The Package Leaflet is updated accordingly. The RMP version 9.8 has also been submitted. In addition, the MAH took the opportunity to introduce a minor editorial change to the Product Information

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

5.3.2. Avacopan - TAVNEOS (CAP) - EMEA/H/C/005523/II/0015, Orphan

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Liana Martirosyan

Scope: Update of sections 4.5 and 5.2 of the SmPC based on final results from study CL020_168; this is an open-label, phase 1 study to evaluate the effect of repeated oral doses of avacopan on the pharmacokinetics of a single dose of simvastatin in healthy volunteers; the Package Leaflet is updated accordingly. The updated RMP version 2.0 has also been submitted. In addition, the 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

5.3.3. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/II/0046/G

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: A grouped application consisting of:
C.I.4: Update of sections 4.2, 4.4, 4.6 and 4.8 of the SmPC in order to add the immune-mediated adverse reactions sclerosing cholangitis, arthritis, polymyalgia rheumatica, and Sjogren's syndrome based on post-marketing data and literature. The Package Leaflet is updated accordingly. The RMP version 7.3 has also been submitted.

C.I.4: Update of section 4.8 of the SmPC in order to update the immunogenicity information based on results from studies EMR100070-003, B9991003 and 100/B9991001. Study EMR100070-003 is a Phase 2, single-arm, open label, multicenter study to investigate the clinical activity and safety of avelumab in patients with mMCC. T. Study B9991003 is a Phase 3 multinational, multicenter, randomized (1:1), open-label, parallel 2 - arm study of avelumab in combination with axitinib versus sunitinib monotherapy in the 1L treatment of participants with aRCC. Study 100/B9991001 is a Phase 3, multicenter, multinational, randomized, open-label, parallel-arm efficacy and safety study of avelumab plus best

supportive care (BSC) versus BSC alone as a maintenance treatment in adult participants with locally advanced or metastatic UC whose disease did not progress after completion of 1L platinum-containing chemotherapy

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

5.3.4. Baloxavir marboxil - XOFLUZA (CAP) - EMEA/H/C/004974/X/0022

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Extension application to add a new pharmaceutical form (granules) associated with three new strengths (10, 30 and 40 mg) packaged in sachet (PET/alu/PET).

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

5.3.5. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/II/0029

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the final report from study PS0014 (BE BRIGHT) listed as a category 3 study in the RMP. This is a multicenter, open-label extension (OLE) study to assess the long-term safety, tolerability, and efficacy of bimekizumab in adult study participants with moderate to severe plaque PSO who completed 1 of the 3 completed feeder studies. The RMP version 2.2 has also been submitted

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

5.3.6. Bulevirtide - HEPCLUDEX (CAP) - EMEA/H/C/004854/II/0034, Orphan

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 4.8 of the SmPC in order to update safety information based on final results from study MYR204 listed as a category 3 study in the RMP; this is a multicenter, open-label, randomized Phase 2b clinical study to assess efficacy and safety of bulevirtide in combination with pegylated interferon alfa-2a in patients with chronic hepatitis delta. The RMP version 4.2 has also been submitted

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

5.3.7. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/II/0069

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of paediatric patients with type 2 diabetes mellitus aged 10 years old and older for INVOKANA, based on final results from

study JNJ-28431754DIA3018 as well as study JNJ-28431754DIA1055. Study JNJ-28431754DIA3018 is a double-blind, placebo-controlled, 2-arm, parallel-group, multicenter Phase 3 study in participants with T2DM >10 and <18 years of age who had inadequate glycemic control (ie, HbA1c of >6.5% to <11.0%). 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 13.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor changes to the PI and 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

5.3.8. 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) - Change in the immediate packaging of the biological finished product Ilaris.
The updated RMP version 14.0 has also been submitted

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

5.3.9. Capivasertib - TRUQAP (CAP) - EMEA/H/C/006017/II/0001

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update the posology recommendation and the warning regarding Diabetic Ketoacidosis (DKA) and add it to the list of adverse drug reactions (ADRs) with frequency uncommon based on a safety review. The Package Leaflet is updated accordingly. The RMP version 2 has also been submitted. In addition, the MAH took the opportunity to remove post authorisation measures which were added to Annex II in error, to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.4

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

5.3.10. Casirivimab, Imdevimab - RONAPREVE (CAP) - EMEA/H/C/005814/II/0017

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of paediatric patients from 2 to less than 12 years old, weighing at least 10kg, who do not require supplemental oxygen and who are at increased risk of progression to severe COVID-19 for Ronapreve, based on final results from study COV-2067; this was a seamless, adaptive, Phase 3, randomized, double-blinded, placebo-controlled, multi-center study to evaluate the efficacy, safety, and tolerability of casirivimab+imdevimab combination therapy in paediatric and adult outpatients with mild to moderate COVID-19. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the

SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted

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

5.3.11. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/II/0022/G, Orphan

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: 1. Type II (B.II.e.1.b.2) An updated RMP version 2.6 has also been submitted
2. Type IB (B.II.e.5.a.2)
3. Type II (B.II.a.3.b.5)
4. Type II (B.II.a.5)
5. Type II (B.II.b.1.c)
6. Type IA (B.II.b.2.a)
7. Type II (B.I.a.1.e)
8. Type II (B.I.a.1.j)
9. Type II (B.I.z)

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

5.3.12. 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

5.3.13. Glofitamab - COLUMVI (CAP) - EMEA/H/C/005751/II/0005, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Extension of indication to include in combination with gemcitabine and oxaliplatin the treatment of adult patients with relapse or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS) who are not candidates for autologous stem cell transplant (ASCT) for COLUMVI, based on results of primary and updated analyses from study GO41944 (STARGLO) listed as a Specific Obligation in the Annex II of the Product Information, as well supportive data from the Phase Ib study GO41943. Study GO41944

(STARGLO) is a Phase III, open-label, multicenter, randomized study of glofitamab in combination with GemOx (Glofit-GemOx) vs. rituximab in combination with GemOx (R-GemOx) in patients with R/R DLBCL. 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 Annex II and Package Leaflet are updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and 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

5.3.14. Human normal immunoglobulin - HYQVIA (CAP) - EMEA/H/C/002491/II/0102

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report from study 161505; this is a Phase 3b, open-label, non-controlled, multicenter study to assess the long-term tolerability and safety of immune globulin infusion 10% (human) with recombinant human hyaluronidase (HYQVIA/HyQvia) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). The RMP version 16.0 has also been submitted

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

5.3.15. Influenza quadrivalent vaccine (rDNA[3]) - SUPEMTEK (CAP) - EMEA/H/C/005159/II/0021/G

Applicant: Sanofi Pasteur

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped application comprising two type II variations as follows:
C.I.6.a – Extension of indication to include the treatment of children 9 years of age and older for Supemtek, based on final results from study VAP00027; this is a Phase III, non-randomized, open-label, uncontrolled study to demonstrate the non-inferior HAI immune response of RIV4 for the 4 strains in participants aged 9 to 17 years vs participants aged 18 to 49 years; 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 2.0 of the RMP has also been submitted.
C.I.4 - Update of sections 4.8 and 5.1 of the SmPC in order to update paediatric information based on final results from study VAP00026; this is a Phase III, randomized, modified double-blind, active-controlled 2-arm to demonstrate the non-inferior HAI immune response of RIV4 vs licensed IIV4 for the 4 strains based on the egg-derived antigen in all participants. 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

[3] Ribosomal deoxyribonucleic acid

5.3.16. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - FLUCELVAX TETRA (CAP) - EMEA/H/C/004814/II/0047

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of adults and children from 6 months of age and older for FLUCELVAX TETRA based on final results from study V130_14. This is a phase 3, randomized, observer-blind, multicenter study to evaluate the efficacy, immunogenicity, and safety of Seqirus' Cell-Based Quadrivalent Subunit Influenza Virus Vaccine (QIVc) compared to a non-influenza vaccine when administrated in healthy subjects aged 6 months through 47 months. 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 3.3 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. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/II/0126

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Monica Martinez Redondo

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

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

5.3.18. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0056, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy data based on final results from study VX19-445-107 (Study 107); this is a Phase 3, Open-label Study Evaluating the Long-term Safety and Efficacy of ELX/TEZ/IVA Combination Therapy in Subjects With Cystic Fibrosis Who Are 6 Years of Age and Older. The RMP version 9.2 has also been submitted

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

5.3.19. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/II/0053

Applicant: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of juvenile idiopathic arthritis for TALTZ, based on week 16 results from study I1F-MC-RHCG; this is a multicenter, open-label, efficacy, safety, tolerability, and pharmacokinetic study (COSPIRIT-JIA) of subcutaneous ixekizumab with adalimumab reference arm, in children from 2 to less than 18 years of age with juvenile idiopathic arthritis subtypes of enthesitis-related arthritis (including juvenile-onset ankylosing spondylitis) and juvenile psoriatic arthritis was performed to evaluate the efficacy and safety of ixekizumab for 16 weeks after treatment initiation. 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 8.1 of the RMP has also been submitted. Furthermore, the PI is in line with the latest QRD template version 10.4

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

5.3.20. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/II/0042

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include the use of SAXENDA for weight management in children from the age of 6 years to less than 12 years based on results from study NN8022-4392; this is a 56-week, double-blind, randomised, placebo-controlled study investigating safety and efficacy of liraglutide on weight management in children with obesity aged 6 to <12 years. 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 34.0 of the RMP has also been submitted

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

5.3.21. Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/II/0043/G

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: A grouped application consisting of:
C.I.6 (Type II): Extension of indication for Breyanzi to include treatment of adult patients with 3rd line + follicular lymphoma (FL) based on final results from the pivotal study JCAR017-FOL-001 (FOL-001, TRANSCEND-FL). This is a phase 2, open-label, single-arm, multicohort, multicenter study to evaluate efficacy and safety of JCAR017 in adult subjects with relapsed or refractory (r/r) follicular Lymphoma (FL) or marginal zone lymphoma (MZL). As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.0 of the RMP is being submitted. Furthermore, as part of the application the MAH is requesting a 1-year extension of the market protection.

B.II.d.1.e (Type II)
B.II.d.1.a (Type IB)
B.II.d.1.a (Type IB)

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

and 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. Olipudase alfa - XENPOZYME (CAP) - EMEA/H/C/004850/II/0012/G, Orphan

Applicant: Sanofi B.V.

PRAC Rapporteur: Martin Huber

Scope: A grouped application consisting of:
C.I.4: Update of sections 4.4 and 4.8 of the SmPC in order to update safety information based on final results from study DFI12712 ASCEND, listed as a category 3 study in the RMP; this is a Phase 2/3, multicenter, randomised, double-blinded, placebo-controlled, repeat-dose study to evaluate the efficacy, safety, pharmacodynamics and pharmacokinetics of olipudase alfa in patients with AMSD. The Package Leaflet is updated accordingly. The RMP version 3.0 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 implement editorial changes to the SmPC.

C.I.4: Update of sections 4.4 and 4.8 of the SmPC in order to update safety information based on final results from study LTS13632 listed as a category 3 study in the RMP; this is a long-term study the ongoing safety and efficacy of olipudase alfa in patients with ASMD. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted

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

5.3.24. Rozanolixizumab - RYSTIGGO (CAP) - EMEA/H/C/005824/II/0006, Orphan

Applicant: UCB Pharma

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 5.1 of the SmPC based on final results from study MG0007 listed as a specific a category 3 study in the RMP; this is a randomized, open-label extension study to evaluate the long-term safety, tolerability, and efficacy of repeated 6-week treatment cycles of rozanolixizumab based on myasthenia gravis worsening in adult study participants with generalized myasthenia gravis. The RMP version 1.1 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 update the PI in accordance with the latest EMA excipients guideline

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

5.3.25. Trastuzumab - ENHERTU (CAP) - EMEA/H/C/005124/II/0048

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include treatment of adult patients with unresectable or metastatic HER2-low or HER2-ultralow breast cancer (BC) who have received at least one endocrine therapy in the metastatic setting for ENHERTU, based on results from study D9670C00001 (DESTINY-Breast06); this is a phase 3, randomized, multicentre, open-label study of trastuzumab deruxtecan (DS-8201a) compared with investigator's choice chemotherapy in, hormone receptor-positive, HER2-low and HER2-ultralow BC patients whose disease has progressed on endocrine therapy in the metastatic setting. 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 8.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI, to update the list of local representatives in the Package Leaflet and to update the PI according to the Excipients Guideline

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

5.3.26. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/II/0071/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Karin Erneholm

Scope: A grouped application consisting of:
C.I.4 (Type II): Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on interim results from study BO27938 (KATHERINE) listed as a PAES in the Annex II and as a category 3 study in the RMP. This is a Randomized, Multicenter, Open Label Phase III Study to Evaluate the Efficacy and Safety of Trastuzumab Emtansine Versus Trastuzumab as Adjuvant Therapy for Patients with HER2-Positive Primary Breast Cancer who have Residual Tumor Present Pathologically in the Breast or Axillary Lymph Nodes Following Preoperative Therapy. The Package Leaflet is updated in

accordance. The RMP version 16.0 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, to update the PI in accordance with the latest EMA excipients guideline, and to implement editorial changes to the PI. Furthermore, the MAH took the opportunity to update Annex II-D and to implement editorial changes to the Labelling section.
A.4 (Type I)

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

5.3.27. Ustekinumab - PYZCHIVA (CAP) - EMEA/H/C/006183/II/0005/G

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Type II B.IV.1.c
Type IB C.I.2.a

To update section 4.6 Fertility, Pregnancy and lactation of the SmPC to update information on pregnancy following assessment of the same change for the reference product Stelara (EMEA/H/C/000958).
An updated RMP (version 4.0) is provided

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

5.3.28. Ustekinumab - WEZENLA (CAP) - EMEA/H/C/006132/II/0003/G

Applicant: Amgen Technology (Ireland) Unlimited Company

PRAC Rapporteur: Rhea Fitzgerald

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

The RMP version 1.0 has also been submitted.

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

5.3.29. Valoctocogene roxaparvovec - ROCTAVIAN (CAP) - EMEA/H/C/005830/II/0014, Orphan

Applicant: BioMarin International Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Update of the Annex II in order to propose changes to the current marketing authorisation obligations for ROCTAVIAN. The RMP version 1.3 has also been submitted.

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

5.3.30. 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

5.3.31. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/X/0023

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (160 mg film-coated tablets)

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. 5-aminolevulinic acid[4] - GLIOLAN (CAP) - PSUSA/00000009/202403

Applicant: Photonamic GmbH & Co. KG

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aprepitant - EMEND (CAP) - PSUSA/00000229/202403

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[4] Glioma indication only

6.1.3. Atogepant - AQUIPTA (CAP) - PSUSA/00000100/202403

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Avacopan - TAVNEOS (CAP) - PSUSA/00010967/202403

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Belimumab - BENLYSTA (CAP) - PSUSA/00009075/202403

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bosutinib - BOSULIF (CAP) - PSUSA/00010073/202403

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. COVID-19 Vaccine (recombinant, adjuvanted) - BIMERVAX (CAP) - PSUSA/00011045/202403

Applicant: Hipra Human Health S.L.

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Dupilumab - DUPIXENT (CAP) - PSUSA/00010645/202403

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Duvelisib - COPIKTRA (CAP) - PSUSA/00010939/202403

Applicant: Secura Bio Limited

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Enalapril maleate[5] - AQUMELDI (CAP) - PSUSA/00000201/202403

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Etrasimod - VELSIPITY (CAP) - PSUSA/00000273/202404

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Filgotinib - JYSELECA (CAP) - PSUSA/00010879/202403

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Fluticasone furoate, umeclidinium, vilanterol - ELEBRATO ELLIPTA (CAP); TRELEGY ELLIPTA (CAP) - PSUSA/00010653/202403

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[5] Centrally authorised product for use in children below the age of 18 only

6.1.14. Fosaprepitant - IVEMEND (CAP) - PSUSA/00001471/202403

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Fostamatinib - TAVLESSE (CAP) - PSUSA/00010819/202404

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Futibatinib - LYTGOBI (CAP) - PSUSA/00000068/202403

Applicant: Taiho Pharma Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Glofitamab - COLUMVI (CAP) - PSUSA/00000067/202403

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Guanfacine - INTUNIV (CAP) - PSUSA/00010413/202403

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Human coagulation factor X - COAGADEX (CAP) - PSUSA/00010481/202403

Applicant: BPL Bioproducts Laboratory GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Idecabtagene vicleucel - ABECMA (CAP) - PSUSA/00010954/202403

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.21. Ipilimumab - YERVOY (CAP) - PSUSA/00009200/202403

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Ixekizumab - TALTZ (CAP) - PSUSA/00010493/202403

Applicant: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Lasmiditan - RAYVOW (CAP) - PSUSA/00011011/202404

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Lutetium (^{177}LU) vipivotide tetraxetan - PLUVICTO (CAP) - PSUSA/00011031/202403

Applicant: Novartis Europharm Limited

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Maralixibat - LIVMARLI (CAP) - PSUSA/00011032/202403

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Mirikizumab - OMVOH (CAP) - PSUSA/00000049/202403

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Naldemedine - RIZMOIC (CAP) - PSUSA/00010753/202403

Applicant: Shionogi B.V.

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Nintedanib[6] - OFEV (CAP) - PSUSA/00010319/202404

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Niraparib - ZEJULA (CAP) - PSUSA/00010655/202403

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Ocrelizumab - OCREVUS (CAP) - PSUSA/00010662/202403

Applicant: Roche Registration GmbH

[6] Respiratory indication only

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Olipudase alfa - XENPOZYME (CAP) - PSUSA/00011003/202403

Applicant: Sanofi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Pemigatinib - PEMAZYRE (CAP) - PSUSA/00010923/202404

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Risankizumab - SKYRIZI (CAP) - PSUSA/00010765/202403

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Selinexor - NEXPOVIO (CAP) - PSUSA/00010926/202403

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Selumetinib - KOSELUGO (CAP) - PSUSA/00010936/202404

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Siponimod - MAYZENT (CAP) - PSUSA/00010818/202403

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Tepotinib - TEPMETKO (CAP) - PSUSA/00010979/202403

Applicant: Merck Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Tucatinib - TUKYSA (CAP) - PSUSA/00010918/202404

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Vardenafil - LEVITRA (CAP) - PSUSA/00003098/202403

Applicant: Bayer AG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Velmanase alfa - LAMZEDE (CAP) - PSUSA/00010677/202403

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Zilucoplan - ZILBRYSQ (CAP) - PSUSA/00000169/202403

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Karin Erneholm

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. Colesevelam - CHOLESTAGEL (CAP); NAP - PSUSA/00000864/202403

Applicant(s): CHEPLAPHARM Arzneimittel GmbH (Cholestagel), various

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Dexmedetomidine - DEXDOR (CAP); NAP - PSUSA/00000998/202403

Applicant(s): Orion Corporation, various

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Esomeprazole - NEXIUM CONTROL (CAP); NAP - PSUSA/00001269/202403

Applicant(s): GlaxoSmithKline Dungarvan Ltd (Nexium Control), various

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Gozetotide - LOCAMETZ (CAP); NAP - PSUSA/00011030/202403

Applicant(s): Novartis Europharm Limited, various

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Spironolactone - QAIALDO (CAP); NAP - PSUSA/00002780/202403

Applicant(s): Nova Laboratories Ireland Limited (Qaialdo), various

PRAC Rapporteur: Terhi Lehtinen

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. Barnidipine (NAP) - PSUSA/00000300/202403

Applicant(s): various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Bilastine (NAP) - PSUSA/00003163/202403

Applicant(s): various

PRAC Lead: Roxana Dondera

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Calcium chloride, glutamic acid, glutathione, histidine, lactobionic acid, magnesium chloride, mannitol, potassium chloride, sodium hydroxide (NAP) - PSUSA/00009162/202403

Applicant(s): various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Chlorphenamine maleate, paracetamol (NAP) - PSUSA/00000703/202403

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Erythromycin[7] (NAP) - PSUSA/00010809/202403

Applicant(s): various

PRAC Lead: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Ezetimibe, simvastatin (NAP) - PSUSA/00001347/202403

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Fluorodopa (^{18}F) (NAP) - PSUSA/00010002/202403

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Fluprednidene (NAP) - PSUSA/00010097/202403

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Fluprednidene, gentamicin (NAP) - PSUSA/00010098/202403

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[7] Topical use only

6.3.10. Highly refined fish oil, glycerol, purified egg phosphatide (NAP) - PSUSA/00010802/202403

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Human anti-d immunoglobulin (NAP) - PSUSA/00001614/202403

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Lanthanum (NAP) - PSUSA/00003175/202403

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Metamizole (NAP) - PSUSA/00001997/202403

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Nitrazepam (NAP) - PSUSA/00002170/202403

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Olodaterol (NAP) - PSUSA/00010245/202403

Applicant(s): various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Oxycodone (NAP) - PSUSA/00002254/202404

Applicant(s): various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Inn (NAP) - Procedure

Applicant(s): various

PRAC Lead: Name Surname

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/LEG 279.1

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's responses to LEG 279 [Cumulative safety review on dental disorders, increased parathyroid hormone and congenital anomalies] RSI as adopted in May 2024

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0025, Orphan

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC in order to propose a combined Adverse Drug Reaction table for Dravet Syndrome and Lennox-Gastaut syndrome following PSUSA procedure EMEA/H/C/PSUSA/00010907/202306. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

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

Action: For adoption of PRAC Assessment Report

6.5.3. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0055, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.6 of the SmPC in order to amend the existing wording on exposure during pregnancy following PSUR procedure (EMEA/H/C/PSUSA/00010868/202310)

Action: For adoption of PRAC Assessment Report

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

Applicant: Orexigen Therapeutics Ireland Limited

Scope: Re-examination of variation II/63 concluded with negative PRAC recommendation in July 2024

Action: Feedback from AHEG Chair and adoption of re-examination PRAC Assessment Report

6.5.5. Relugolix - ORGOVYX (CAP) - EMEA/H/C/005353/II/0024

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Karin Erneholm

Scope: Update of section 4.8 of the SmPC in order to amend the frequency of an existing adverse drug reactions (ADRs) 'Myocardial infarction' from 'rare' to 'uncommon' following PSUSA 00010994/202401 procedure and based on the current available clinical trial data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to add editorial changes

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[8]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[9]

7.1.1. Exagamglogene autotemcel - CASGEVY (CAP) - EMEA/H/C/PSA/S/0113.1

Applicant: Vertex Pharmaceuticals (Ireland) Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Substantial amendment to a protocol for a long-term registry-based study of patients with transfusion-dependent β-thalassemia (TDT) or sickle cell disease (SCD) treated with exagamglogene autotemcel (exa-cel) [MAH's response to PSA/S/0113]

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

7.1.2. Valproate (NAP)- EMEA/H/N/PSP/J/0094.5

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

PRAC Rapporteur: Liana 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 follow up: retrospective study of multiple European data sources

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

7.1.3. Valproate (NAP) - EMEA/H/N/PSP/J/0108

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

PRAC Rapporteur: Liana Martirosyan

Scope: Paternal exposure to valproate, further investigation on the risk of Neuro Developmental Disorders (NDD) and Congenital Malformation (CM) in Offspring: A Non-Interventional Post-Authorization Safety Study (PASS)

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

[8] 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
[9] In accordance with Article 107n of Directive 2001/83/EC

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[10]

7.2.1. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 006

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Petar Mas

Scope: ***Study Protocol B7451120***
Title: A Prospective Active Surveillance Study to Monitor Growth, Development, and Maturation Among Adolescents with Atopic Dermatitis Exposed to Abrocitinib (as listed in PART III of the EU Risk Management Plan (Version 4.4) agreed during the Type II Variation (Procedure No. EMEA/H/C/005452/II/0010)

Action: For adoption of advice to CHMP

7.2.2. Atogepant - AQUIPTA (CAP) - EMEA/H/C/005871/MEA 003.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: MAH's responses to MEA 003 [***Atogepant pregnancy exposure registry: Study P22-392***] RSI as adopted in May 2024
Study P22-392 aims to prospectively evaluate maternal, fetal, and infant outcomes through 12 months of age among women exposed to atogepant during pregnancy
Protocol and Interim Study Result

Action: For adoption of advice to CHMP

7.2.3. Atogepant - AQUIPTA (CAP) - EMEA/H/C/005871/MEA 004.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: MAH's responses to MEA 004 [***Study P22-419***/ Pregnancy Study] RSI as adopted in 30 May 2024.
Study P22-419 aims to describe and compare the incidence of pregnancy outcomes in women with migraine who are exposed to atogepant during pregnancy
Protocol and Interim Study

Action: For adoption of advice to CHMP

7.2.4. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/MEA 007.2

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

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

Scope: MAH's responses to MEA 007.1 [***Revised Protocol***] as adopted in June 2024. To Evaluate the Risk of Malignancies in Patients with Myasthenia Gravis (MG) Treated with Efgartigimod

Action: For adoption of advice to CHMP

7.2.5. Exagamglogene autotemcel - CASGEVY (CAP) - EMEA/H/C/005763/MEA 011

Applicant: Vertex Pharmaceuticals (Ireland) Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: ***Protocol v. 1.0 / Study no VX24-290-102***
Title: Healthcare Professional Survey (HCP) to Assess the Effectiveness of the Additional Risk Minimization Measures (aRMM) for Casgevy (exagamglogene autotemcel)

Action: For adoption of advice to CAT and CHMP

7.2.6. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 001.12

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: ***REVISED PROTOCOL for PASS Study TEG4001*** (Version 4.2)
A Prospective, Non-interventional, Long-term, Multinational Cohort Safety Study of Patients with Hereditary Transthyretin Amyloidosis with Polyneuropathy (hATTR-PN)

Action: For adoption of advice to CHMP

7.2.7. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/MEA 009.8

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: ***Amended PASS Protocol (v 13.2) / Study number: EVM-18888***
Title: Linaclotide Safety Study for the Assessment of Diarrhoea Complications and Associated Risk Factors in Selected European Populations with Irritable Bowel Syndrome with Constipation (IBS-C)

Action: For adoption of advice to CHMP

7.2.8. Mirikizumab - OMVOH (CAP) - EMEA/H/C/005122/MEA 001.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Hrabcik

Scope: MAH's response to questions regarding MEA 001.1 and a Revised Protocol [***Protocol I6T-MC-B003***] as adopted in July 2024.
Observational Study of Pregnancy and Infant Outcomes Among Women Exposed to

Mirikizumab During Pregnancy in US-based Administrative Claims Data. (RMP v.0.4)

Action: For adoption of advice to CHMP

7.2.9. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[11]) - EMEA/H/W/002300/MEA 003.11

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 003.10 [Amended Protocol (version 3) for PASS EPI-MALARIA-003] RSI as adopted in July 2024.
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

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[12]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[13]

7.4.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0219

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Karin Bolin

Scope: Submission of the final report from study P10-262 listed as a category 3 study in the RMP. This is a long-term, multi-center, longitudinal, post-marketing observational registry to assess long-term safety and effectiveness of Humira (adalimumab) in children with moderately to severely active polyarticular or polyarticular-course juvenile idiopathic arthritis (JIA). The RMP version 16.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.2. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/WS2620/0092; Dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/WS2620/0047; Dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/WS2620/0056; Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/WS2620/0118

Applicant: ViiV Healthcare B.V.

[11] 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)

[12] In accordance with Article 107p-q of Directive 2001/83/EC
[13] 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

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.6 of the SmPC in order to update information about the use of DTG-containing regimens in pregnancy and at conception based on final results from non-interventional Tsepamo study and the Eswatini Birth Outcomes Surveillance study. In addition, data from other cohort studies and pregnancy registries, including the APR, DOLOMITE-EPPICC (Study 208613) and DOLOMITE-NEAT-ID Network study (Study 208759) both listed as category 3 studies in the RMP; and the US Chart Review (Study 212976) as well as data from literature are included. DOLOMITE-EPPICC (Study 208613) is a s a non-interventional study to Assess "real-world" maternal and foetal outcomes following DTG use during pregnancy and to describe patterns of DTG utilization; DOLOMITE NEAT ID Network Study (208759) is a non-interventional, multi-site observational study to define the safety and effectiveness of Dolutegravir use in HIV positive pregnant women. The Package Leaflet is updated accordingly. The RMP version 19 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to sections 4.4 and 4.5 of the SmPC

Action: For adoption of PRAC Assessment Report

7.4.3. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/II/0056

Applicant: Eisai GmbH

PRAC Rapporteur: Mari Thorn

Scope: Update of section 5.1 of the SmPC in order to update the safety and efficacy information for the current HCC indication based on final results from study E7080-M000-508 (STELLAR), listed as a category 3 PASS in the RMP; this is a multicentre non-interventional, observational Phase 4 study to evaluate the safety and tolerability of lenvatinib in patients with advanced or unresectable HCC. The RMP version 17.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.4. Pasireotide - SIGNIFOR (CAP) - EMEA/H/C/002052/II/0070, Orphan

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report from study CSOM230B2410 listed as a category 3 PASS in the RMP. This is a non-interventional, multinational, multi-centre post-marketing study to further document the safety and efficacy of pasireotide s.c. administered in routine clinical practice in patients with Cushing's disease. The RMP version 8.0 has also been submitted

Action: For adoption of PRAC Assessment Report

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: A grouped application comprised of two Type II Variations, as follows:
C.I.4: Update of the Annex II based on final results from study B3461001 (THAOS) listed as a category 3 study in the RMP. This is a global, multi-center, longitudinal, observational survey of patients with documented transthyretin gene mutations or wild-type transthyretin amyloidosis.
C.I.13: Submission of the final report from study B3461042 listed as a category 3 study in the RMP. This is a post-marketing safety surveillance study in Japanese patients with AATR-PN.
The RMP version 10.0 has also been submitted. In addition, the MAH took the opportunity to provide B3461028 Clinical Study Report (CSR) Errata

Action: For adoption of PRAC Assessment Report

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

7.5.1. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050.7

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's responses to MEA 050.6 [*** FORTH ANNUAL INTERIM REPORT***/ PASS C18477-ONC-50025] as adopted in June 2024.
Study Title: A post-authorisation long term safety cohort study in acute promyelocytic leukaemia (APL) patients treated with Trisenox

Action: For adoption of advice to CHMP

7.5.2. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/SOB 009.4

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: MAH's response to SOB 009.3 [***Study BLU-285-1406***] as adopted in July 2024:
Study BLU-285-1406 is an imposed non-interventional PASS aiming to confirm the safety and efficacy of avapritinib in the treatment of adult patients with unresectable or metastatic GIST harbouring the PDGFRA D842V mutation, given as Specific Obligation 3 (SOB3) of the Conditional Marketing Authorisation for AYVAK
The interim report should include an update of the MAH’s efforts to include data from AVIATOR2020. If the MAH has found a way to include patient data from this registry, the MAH should discuss how these data will be incorporated in study 1406, which methodological challenges are faced and how these will be addressed.
Third Progress Report / Study BLU-285-1406

Action: For adoption of advice to CHMP

7.5.3. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/MEA 006.7

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: From Initial MAA:
PASS Study ALN-AS1-006
Company Sponsored AHP Registry
A global observational longitudinal prospective registry of patients with acute hepatic porphyria (AHP). [ELEVATE]
THIRD INTERIM ANNUAL REPORT

Action: For adoption of advice to CHMP

7.5.4. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/MEA 009.9

Applicant: AbbVie Deutschland GmbH & Co. KGGPRAC Rapporteur: Martin HuberG

Scope: ***Study Progress Report (v. 1.1) / Study no EVM-18888***
Title: Linaclotide Safety Study for the Assessment of Diarrhea Complications and Associated Risk Factors in Selected European Populations with IBS-C

Action: For adoption of advice to CHMP

7.5.5. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.16

Applicant: Gruenenthal GmbH

PRAC Rapporteur: Eamon O'Murchu

Scope: MAH Response to MEA 006.15 [Study No. D3820R00009 (EUPAS12669)] RSI as adopted in February 2024.

Action: For adoption of advice to CHMP

7.5.6. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 032.5

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eamon O'Murchu

Scope: MAH's responses to MEA 032.4 [***Progress Report / Study No.: 2868371***] as adopted in February 2024

Action: For adoption of advice to CHMP

7.5.7. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.19

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's responses to MEA 044.18 [6th annual report of the observational PASS

(EUPAS19506) of Ustekinumab in the treatment of paediatric patients aged 6 years and older with moderate to severe plaque psoriasis] as adopted in June 2024

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 024.5

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: MAH's responses to MEA 024.4 [***Progress Report / Study No.: 2868371***] as adopted in February 2024

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

7.8. Ongoing Scientific Advice

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

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Cerliponase alfa - BRINEURA (CAP) - EMEA/H/C/004065/S/0047 (without RMP)

Applicant: BioMarin International Limited

PRAC Rapporteur: Mari Thorn

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/S/0061 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Nelarabine - ATRIANCE (CAP) - EMEA/H/C/000752/S/0068 (without RMP)

Applicant: Sandoz Pharmaceuticals d.d.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Smallpox vaccine (live modified vaccinia virus Ankara) - IMVANEX (CAP) - EMEA/H/C/002596/S/0107 (with RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Vestronidase alfa - MEPSEVII (CAP) - EMEA/H/C/004438/S/0042 (without RMP)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Maria del Pilar Rayon

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. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/R/0047 (with RMP)

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.2. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0076 (with RMP)

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/R/0035 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Arsenic trioxide - ARSENIC TRIOXIDE MYLAN (CAP) - EMEA/H/C/005235/R/0012 (without RMP)

Applicant: Mylan Ireland Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Cefiderocol - FETCROJA (CAP) - EMEA/H/C/004829/R/0022 (with RMP)

Applicant: Shionogi B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Cholera vaccine, oral, live - VAXCHORA (CAP) - EMEA/H/C/003876/R/0024 (without RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Indacaterol, mometasone - ATECTURA BREEZHALER (CAP) - EMEA/H/C/005067/R/0031 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Indacaterol, mometasone - BEMRIST BREEZHALER (CAP) - EMEA/H/C/005516/R/0026 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Insulin lispro - LYUMJEV (CAP) - EMEA/H/C/005037/R/0019 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Isatuximab - SARCLISA (CAP) - EMEA/H/C/004977/R/0033 (without RMP)

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Monica Martinez Redondo

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/R/0028 (without RMP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. 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

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

9.1.1. Risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders connected with human centrally authorised products

Scope: Pharmacovigilance inspection programme 2024-2027 (2024 revision)

Action: For adoption

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. Levothyroxine (NAP) - FR/H/xxxx/WS/388

Applicant: IBSA PHARMA SAS

PRAC Lead: Tiphaine Vaillant

Scope: PRAC consultation on a worksharing variation procedure to revise, in the product information of levothyroxine-containing medicinal products (capsules and oral solution), the information regarding the drug-drug interaction between levothyroxine and proton-pump inhibitors (PPIs) as agreed in the last PSUSA procedure (PSUSA/00001860/202201) adopted by PRAC in October 2022, following results of 2 drug interaction studies, on request for France

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. Vote by proxy

None

12.1.3. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q3 2024

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2025

PRAC lead: Ulla Wändel Liminga, Liana Martirosyan

Action: For discussion

12.8. Planning and reporting

12.8.1. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q3 2024 and predictions

Action: For discussion

12.8.2. PRAC workload statistics – Q3 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 single assessment (PSUSA) – reminder session on agreed approach post pilot on Section 6 "Other Considerations" of the PSUSA assessment report

PRAC lead: Ulla Wändel Liminga, Liana Martirosyan

Action: For discussion

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: **Action:** For discussion

12.10.3. PSURs repository

None

12.10.4. Union reference date list – consultation on the draft list

Action: For adoption

12.11. Signal management

None

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. 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. Draft PRAC Interest Group (IG) impact workplan 2025/2026

PRAC lead: Liana Martirosyan

Action: For discussion

12.20.2. Good Pharmacovigilance Practices (GVP) module XVI – Addendum on pregnancy - update

PRAC lead: Ulla Wändel Liminga

Action: For discussion

12.20.3. Impact study on the dissemination of additional risk minimisation measures (RMM) for patients and healthcare professionals in EU Member States

PRAC lead: Liana Martirosyan

Action: For discussion

12.21. Others

12.21.1. Comparative effectiveness and safety studies using the target trial emulation and estimand frameworks

Action: For discussion

12.21.2. Draft template for qualification of patient registries

Action: For discussion

12.21.3. EMA-HMA catalogues of real-world data sources and non-interventional studies

Action: For discussion

12.21.4. IRIS training plan

Action: For discussion

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

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)

Signals assessment and prioritisation
(Item 4 of the PRAC agenda)

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

Risk Management Plans (RMPs)
(Item 5 of the PRAC agenda)

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

Assessment of Periodic Safety Update Reports (PSURs)
(Item 6 of the PRAC agenda)

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

Post-authorisation Safety Studies (PASS)
(Item 7 of the PRAC agenda)

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

Product related pharmacovigilance inspections
(Item 9 of the PRAC agenda)

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

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