EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

24 June 2026
EMA/PRAC/128532/2026
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 04-07 May 2026

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

Health and safety information

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

Disclaimers

Some of the information contained in the minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scope 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, the minutes are a working document primarily designed for PRAC members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes 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

The Chairperson opened the 04-07 May 2026 meeting by welcoming all participants. The meeting was held in-person.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics. Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. No new or additional competing interests were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

Discussions, deliberations and voting took place in full respect of the restricted involvement of Committee members and experts in line with the relevant provisions of the Rules of Procedure (EMA/PRAC/567515/2012 Rev.3). All decisions taken at this meeting were made in the presence of a quorum of members. All decisions, recommendations and advice were agreed by consensus, unless otherwise specified. The members of the EEA-EFTA states agreed with the recommendation of PRAC, unless otherwise specified.

The Chair thanked the departing member for their contributions to the Committee.

The EMA Secretariat announced the names of the Committee members who delegated their vote via proxy and the Committee members who received such proxy.

1.2. Agenda of the meeting on 04-07 May 2026

The agenda was adopted with some modifications upon request from the members of the Committee and the EMA secretariat as applicable.

1.3. Minutes of the previous meeting on 07-10 April 2026

The minutes were adopted with some amendments received during the consultation phase and will be published on the EMA website.

Post-meeting note: the PRAC minutes of the meeting held on 07-10 April 2026 were published on the EMA website on 08 June 2026 (EMA/PRAC/117688/2026).

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]

For further details, see also the adopted PRAC recommendations on signals under the corresponding month.

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

See also Annex I 14.1.

4.1.1. Alprazolam (NAP); amitriptyline hydrochloride / medazepam (NAP); amitriptyline / chlordiazepoxide (NAP); bromazepam (NAP); bromazepam / propantheline bromide (NAP); brotizolam (NAP); chlordiazepoxide (NAP); chlordiazepoxide / clidinium bromide (NAP); cinolazepam (NAP); clidinium bromide / diazepam (NAP); clobazam (NAP); cyclobarbital calcium / diazepam (NAP);clonazepam (NAP); clorazepate

[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

(NAP); clotiazepam (NAP); cloxazolam (NAP); delorazepam (NAP); diazepam (NAP); diazepam / gamma-amino-beta-hydroxybutyric acid (NAP); diazepam / isopropamide iodide (NAP); diazepam / octatropine methylbromide (NAP); diazepam / otilonium bromide (NAP); diazepam / sulpiride (NAP); diazepam / sulpiride / pyridoxine hydrochloride (NAP); estazolam (NAP); ethyl loflazepate (NAP); etizolam (NAP); flunitrazepam (NAP); flurazepam (NAP); ketazolam (NAP); loprazolam (NAP); lorazepam (NAP); lormetazepam (NAP); medazepam (NAP); mexazolam (NAP); midazolam - BUCCOLAM (CAP), NAP; nitrazepam (NAP); nordazepam (NAP); oxazepam (NAP); pinazepam (NAP); prazepam (NAP); remimazolam – BYFAVO (CAP), NAP; temazepam (NAP); tofisopam (NAP); triazolam (NAP); trimebutine maleate / medazepam (NAP)

Applicants: Neuraxpharm Pharmaceuticals S.L. (Buccolam), Paion Pharma GmbH (Byfavo), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Signal on miscarriage associated with in utero exposure to benzodiazepines (including fixed-dose combinations)

EPITT 20272 – New signal

Lead Member State(s): DK, PL, SI, NL, FR, FI, ES, BE, IT, HU, MT, AT, DE, PT, SK, IE, EE

Background

Benzodiazepines are central nervous system (CNS) depressants commonly used for the treatment of anxiety and sleep disorders.

During routine signal detection activities, a signal of miscarriage associated with in utero exposure to benzodiazepines (including fixed-dose combinations) was identified by France, based on the most recent published pharmacoepidemiological studies: Ishikawa et al.[3], Li et al.[4], Picot et al.[5]. France confirmed that the signal needed further analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from literature, PRAC has agreed that further review of available data by PRAC is warranted.

PRAC appointed Tiphaine Vaillant as PRAC Rapporteur for the signal.

Summary of recommendation(s)

- An updated PRAC Rapporteur's assessment report should be provided by 28 September 2026, focusing on pharmacoepidemiological data, taking into consideration also any other relevant publications or data, primarily those published over the last ten years, including EU data representative of current clinical practice within the EU. In addition, a discussion on the potential of residual confounding and other factors influencing interpretation of the observed association, on methodological limitations related to exposure assessment and comparator selection within the available pharmacoepidemiological literature, on contextualisation of the observed associations in

[3] Ishikawa T, Sakai T, Iwama N, et al. Association between exposure to atypical antipsychotics during pregnancy and risk of miscarriage. Acta Psychiatr Scand. 2024 Dec;150(6):562-572.
[4] Li BM, Wei SY, Chuang MT, Lai EC. Benzodiazepine Use in Pregnancy and the Risk of Pregnancy Outcomes. JAMA Intern Med. 2026 Feb 1;186(2):215-223.
[5] Picot C, Piroux Y, Pleau J, Bérard A, Cucherat M, Cottin J. Risk of miscarriage after benzodiazepine use during pregnancy: updated systematic review and meta-analysis. BMC Pregnancy Childbirth. 2026 Jan 26;26(1):175.

relation to baseline risks associated with underlying diseases and the absolute risk related to the association, on dose-response effects and on the impact of duration of use, as well as on a biological plausibility and the extent to which mechanistic considerations may support interpretation of epidemiological findings should also be included. Additionally, a discussion should be provided to determine whether the currently available data allow the observed association to be considered a class effect for benzodiazepines, or whether significant differences exist between individual substances which would warrant product-specific conclusions. The Rapporteur should also examine the need to update the product information (PI) and/or risk management plan (RMP) of concerned products.

- A 60-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.2. Amoxicillin (NAP); amoxicillin/clavulanic acid (NAP)

Applicant(s): various

PRAC Rapporteur: Dennis Lex (amoxicilin/clavulanic acid); Jan Neuhauser (amoxicilin)

Scope: Signal of encephalopathy

EPITT 20264 – New signal

Lead Member States: AT, DE

Background

Amoxicillin is a semi-synthetic broad spectrum penicillin antibiotic and clavulanic acid a beta lactamase inhibitor. In combination, amoxicillin/clavulanate is indicated for the treatment of infections of the upper respiratory tract, lower respiratory tract infections, genito-urinary tract infections, skin and soft tissue infections, bone and joint infections and perioperative antibiotic prophylaxis during surgical procedures.

During routine signal detection activities, a signal of encephalopathy was identified by France, based on 149 cases retrieved in French National Pharmacovigilance database.

Discussion

Having considered the available evidence from case reports in EudraVigilance and the literature, PRAC agreed that the signal should be addressed as part of the next PSUSA procedures.

Summary of recommendation(s)

- The innovator marketing authorisation holder (MAH) of amoxicillin containing medicinal products (Sandoz/Novartis Ospamox) and amoxicillin-clavulanate containing medicinal products (GlaxoSmithKline [GSK]) should submit within the PSUR with data lock point 07/03/2027 a cumulative review of all cases of encephalopathy with relevant preferred terms (PTs) within the standardised MedDRA query (SMQ) ´Non-infectious encephalopathy/delirium´ (except those only including already labelled neurological ADRs of amoxicillin (as e.g. ´convulsions´)) associated with amoxicillin as a suspect drug. This analysis should include a review of the published literature, data from spontaneous reports and reports from studies including all cases in EudraVigilance database, as well as a discussion on possible biological plausibility and mechanism of

this association. Additionally, the MAH should perform a causality assessment of all cases using the WHO-UMC causality assessment criteria and discuss whether a causal relationship between the administration of amoxicillin-clavulanate and the risk of ´encephalopathy´ can be established and if this relationship is dose-dependent. The MAH should also discuss the need for any potential amendment to the product information (PI) and/ or the risk management plan (RMP), particularly regarding highdose use or vulnerable patient populations and make accordingly a proposal for the changes to the relevant sections within this discussion.

- PRAC will assess the cumulative review within the PSUR procedure PSUSA/00000187/202703 and PSUSA/00000188/202703.

4.1.3. Exenatide – BYDUREON (CAP), BYETTA (CAP); insulin icodec / semaglutide - KYINSU (CAP); semaglutide – KAYSHILD (CAP), OZEMPIC (CAP), RYBELSUS (CAP), WEGOVY (CAP), WEGOVY FLEXTOUCH (CAP)

Applicants: AstraZeneca AB (Bydureon, Byetta), Novo Nordisk A/S (Ozempic, Kayshild, Kyinsu, Rybelsus, Wegovy, Wegovy flextouch)

PRAC Rapporteur: Mari Thorn

Scope: Signal of peripheral neuropathies

EPITT 20270 – New signal

Lead Member State(s): SE

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

During routine signal detection activities, a signal of peripheral neuropathies was identified by EMA, based on 18 cases retrieved from literature (exposed to dulaglutide, tirzepatide and semaglutide). The Rapporteur confirmed that the signal for semaglutide needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from the literature, as well as the known association between semaglutide and non-arteritic anterior ischaemic optic neuropathy (NAION) and acute worsening of diabetic retinopathy, PRAC agreed that further evaluation on the signal is warranted.

PRAC appointed Mari Thorn as Rapporteur for the signal.

Summary of recommendation(s)

- The marketing authorisation holder (MAH) for semaglutide (Novo Nordisk A/S) should submit a review of the semaglutide randomised clinical trials (RCTs) such as the Cardiovascular Outcomes Trials (CVOT) (i.e. SUSTAIN 6, PIONEER 6, SELECT, SOUL) and other relevant RCTs (e.g. FLOW and STRIDE) to evaluate for any imbalances between semaglutide and control arm concerning the MedDRA high-level group term (HLGT) peripheral neuropathies. The MAH should also perform a critical appraisal of any relevant published observational studies, including but not limited to the study by

Triplett et al. 2025[6], Fan et al. 2024[7]; García-Casares et al. 2023[8]. Additionally, the MAH should discuss the biological plausibility and potential mechanism of this association considering the specific type of peripheral neuropathies and discuss the need for any potential amendment to the product information and/or the risk management plan and make accordingly a proposal for changes to the relevant sections within this discussion.

- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.2. Signals follow-up and prioritisation

4.2.1. Pancreatin (NAP)

Applicant(s): various

PRAC Rapporteur: Dennis Lex

Scope: Signal of infection due to viral transmission

EPITT 20205 – Follow-up to October 2025

Background

For background information, see PRAC minutes October 2025.

The marketing authorisation holder (MAH) replied to the request for information on the signal of infection due to viral transmission and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance, literature including epidemiological studies, including the responses from the MAHs for products containing porcine pancreatin, PRAC agreed that there is sufficient evidence to support a potential association between pancreatic enzyme replacement treatment (PERT) and the risk of hepatitis E virus (HEV) infection, and that the product information should be updated to include a warning to address this risk.

Summary of recommendation(s)

- The MAH should submit to the national competent authorities (NCAs), within 60 days, a variation to update the product information[9]. In addition, the MAHs of the medicinal products within the scope of this recommendation should review their quality systems, including manufacturing processes and currently implemented control measures, with the aim of minimising the potential risk of viral transmission. MAHs should assess whether changes to existing processes and controls are warranted and submit the outcome of this assessment, together with a proposed action plan (including planned actions and timelines), to the relevant NCAs through an appropriate regulatory

[6] Triplett JD, Pinto MV, Young NP, Staff NP, Chinmay MS, Horowitz M, et al. GLP-1RA-Associated Diabetic Lumbosacral Radiculoplexus and Common Fibular Neuropathies: A Case-Control Evaluation. Neurology. 2025 Aug 12;105(3):e213916. doi:10.1212/WNL.0000000000213916 PubMed PMID: 40694751

[7] Fan, S., Qiu, Y., Liu, J., Zhu, T., Wang, C., Liu, D., Yan, L., & Ren, M. (2025). Effect of the glucagon-like peptide-1 receptor agonists on diabetic peripheral neuropathy: A meta-analysis. Journal of Neurochemistry, 169, e16242. https://doi.org/10.1111/jnc.16242

[8] García-Casares, N., González-González, G., de la Cruz-Cosme, C. et al. Effects of GLP-1 receptor agonists on neurological complications of diabetes. Rev Endocr Metab Disord 24, 655–672 (2023). https://doi.org/10.1007/s11154-023-09807-3

[9] Update of SmPC section 4.4. The package leaflet is updated accordingly.

procedure at the earliest opportunity and no later than three months following publication of the PRAC recommendation. Any subsequent changes to manufacturing processes or control measures should thereafter be submitted through applicable variation procedures.

4.3. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

PRAC provided advice to CHMP on the proposed RMPs for a number of products (identified by active substance below) that are under evaluation for initial marketing authorisation. Information on the PRAC advice will be available in the European Public Assessment Reports (EPARs) to be published at the end of the evaluation procedure.

Please refer to the CHMP pages for upcoming information (http://www.ema.europa.eu/Committees>CHMP>Agendas, minutes and highlights).

See also Annex I 15.1.

5.1.1. Arimoclomol (CAP MAA) - EMEA/H/C/006736, Orphan

Scope (pre D-180 phase): Treatment of Niemann-Pick disease type C (NPC) in patients aged 6 months and older in combination with miglustat

5.1.2. Cefepime / Zidebactam (CAP MAA) - EMEA/H/C/006799

Scope (pre D-90 phase, accelerated assessment): Treatment of a number of infections in adults

5.1.3. Icotrokinra hydrochloride (CAP MAA) - EMEA/H/C/006730

Scope (pre D-180 phase): Treatment of plaque psoriasis in adults and adolescents 12 years or older

5.1.4. Obicetrapib (CAP MAA) - EMEA/H/C/006516

Scope (pre D-180 phase): Treatment of primary hypercholesterolaemia or mixed dyslipidaemia

5.1.5. Obicetrapib / Ezetimibe (CAP MAA) - EMEA/H/C/006517

Scope (pre D-180 phase): Treatment of primary hypercholesterolaemia or mixed dyslipidaemia

5.1.6. Ranibizumab (CAP MAA) - EMEA/H/C/006527

Scope (pre D-180 phase): Treatment of neovascular (wet) age-related macular degeneration (AMD)

5.1.7. Senaparib (CAP MAA) - EMEA/H/C/006708

Scope (pre D-180 phase): Maintenance treatment of advanced epithelial high-grade ovarian, fallopian tube or primary peritoneal cancer

5.1.8. Sufentanil / Ketamine (CAP MAA) - EMEA/H/C/006395, PUMA

Scope (pre D-180 phase): Treatment of acute pain in children aged 1 to less than 18 years

5.1.9. Tafamidis (CAP MAA) - EMEA/H/C/006711

Scope (pre D-180 phase): Treatment of hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM)

5.1.10. Trilaciclib (CAP MAA) - EMEA/H/C/006709

Scope (pre D-180 phase): Prevention of chemotherapy-induced myelosuppression when administered prior to platinum/etoposide- or topotecan-containing regimens for extensive-stage small cell lung cancer (ES-SCLC)

5.2. Medicines in the post-authorisation phase – PRAC-led procedures

See also Annex I 15.2

5.2.1. Atazanavir – REYATAZ (CAP); Atazanavir / Cobicistat – EVOTAZ (CAP) – EMA/VR/0000288444

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of an updated RMP version 16 in order to propose the removal of the continued prospective monitoring via the Antiretroviral Pregnancy Registry (APR) as an additional pharmacovigilance activity.

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

PRAC is evaluating a type II variation procedure for Reyataz (atazanavir) and Evotaz (atazanavir/cobicistat) to update the RMPs to remove the continued prospective monitoring via the Antiretroviral Pregnancy Registry (APR) as an additional pharmacovigilance activity. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

S**ummary of advice**

- The RMP version 16.1 for Reyataz (atazanavir) and RMP version 9.2 for Evotaz (atazanavir/cobicistat) in the context of the variation under evaluation by PRAC and CHMP are considered acceptable.
- PRAC supported the removal of all safety concerns from the RMPs in line with GVP Module V Revision 2, with continued monitoring of these risks through PSURs. It also supported the removal of the prospective monitoring via the Antiretroviral Pregnancy Registry (APR) as an additional pharmacovigilance activity from the RMP.

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

See also Annex I 15.3

5.3.1. Glycopyrronium – SIALANAR (CAP) – EMA/X/0000287532

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Zane Neikena

Scope: Extension application to introduce a new pharmaceutical form associated with two new strengths (0.68 mg and 1.36 mg orodispersible tablets).

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

CHMP is evaluating a line extension for Sialanar, a centrally authorised product containing glycopyrronium, to introduce a new pharmaceutical form. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

Summary of advice

- The RMP for Sialanar (glycopyrronium) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 4.1 is submitted. PRAC considered that the MAH should update the list of safety concerns by renaming the important potential risk 'anticholinergic side effects due to dosing errors' to 'anticholinergic side effects due to dosing errors, including when switching between glycopyrronium products' and remove 'dosing errors when switching between glycopyrronium products' as missing information from the RMP. Regarding the pharmacovigilance plan, PRAC agreed that routine pharmacovigilance is sufficient to identify and characterise the risks of the medicinal product. Regarding risk minimisation measures, PRAC considered that the product information should contain sufficiently detailed recommendations for the risk minimisation measures to prevent overdosing and underdosing when switching between different Sialanar formulations. In addition, PRAC considered that the physician educational material that contains the prescriber checklist should be removed from the RMP and that the educational material for caregivers should be renamed as 'guide for risk minimisation for patient's caregiver' and be updated to address information also on Sialanar orodispersible tablets including the dose administration table. As a consequence, Annex II D. Conditions or restrictions with

regard to the safe and effective use of the medicinal product should be revised accordingly.

5.3.2. Obinutuzumab – GAZYVARO (CAP) – EMA/VR/0000327013

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

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

C.6.a: Extension of indication to include treatment of adult patients with active systemic lupus erythematosus (SLE) who are receiving standard therapy, for GAZYVARO, based on the results from study CA42750 (ALLEGORY); this is a Phase III, randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of obinutuzumab in patients with SLE treated with standard-of-care therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the SmPC with minor edits. Version 12 of the RMP has also been submitted.

C.4: Update of section 4.2 of the SmPC to introduce short duration infusion (SDI) as method of administration for SLE patients, supported by previously submitted data in patients with Follicular Lymphoma and by simulations conducted using an integrated population PK model to estimate exposures following administration as an SDI to SLE patients.

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

CHMP is evaluating an extension of the therapeutic indication for Gazyvaro, a centrally authorised product containing obinutuzumab. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

Summary of advice

- The RMP for Gazyvaro (obinutuzumab) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 12 is submitted.
- PRAC supported the inclusion of the long-term extension of the ALLEGORY study as a category 3 study in the RMP and considered that 'long-term safety in lupus nephritis patients' as missing information in the RMP should be rephrased to 'long term safety in SLE (including lupus nephritis)'.

6. Periodic safety update reports (PSURs)

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

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website

See also Annex I 16.1

6.1.1. Amikacin – ARIKAYCE LIPOSOMAL (CAP) – EMA/PSUR/0000321506

Applicant: Insmed Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010882/202509)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Arikayce liposomal, a centrally authorised medicine containing amikacin and issued a recommendation on its marketing authorisation(s).

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Arikayce liposomal (amikacin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include eye irritation (following accidental eye exposure to the aerosol), acute kidney injury, renal failure and blood creatinine increased as undesirable effects with a frequency 'not known'. In addition, the product information should be updated to include the risk of accidental exposure. Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAH should address results of the ongoing INS-16 (ENCORE) clinical trial and summarise cases of accidental/occupational exposure associated with medication errors. Furthermore, the MAH should closely monitor the following specific topics: drug resistance, laryngeal ulceration, peripheral neuropathy and tremor, and provide a cumulative review of cases associated with the preferred terms pneumonia lipoid and interstitial lung disease.

The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

6.1.2. Chikungunya vaccine (live) – IXCHIQ (CAP) – EMA/PSUR/0000327923

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011058/202511)

Background

PRAC discussed the preliminary assessment report of the PSUSA for Ixchiq, a centrally authorised medicine containing chikungunya vaccine (live). PRAC will adopt a PRAC recommendation at the June 2026 plenary meeting.

[10] Update of SmPC sections 4.8 and 6.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

6.1.3. Concizumab – ALHEMO (CAP) – EMA/PSUR/0000321510

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011105/202509)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Alhemo, a centrally authorised medicine containing concizumab and issued a recommendation on its marketing authorisation(s).

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Alhemo (concizumab) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- The MAH should address the possible need to update the additional risk minimization measures (aRMM) tools (i.e. remove the healthcare professional (HCP) guide and the patient guide) and to update the aRMM messages for thromboembolic events (i.e. elaborate the patient card as a consequence of the discontinuation of HCP guide and patient guide), within an upcoming regulatory procedure affecting the RMP, or at the latest 6 months after PRAC recommendation as a separate type II variation. In addition, PRAC did not find it warranted to include a follow-up questionnaire for 'thromboembolic events' in the RMP.

The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC. The frequency of submission of the subsequent PSURs should be changed from 6-monthly to early and the list of Union reference dates (EURD list) will be updated accordingly.

6.1.4. Tobramycin – VANTOBRA (CAP) – EMA/PSUR/0000321512

Applicant: Pari Pharma GmbH

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010370/202509)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Vantobra, a centrally authorised medicine containing tobramycin (nebuliser solution) and issued a recommendation on its marketing authorisation(s).

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Vantobra (tobramycin (nebuliser solution)) in the approved indication(s) remains unchanged.

- Nevertheless, the product information should be updated to amend the warning regarding nephrotoxicity and to include acute kidney injury (AKI) as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[11].
- In the next PSUR, the MAH should provide an update on the potential risk for systemic toxicity in patients treated with inhaled tobramycin after lung transplantation, providing a comparison between non-lung transplant patients and lung-transplant patients, particularly in cystic fibrosis patients.

The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC.

6.1.5. Trabectedin – YONDELIS (CAP) – EMA/PSUR/0000321523

Applicant: Pharma Mar S.A.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00003001/202509)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Yondelis, a centrally authorised medicine containing trabectedin and issued a recommendation on its marketing authorisation(s).

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Yondelis (trabectedin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include acute kidney injury as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAH should provide a cumulative review of cases of renal impairment and of renal failure, including a discussion on the possible mechanism as well as on the need to update the product information.

The next PSUR should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC.

6.2. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)

See Annex I 16.2

[11] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[12] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

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

See Annex I 16.3

6.4. Follow-up to PSUR/PSUSA procedures

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

See also Annex I 16.5

6.5.1. Sapropterin – KUVAN (CAP) – EMA/VR/0000301983

Applicant: Biomarin International Limited

PRAC Rapporteur: Eamon O Murchu

Scope: Update of section 4.6 of the SmPC in order to update pregnancy information based on a cumulative pregnancy data analysis, following the PRAC request in the PSUR assessment for PSUR/0000257835. In addition, the MAH took the opportunity to introduce a minor editorial change to the PI.

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit a variation to update the product information related to pregnancy based on a cumulative pregnancy data analysis. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

Summary of recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed to update to section 4.6 of the SmPC to reflect that the data available (including data from registry studies) are limited to conclude on malformative or foeto-neonatal toxicity. Additionally, existing text regarding uncontrolled maternal phenylalanine levels during pregnancy was revised to provide additional details on the associated high incidence of intellectual impairment, microcephaly, cardiac anomalies, growth restriction and facial dysmorphism in the offspring.

6.6. Expedited summary safety reviews[13]

None

[13] 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

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[14]

See also Annex I 17.1

7.1.1. Lecanemab – LEQEMBI (CAP) – EMA/PASS/0000267311

Applicant: Eisai GmbH

PRAC Rapporteur: Eva Jirsová

Scope: PASS protocol [107n]: Study BAN2401-G000-505; A prospective observational registry study to evaluate the use and safety of LEQEMBI in routine clinical practice (EEA)

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

In order to fulfil the obligation to conduct a PASS imposed in accordance with Article 107n(3) of Directive 2001/83/EC, the MAH submitted on 29.04.2025 a PASS protocol version 1.0 to the EMA for Leqembi (lecanemab). On 26th January 2026, protocol version 3.0 was submitted for review by PRAC.

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 3.0-in accordance with Article 107n of Directive 2001/83/EC, PRAC objected to the draft protocol for the above listed medicinal product(s), as the Committee considered that that the design of the study did not fulfil the study at this stage.
- PRAC therefore recommended that the MAH should further explore existing registry initiatives that include patients in the EU, with an aim to undertake this study leveraging on existing data sources. The MAH should demonstrate having performed a systematic and comprehensive search of all relevant EU registries and a sufficient feasibility assessment for each identified registry, including their ability to reliably and timely deliver the data required for the PASS. In addition, the MAH should provide a clear and realistic timeline for completing a thorough feasibility assessment of any potentially eligible registry with respect to their ability to deliver the data required for the PASS. In case feasibility assessments yield negative results across all identified registry initiatives, the next proposal should include clear, specific and operational commitments on data sharing and interoperability, sufficient to ensure the generation of PASS-relevant data.
- A revised PASS protocol should be resubmitted within 60 days. The PRAC review of the revised protocol will follow a 60-day procedure.

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

7.1.2. Obecabtagene autoleucel – AUCATZYL (CAP) – EMA/PASS/0000300590

Applicant: Autolus GmbH

PRAC Rapporteur: Karin Erneholm

Scope: PASS protocol [107n]: Prospective, international, non-interventional study to assess the short- and long-term safety and effectiveness of adult patients with relapsed or refractory B cell acute lymphoblastic leukemia receiving Aucatzyl treatment.

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

In order to fulfil the obligation to conduct a PASS imposed in accordance with Article 107n(3) of Directive 2001/83/EC, the MAH submitted on 11 September 2025 a PASS protocol version 1.3 to the EMA. A revised PASS protocol (version 1.4) together with responses to the RSI were submitted by the MAH on 23 February 2026 for review by PRAC.

Endorsement/Refusal of the protocol

- Based on the PRAC review of the PASS protocol version 1.4 and in accordance with Article 107n(2)(a) of Directive 2001/83/EC, PRAC considered that the study is non-interventional and the PASS protocol can be endorsed.

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[15]

See also Annex I 17.2

7.2.1. Garadacimab – ANDEMBRY (CAP) – EMA/PAM/0000267718

Applicant: CSL Behring GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Feasibility and protocol assessment of the Non-Interventional Post Authorisation Safety Study CSL312_5006 to assess the long-term safety in adults and adolescents.

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

As part of the RMP for Andembry (garadacimab), the MAH for was required to assess the long-term safety in adults and adolescents. The MAH submitted a protocol (version 1.0) and a feasibility assessment for the study, as well as responses to RSIs, which were assessed by the Rapporteur. PRAC was requested to provide advice to CHMP on the protocol submitted by the MAH.

Summary of advice

[15] 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

- PRAC considered that, in absence of a specific long-term safety concern, and considering the limitations of the research methods, the study may not significantly contribute to the characterization of long-term safety beyond routine pharmacovigilance.
- Therefore, PRAC considered that the PASS should be removed from the RMP and the safety concerns should be followed up by routine pharmacovigilance including PSURs. As a consequence, the MAH should update the RMP to align with the outcome of this procedure within 6 months of the finalisation of this procedure.

7.3. Results of PASS imposed in the marketing authorisation(s)[16]

None

7.4. Results of PASS imposed and non-imposed in the marketing authorisation(s)[17]

See Annex I 17.4

7.5. Interim results and other post-authorisation measures for imposed and non-imposed studies

See also Annex I 17.5

7.5.1. Etuvetidigene autotemcel – WASKYRA (CAP) – EMA/PAM/0000334844

Applicant: Fondazione Telethon Ets

PRAC Rapporteur: Jo Robays

Scope: Submission of an updated PASS protocol (version 3.0) for the imposed interventional Post-Approval Safety Study (PASS) WAS-TLT003-01, a Category 1- Required additional pharmacovigilance activity. The protocol is submitted within three months of the EC Decision as defined in the approved RMP (version 0.6)

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

The MAH submitted an updated PASS protocol (version 3.0) for the imposed interventional Post-Approval Safety Study (PASS) WAS-TLT003-01, a Category 1- Required additional pharmacovigilance activity, for review by PRAC.

Summary of advice

- PRAC concluded that a protocol resubmission is not required, as the recommended changes may be implemented via a protocol update without reassessment, provided they are implemented as requested in the assessment report. Additionally, the MAH should submit for assessment the statistical analysis plan of the study.

[16] In accordance with Article 107p-q of Directive 2001/83/EC
[17] 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

7.5.2. Niraparib / Abiraterone acetate – AKEEGA (CAP) – EMA/PAM/0000302057

Applicant: Janssen Cilag International

PRAC Rapporteur: Jan Neuhauser

Scope: Interim Study report for PCSONCA0485: Post authorization safety study to characterize the risk of second primary malignancies (SPM) including MDS/AML among metastatic prostate cancer patients exposed to AKEEGA.

Background

For background information on substance(s) and indication(s) of centrally authorised product(s) identified as 'CAP', see Human medicine European public assessment report (EPAR) on the EMA website.

The MAH had committed to perform a PASS according to the RMP. The first interim report of the study was submitted by the MAH and assessed by the Rapporteur for PRAC review.

Summary of advice

- Based on the PRAC Rapporteur's assessment and the responses provided by the MAH, PRAC agreed with the MAH's proposal to terminate the study. PRAC also concluded that routine pharmacovigilance activities are sufficient to further monitor the risks of myelodysplastic syndromes (MDS) and acute myeloid leukaemia (AML) and therefore agreed that these risks should be further monitored in PSURs. The MAH should remove the study from the RMP at the next regulatory opportunity.

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

8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2

8.3. Renewals of the marketing authorisation

See Annex I 18.3

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 minutes.

9.3. Others

None

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

None

11. Scientific advice procedures

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

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The Chair thanked Mari Thorn for her contribution as a member representing Sweden.

12.1.2. Vote by proxy

Georgia Gkegka (Greece) granted a proxy to Panagiotis Psaras (Cyprus) and Annalisa Capuano granted a proxy to Maria Teresa Herdeiro, covering the entire meeting.

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

12.4.1. PRAC strategic review and learning meeting (SRLM) under the Cyprus presidency of the European Union (EU) Council – Pafos, Cyprus, 12 – 13 May 2026 - update

PRAC lead: Panagiotis Psaras

PRAC was informed on the final agenda for the 'PRAC strategic review and learning meeting (SRLM)', to be held on 12-13 May 2026 in Pafos, Cyprus, under the Cypriotic presidency of the Council of the European Union (EU).

12.5. Cooperation with International Regulators

12.5.1. International Conference on Harmonisation (ICH) E23 guideline - update

PRAC lead: Carla Torre

The EMA Secretariat presented to PRAC an update on the progress of the drafting activities for the International Conference on Harmonisation (ICH) E23 guideline - Considerations for the Use of Real-World Evidence (RWE) to Inform Regulatory Decision Making with a focus on Effectiveness of Medicines. The EMA Secretariat also presented the next steps and the timeline for the guideline finalization. PRAC noted the information.

12.6. Contacts of 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) and technology forecast: April 2026 – December 2028

The EMA Secretariat presented to PRAC an overview of the forecast of the marketing authorisation applications pipeline for 2026-2028. PRAC noted the information.

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

In line with the criteria for plenary presentation of updates to the EURD List adopted by PRAC in December 2021, PRAC endorsed the draft revised EURD list, version *May 2026*, reflecting the PRAC's comments impacting on the data lock point (DLP) and PSUR submission frequencies of the substances/combinations. PRAC endorsed the newly allocated Rapporteurs for upcoming PSUSAs in accordance with the principles previously endorsed by PRAC (see PRAC minutes April 2013).

Post-meeting note: following the PRAC meeting of May 2026, the updated EURD list was adopted by CHMP and CMDh at their *May 2026* meetings and published on the EMA website, see: Home> Human Regulatory>Post-authorisation>Pharmacovigilance>Periodic safety update reports>> List of Union reference dates and frequency of submission of periodic safety update reports (PSURs)

12.11. Signal management

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

PRAC lead: Dennis Lex

The EMA Secretariat presented a summary of the meeting of the SMART Methods group that took place on 04 March 2026. PRAC noted the information.

12.12. Adverse drug reactions reporting and additional monitoring

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

PRAC was informed on the updates made to the list of products under additional monitoring.

Post-meeting note: The updated additional monitoring list was published on the EMA website, see: Home>Human Regulatory>Post-authorisation>Pharmacovigilance>Medicines under additional monitoring>List of medicines under additional monitoring

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. Study on the implementation of controlled access to and distribution of medicinal products in EU Member States (SC02/EMA/2020/46/TDA/L4.02) - regulatory follow-up

PRAC lead: Liana Martirosyan

The PRAC Sponsor presented the results the study "Implementation of controlled access to and distribution of medicinal products in European Union (CONTROL EU)" (EUPAS1000000313). This mixed-methods study was conducted under the remit of the PRAC Impact Strategy to investigate how EU level requirements for risk minimisation control tools for medicinal products are implemented in Member States, including enablers and barriers for successful regulatory and clinical practice implementation. In line with the process for regulatory follow-up on impact research, the PRAC Sponsors' critical appraisal of the results was discussed.

PRAC agreed that there was no need for regulatory follow-up or stakeholder communication at this point in time. The proposed recommendations to facilitate implementation of risk minimisation control tools will be further reviewed and prioritised to update existing regulatory guidance as appropriate.

12.21. Others

None

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[18]

As per the agreed criteria for new signal(s), PRAC adopted without further plenary discussion the recommendation of the Rapporteur to request MAH(s) to submit a cumulative review following standard timetables[19].

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

14.1.1. Dapagliflozin – EDISTRIDE (CAP); DAPAGLIFLOZIN VIATRIS (CAP); FORXIGA (CAP), NAP; dapagliflozin / metformin – EBYMECT (CAP), XIGDUO (CAP), NAP; dapagliflozin / saxagliptin – QTERN (CAP); dapagliflozin/sitagliptin (NAP)

Applicants: AstraZeneca AB (Ebymect, Edistride, Forxiga, Qtern, Xigduo), Viatris Limited (Dapagliflozin Viatris), various

PRAC Rapporteur: Mari Thorn

Scope: Signal of lichen sclerosus

EPITT 20259 – New signal

Lead Member State(s): SE

14.1.2. Ixekizumab - TALTZ (CAP)

Applicants: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Signal of Behcet's syndrome

EPITT 20269 – New signal

Lead Member State(s): DE

14.1.3. Semaglutide – OZEMPIC (CAP), RYBELSUS (CAP), WEGOVY (CAP), WEGOVY FLEX TOUCH (CAP), KAYSHILD (CAP); insulin icodec / semaglutide - KYINSU (CAP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Signal of gastrointestinal volvulus

EPITT 20260 – New signal

Lead Member State(s): SE

[18] 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

[19] Either MAH(s)'s submission within 60 days followed by a 60 day-timetable assessment or MAH's submission cumulative review within an ongoing or upcoming PSUR/PSUSA procedure (if the DLP is within 90 days), and no disagreement has been raised before the meeting

14.1.4. Tocilizumab – AVTOZMA (CAP); RoACTEMRA (CAP); TOCILIZUMAB STADA (CAP); TUYORY(CAP); TYENNE (CAP)

Applicants: Celltrion Healthcare Hungary Kft. (Avtozma), Fresenius Kabi Deutschland GmbH (Tyenne), Gedeon Richter (Tuyory), Roche Registration GmbH (RoActemra), STADA Arzneimittel AG (Tocilizumab STADA)

PRAC Rapporteur: Dirk Mentzer

Scope: Signal of cutaneous vasculitis

EPITT 20261 – New signal

Lead Member State(s): DE

14.2. Signals follow-up and prioritisation

None

14.3. Variation procedure(s) resulting from signal evaluation

None

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

As per the agreed criteria, PRAC endorsed without further plenary discussion the conclusions of the Rapporteur on the assessment of the RMP for the medicine(s) mentioned below under evaluation for initial marketing authorisation application. Information on the medicines containing the active substance(s) listed below will be made available following the CHMP opinion on their marketing authorisation(s).

15.1.1. Azacitidine (CAP MAA) - EMEA/H/C/006695

Scope (pre D-180 phase): Treatment of myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML)

15.1.2. Ranibizumab (CAP MAA) - EMEA/H/C/006926

Scope (pre 60phase): 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), visual impairment due to choroidal neovascularisation (CNV)

15.1.3. Ruxolitinib hemifumarate (CAP MAA) - EMEA/H/C/006618

Scope (pre D-180 phase): Treatment of myelofibrosis (MF), polycythaemia vera (PV) and Graft versus host disease (GvHD)

15.2. Medicines in the post-authorisation phase – PRAC-led procedures

As per the agreed criteria, PRAC endorsed without further plenary discussion the conclusions of the Rapporteur on the assessment of the variation procedure for the medicine(s) mentioned below.

15.2.1. Lecanemab – LEQEMBI (CAP) – EMA/VR/0000302769

Applicant: Eisai GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Submission of an updated RMP version 1.1 in order to propose an update to PASS study deadlines. In addition, the MAH has taken the opportunity to update Annex II accordingly.

15.2.2. Pegcetacoplan – ASPAVELI (CAP) – EMA/VR/0000333829

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of an updated RMP (version 5.1) in order to revise the patient number in the category 3 post-authorization safety study (PASS) Sobi.PEGCET-301 and the milestone date for the clinical study report for the Category 3 study APL2-307.

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

15.3.1. Abiraterone acetate – ABIRATERONE MYLAN (CAP); NAP – EMA/VR/0000291298

Applicants: Mylan Pharmaceuticals Limited, various

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped application comprising of 3 Extension of indication variations for ABIRATERONE MYLAN, as follows:

C.I.6: to update the currently approved indication for metastatic hormone sensitive prostate cancer (mHSPC) patients to also include non-high risk mHSPC

C.I.6: to include the treatment of newly diagnosed mHSPC in adult men in combination with androgen deprivation therapy (ADT) and docetaxel in patients who are fit for chemotherapy

C.I.6: to include the treatment of newly diagnosed high risk non-metastatic hormone sensitive prostate cancer (HSPC) in adult men in combination with ADT and radiotherapy

The variations are based on literature data. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.2 of the RMP has also been submitted.

15.3.2. Adalimumab – IMRALDI (CAP) – EMA/X/0000321285

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Karin Bolin

Scope: Extension application to add a new strength of 80 mg solution for injection in a single dose 0.8 ml pre-filled pen (PFP). This is a grouped line extension application including four quality variations

15.3.3. Alemtuzumab – LEMTRADA (CAP) – EMA/VR/0000335041

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: A grouped application consisting of:

C.4: Update of section 4.4 of the SmPC in order to add a new warning on vasculitis following request from Saudi Arabia and based on data from clinical studies and post-authorisation data sources. The RMP version 14.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI.

C.4: Update of section 5.1 in order to update information on paediatrics based on final results from study EFC13429 (LemKids) listed as a category 3 study in the RMP; this is a phase 3 multi-center, open-label, single-arm, before and after switch study to evaluate the efficacy, safety and tolerability of alemtuzumab in paediatric patients with relapsing remitting multiple sclerosis (RRMS) with disease activity on prior disease modifying therapy. The RMP version 14.0 has also been submitted.

15.3.4. Apixaban – ELIQUIS (CAP) – EMA/VR/0000327005

Applicant: Bristol-Myers Squibb Pfizer EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include neonates in the currently approved indication treatment of venous thromboembolism (VTE) and prevention of recurrent VTE in paediatric patients from birth to less than 18 years of age for ELIQUIS, based on final results from pivotal study CV185325. This is an open-label, multi-centre, randomized, active controlled trial to provide PK data and data on anti-Xa activity to support the extrapolation of efficacy to children, to evaluate safety and efficacy of apixaban in children (full term neonates to less than 18 years of age) who require anticoagulation for venous thromboembolism, and Study 2, modelling and simulation study to derive dosing of apixaban for use in neonates for treatment of venous thromboembolism; As a consequence, section 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 24.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the The Patient Card to mention Eliquis only once on the title page and refer to apixaban throughout the rest of the card.

15.3.5. Atidarsagene autotemcel – LIBMELDY (CAP) – EMA/VR/0000334917

Applicant: Orchard Therapeutics (Netherlands) B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: A grouped application consisting of:

C.12: Submission of the final report from study 201222 listed as a category 3 study in the RMP. This is a Phase I/II clinical trial of haematopoietic stem cell gene therapy for the treatment of metachromatic leukodystrophy (MLD).

C.12: Submission of the final report from study CUP 207394 listed as a category 3 study in the RMP. This is a gene therapy protocol using autologous haematopoietic stem cells for a patient with metachromatic leukodystrophy (MLD).

C.12: Submission of the final report from studies CUP 206258 and HE 205029 listed as category 3 studies in the RMP. These are Expanded Access Programs (EAP) for hematopoietic stem cell gene therapy OTL-200 in subjects with early-onset metachromatic leukodystrophy (MLD).

The RMP version 4.1 has also been submitted.

15.3.6. Belimumab – BENLYSTA (CAP) – EMA/VR/0000306408

Applicant: Glaxosmithkline (Ireland) Limited

PRAC Rapporteur: Karin Bolin

Scope: Submission of the final report from study analysis BEL116559 listed as a category 3 study in the RMP. This is a pooled analyses of elderly (aged ≥65 years) subpopulation treated in select belimumab clinical trials to evaluate the safety of belimumab treatment in elderly patients with systemic lupus erythematosus (SLE). The RMP version 47.0 has also been submitted.

15.3.7. Belzutifan – WELIREG (CAP); Pembrolizumab – KEYTRUDA (CAP) – EMA/VR/0000313634

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Dennis Lex

Scope: Worksharing variation to extend the indication for KEYTRUDA, in combination with belzutifan, and for WELIREG, in combination with pembrolizumab, for the adjuvant treatment of adult patients with clear cell renal cell carcinoma at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions, based on results from study MK-6482-022 (LITESPARK-022). This is a multicenter, double-blind, randomized phase 3 study to compare the efficacy and safety of belzutifan plus pembrolizumab versus placebo plus pembrolizumab, in the adjuvant treatment of clear cell renal cell carcinoma (ccRCC) post nephrectomy. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC for KEYTRUDA and sections 4.1, 4.2, 4.8 and 5.1 of the SmPC for WELIREG are updated. The Package Leaflet for WELIREG is updated in accordance. The RMP version 53.1 for KEYTRUDA and version 2.1 for WELIREG have also been submitted. In addition, the MAH took the opportunity to introduce minor formatting changes to the PI for KEYTRUDA and WELIREG.

15.3.8. Belzutifan – WELIREG (CAP) – EMA/VR/0000326853

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Dennis Lex

Scope: Extension of indication to include in combination with lenvatinib, treatment of adult patients with advanced clear cell renal cell carcinoma that progressed following a PD-1 or PD-L1 inhibitor for WELIREG, based on interim results from study P011V01MK6482 (LITESPARK-011); this is an open-label, randomized, Phase 3 study of belzutifan in combination with lenvatinib vs cabozantinib for treatment in participants with advanced renal cell carcinoma (RCC) who have progressed after prior anti-PD-1/L1 Therapy. 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 1.1 of the RMP has also been submitted.

15.3.9. Cabotegravir – VOCABRIA (CAP) – EMA/VR/0000332087

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Dennis Lex

Scope: Update of sections 4.4, 4.6 and 5.2 of the SmPC in order to update information on pregnancy based on interim results from study HPTN 084/084-01; this is phase 3 double blind safety and efficacy study of long-acting injectable cabotegravir compared to daily oral TDF/FTC for pre-exposure prophylaxis in HIV-uninfected women – Pregnancy Safety and PK Interim Analysis; the Package Leaflet is updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template and to make typographical edits.

15.3.10. Cabotegravir – APRETUDE (CAP) – EMA/VR/0000331993

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Dennis Lex

Scope: Update of sections 4.6 and 5.2 of the SmPC in order to update information and recommendations on pregnancy, based on interim results from the open label extension (OLE) phase of the Phase 3 study HPTN 084 (study 201739) on the use of cabotegravir (CAB) for HIV-1 pre-exposure prophylaxis (PrEP) during pregnancy. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce updates to the information on excipients in alignment with the excipient guideline and to introduce minor editorial and formatting changes to the PI.

15.3.11. Cetuximab – ERBITUX (CAP) – EMA/VR/0000326978

Applicant: Merck Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include in combination with encorafenib treatment of with metastatic colorectal cancer (mCRC) with a BRAF V600E mutation, who have received prior systemic therapy for ERBITUX, based on final results from study ARRAY-818-302 (BEACON-CRC); this is a randomized, open label, 3-arm Phase 3 design that investigated the BRAF inhibitor, encorafenib in combination with cetuximab with or without the mitogen-activated protein kinase (MEK) inhibitor, binimetinib, in patients with BRAF V600E-mutated mCRC whose disease has progressed after 1 or 2 prior regimens in the metastatic setting. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 21.1 of the RMP has also been submitted.

15.3.12. Cetuximab – ERBITUX (CAP) – EMA/VR/0000327014

Applicant: Merck Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include in combination with encorafenib and mFOLFOX6 treatment of metastatic colorectal cancer with a BRAF V600E mutation for ERBITUX, based on interim results from study C4221015 (BREAKWATER); this is an open-label, multicenter, 3-arm, randomized phase 3 study of EC alone or in combination with mFOLFOX6 versus standard-of-care chemotherapy in first-line participants with BRAF V600E-mutant mCR . 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 21.1 of the RMP has also been submitted.

15.3.13. COVID-19 mRNA vaccine – SPIKEVAX (CAP) – EMA/VR/0000335829

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC to update the posology recommendation for the 2 years through 4 years age group, based on final results from the study mRNA-1273-P306 listed as a category 3 study in the RMP; this is an Open-Label, Phase 3 Study to Evaluate the Safety and Immunogenicity of the mRNA Vaccines for SARS-CoV-2 Variants in Participants Aged 6 Months to <6 Years; the Package Leaflet is updated accordingly. The RMP version 14.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.14. Damoctocog alfa pegol – JIVI (CAP) – EMA/VR/0000326847

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

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

C.6.a: Extension of indication to include treatment and prophylaxis of bleeding in previously untreated patients ≥7 years of age with haemophilia A for JIVI, following the guideline for clinical investigation of recombinant and human plasma-derived factor VIII products (EMA/CHMP/BPWP/144552/2009 rev 2). As a consequence, sections 4.1, 4.2, 4.4 and 4.8 of the SmPC are updated. The Package Leaflet is updated accordingly.

C.4: Update of section 4.2 of the SmPC in order to update posology recommendations for patients 7 to <12 years of age, based on integrated analysis results from Part B of the Alfa-PROTECT study (21824) and PROTECT Kids extension study (15912). Alfa-PROTECT is a Phase 3, single-group treatment, open-label study to evaluate the safety of BAY 94-9027 infusions for prophylaxis and treatment of bleeding in previously treated children aged 7 to <12 years with severe hemophilia A. The PROTECT Kids study was a Phase 3, open-label, uncontrolled, multicenter study in previously treated children <12 years of age with severe hemophilia A (>50 prior EDs).

Version 4.1 of the RMP has also been submitted.

15.3.15. Deferasirox – EXJADE (CAP) – EMA/VR/0000333352

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of sections 4.3 and 4.5 of the SmPC in order to remove the existing contraindication for the combination of deferasirox with other iron chelator therapies, based on a cumulative review of the available data. The Package Leaflet is updated accordingly. The RMP version 24.0 has also been submitted.

15.3.16. Difelikefalin – KAPRUVIA (CAP) – EMA/VR/0000316094

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: A grouped application consisting of safety data from three studies of the oral difelikefalin formulation to support the safety of the intravenous difelikefalin formulation:

C.I.13: Submission of the final report from study CR845-310301 listed as a category 3 study in the RMP. This is a multicenter, randomized, double-blind, placebo-controlled 12-week study to evaluate the safety and efficacy of oral difelikefalin in advanced chronic kidney disease subjects with moderate-to-severe pruritus with an up to 52-week long-term extension. The RMP version 3.0 has also been submitted.

C.I.13: Submission of the final report from study CR845-310302 listed as a category 3 study in the RMP. This is a multicenter, randomized, double-blind, placebo-controlled 12-week study to evaluate the safety and efficacy of oral difelikefalin in advanced chronic kidney disease subjects with moderate-to-severe pruritus with an up to 52-week long-term extension

C.I.13: Submission of the final report from study CR845-310501 listed as a category 3 study in the RMP. This is a two-part, multicenter, randomized, double-blind study to evaluate the efficacy and safety of oral difelikefalin as adjunct therapy to a topical corticosteroid for moderate-to-severe pruritus in adult subjects with atopic dermatitis.

15.3.17. Dimethyl fumarate – TECFIDERA (CAP) – EMA/VR/0000320745

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Dennis Lex

Scope: Submission of the final study results from 109MS306 (CONNECT) Part 2 listed as a category 3 study in the RMP; this is a phase 3 efficacy and safety study of BG00012 in pediatric subjects with relapsing-remitting multiple sclerosis (RRMS). The primary objective of Part 2 is to evaluate the long-term safety of BG00012 in subjects who completed Week 96 in Part 1 of Study 109MS306. The secondary objective of Part 2 is to describe the long-term multiple sclerosis outcomes of BG00012 in subjects who completed Week 96 in Part 1 of Study 109MS306. The RMP version 17.1 has also been submitted.

15.3.18. Enfortumab vedotin – PADCEV (CAP) – EMA/VR/0000312495

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include PADCEV, in combination with pembrolizumab, for use as neoadjuvant treatment and continued as adjuvant treatment following radical cystectomy, is indicated for the treatment of adult patients with muscle-invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy, based on interim results from study EV-303/KN-905; this is a randomized phase 3 study evaluating cystectomy with perioperative pembrolizumab and cystectomy with perioperative enfortumab, vedotin and pembrolizumab versus cystectomy alone in participants who are cisplatin-ineligible or decline cisplatin with muscle-invasive bladder cancer. 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 5.0 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 bring the PI in line with the latest QRD template version 10.4.

15.3.19. Epcoritamab – TEPKINLY (CAP) – EMA/VR/0000311043

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Extension of indication to include in combination with rituximab and lenalidomide treatment of patients with relapsed/refractory follicular lymphoma (FL) for Tepkinly, based on interim results from study M20-638; this is a Phase 3, open-label study to evaluate safety and efficacy of epcoritamab in combination with rituximab and lenalidomide (R2) compared to R2 in subjects with relapsed or refractory follicular lymphoma (EPCORE FL-1). 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 3.2.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (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.

15.3.20. Filgotinib – JYSELECA (CAP) – EMA/VR/0000325892

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: Extension of indication to include treatment of axial spondyloarthritis in adult patients with active radiographic axial spondyloarthritis (r-axSpA) and with active non-radiographic axial spondyloarthritis (nr-axSpA) for JYSELECA, based on interim results from study LPG0634-CL-336 (OLINGUITO); this is a Phase 3 randomized, placebo-controlled, double-blind, parallel-group program to evaluate efficacy and safety of filgotinib in adult subjects with active axial spondyloarthritis which provide evidence of the efficacy and safety of filgotinib up to Week 52. 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 7.1 of the RMP has also been submitted.

15.3.21. Florbetapir (18F) – AMYVID (CAP) – EMA/VR/0000333287

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dennis Lex

Scope: Update of section 4.8 of the SmPC in order to revise the frequency category of ADRs and include additional adverse reaction terms related to injection site reactions based on a pooled safety analysis incorporating cumulative florbetapir (18F) exposure data from 26 979 subjects from 48 clinical trials; the Package Leaflet is updated accordingly. The RMP version 6.1 has also been submitted. In addition, the MAH took the opportunity update Annex II.D of the SmPC to align with proposed RMP changes.

15.3.22. Formoterol / Glycopyrronium bromide / Budesonide – RILTRAVA AEROSPHERE (CAP) – EMA/X/0000287672

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Extension application to introduce a new strength (5 µg / 14.4 µg / 160 µg Pressurised inhalation, suspension) associated with a new indication for the "maintenance treatment of asthma in patients 12 years of age and older who are not adequately controlled by a combination of a medium or high dose inhaled corticosteroid and a long-acting beta2-agonist". The RMP (version 3.1) is updated in accordance.

15.3.23. Formoterol / Glycopyrronium bromide / Budesonide – TRIXEO AEROSPHERE (CAP) – EMA/X/0000287664

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Extension application to introduce a new strength (5 µg / 14.4 µg / 160 µg Pressurised inhalation, suspension) associated with a new indication for the "maintenance treatment of asthma in patients 12 years of age and older who are not adequately controlled by a combination of a medium or high dose inhaled corticosteroid and a long-acting beta2-agonist". The RMP (version 3.1) is updated in accordance.

15.3.24. Glecaprevir / Pibrentasvir – MAVIRET (CAP) – EMA/VR/0000316551

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include treatment of Acute HCV for MAVIRET, based on final results from study M20-350; this is a multicenter, single-arm prospective study to evaluate safety and efficacy of GLE/PIB 8-week treatment in adults and adolescents with acute hepatitis C virus (HCV) infection. 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 10.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.25. Glofitamab – COLUMVI (CAP) – EMA/VR/0000327100

Applicant: Roche Registration GmbH

PRAC Rapporteur: Veronika Macurova

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add a new warning on 'haemophagocytic lymphohistiocytosis' and to add it to the list of adverse drug reactions (ADRs) with frequency not known, based on a drug safety report. The Package Leaflet is updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial and administrative changes to the PI.

15.3.26. Inclisiran – LEQVIO (CAP) – EMA/VR/0000293324

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouping of two Type II C.I.6 variations to support the extension of the LEQVIO indication to paediatric patients aged 12 to less than 18 years with heterozygous and homozygous familial hypercholesterolaemia, as follows:

C.I.6: Extension of indication to include the treatment of paediatric patients aged 12 to less than 18 years with heterozygous familial hypercholesterolaemia (HeFH) for LEQVIO based on the final results from study CKJX839C12301 (ORION-16). ORION-16 is a two part (double-blind inclisiran versus placebo [Year 1] followed by open-label inclisiran [Year 2]) randomized multicenter study to evaluate safety, tolerability, and efficacy of inclisiran in paediatric patients (12 to less than 18 years) with heterozygous familial hypercholesterolemia and elevated LDL-cholesterol.

C.I.6: Extension of indication to include the treatment of paediatric patients aged 12 to less than 18 years with homozygous familial hypercholesterolaemia (HoFH) for LEQVIO based on the final results from study CKJX839C12302 (ORION-13). ORION-13 is a two part (double-blind inclisiran versus placebo [Year 1] followed by open-label inclisiran [Year 2]) randomized multicenter study to evaluate safety, tolerability, and efficacy of inclisiran in paediatric patients (12 to less than 18 years) with homozygous familial hypercholesterolemia and elevated LDL-cholesterol.

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 4.0 of the RMP has also been submitted.

15.3.27. Ipilimumab – YERVOY (CAP); Nivolumab – OPDIVO (CAP) – EMA/VR/0000319172

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add 'Myocarditis-Myositis-Myasthenia Gravis Overlap Syndrome' to the list of adverse drug reactions (ADRs) with frequency 'Uncommon' based on postmarketing data and literature. The Package Leaflet is updated accordingly. The RMP version 46 and 52 respectively, had also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.

15.3.28. Lacosamide – LACOSAMIDE UCB (CAP); VIMPAT (CAP) – EMA/VR/0000321459

Applicant: UCB Pharma

PRAC Rapporteur: Karin Bolin

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update clinical information based on final results from study SP0968 and study EP0223. SP0968 was a phase 2/3, multicenter, open-label, randomized, active comparator study that evaluated the PK, efficacy, safety, and tolerability of lacosamide in neonatal study participants with repeated electroencephalographic neonatal seizures compared with an Active Comparator chosen based on standard of care per the local practice and treatment guidelines. EP0223 is a comparative study on long-term neurodevelopmental outcomes in neonates treated with lacosamide versus other antiseizure medications for neonatal seizures. The RMP version 18.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to implement corrections in some local languages in both Vimpat and Lacosamide UCB Product Information.

15.3.29. Octreotide – OCZYESA (CAP) – EMA/VR/0000333073

Applicant: Camurus AB

PRAC Rapporteur: Eamon O Murchu

Scope: Submission of the final report from study HS-19-647, listed as a category 3 study in the RMP. This is a Phase 3, open-label, single-arm, multi-center trial to assess the long-term safety of octreotide subcutaneous depot (CAM2029) in patients with acromegaly. The RMP version 1.1 has also been submitted.

15.3.30. Pegvaliase – PALYNZIQ (CAP) – EMA/VR/0000302032

Applicant: Biomarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

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

C.I.6: Extension of indication to include treatment of adolescent patients aged 12 to <16 years with phenylketonuria (PKU) for PALYNZIQ, based on interim results from study 165-306; this is a Phase 3 open label, randomized, controlled, 2-arm, multicenter study designed to evaluate the safety and efficacy of pegvaliase in adolescent participants 12 to <18 years old with PKU. 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. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI to include editorial changes and remove references to the route of administration of adrenaline (injection) to allow physicians to prescribe any approved adrenaline device.

C.I.4: Update of section 4.6 of the SmPC in order to update information on pregnancy based on a comprehensive assessment of all pregnancy and breastfeeding reports received from all sources.

The RMP version 5.0 has also been submitted.

15.3.31. Pembrolizumab – KEYTRUDA (CAP) – EMA/VR/0000316576

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: A grouped application consisting of:

C.I.6. Extension of indication for KEYTRUDA for subcutaneous use to include treatment of melanoma for adolescents aged 12 years and older based on an extrapolation approach from adults to adolescents using pharmacokinetics modelling and simulation. 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 52.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to implement some minor editorial and formatting changes in the PI.

C.I.6. Extension of indication for KEYTRUDA for subcutaneous use to include treatment of classical Hodgkin lymphoma for adolescents aged 12 years and older based on an extrapolation approach from adults to adolescents using pharmacokinetics modelling and simulation. 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.

15.3.32. Pembrolizumab – KEYTRUDA (CAP) – EMA/VR/0000312515

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include in combination with enfortumab vedotin, as neoadjuvant treatment and then continued after radical cystectomy as adjuvant treatment of adults with muscle invasive bladder cancer (MIBC) who are ineligible for cisplatin containing chemotherapy for KEYTRUDA, based on interim results from study KEYNOTE-905, an open label, randomised, interventional phase 3 study. As consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 51.1 of the RMP has also been submitted.

15.3.33. Ponatinib – ICLUSIG (CAP) – EMA/X/0000296489

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (5 mg hard capsule) grouped with an Extension of Indication to include treatment of paediatric patients aged 6 years and older with chronic phase chronic myeloid leukaemia (CP-CML) who are resistant or intolerant to at least one tyrosine kinase inhibitor for ICLUSIG, based on interim results from study INCB 84344-102 and a final results from early-terminated study Ponatinib-1501; the first is an ongoing open-label, single-arm, Phase 1/2 study evaluating the safety and efficacy of ponatinib MONOTHERAPY for the treatment of R/R leukemias, lymphomas, or solid tumors in pediatric participants. The second is a Phase 1/2, single-arm, open-label, multicenter study designed to evaluate the safety, tolerability, PK, and efficacy of ponatinib when administered IN COMBINATION WITH multiagent CHEMOTHERAPY in pediatric patients with Ph+ ALL, Ph+ MPAL, or Ph-like ALL who had a relapse, were resistant or intolerant to at least 1 prior BCR-ABL1 TKI therapy, or had the T315I mutation. As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.8, 5.1, 5.2, 6.1 and 6.5 of the SmPC are updated. Package Leaflet is updated accordingly. The RMP version 23.4 has also been submitted.

15.3.34. Rucaparib – RUBRACA (CAP) – EMA/VR/0000332297

Applicant: pharmaand GmbH

PRAC Rapporteur: Mari Thorn

Scope: Submission of the updated RMP version 9.0 in order to revise the originally anticipated overall survival (OS) maturity threshold for the ATHENA MONO study.

15.3.35. Sacituzumab govitecan – TRODELVY (CAP) – EMA/VR/0000312649

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication for treatment of adult patients with PD-L1-negative metastatic triple- negative breast cancer or PD-L1-positive metastatic triple-negative breast cancer previously treated with an anti-PD-(L)1 agent in the curative setting for Trodelvy, based on results from study GS-US-592-6238 (ASCENT-03), which is a phase 3 study of sacituzumab govitecan (IMMU-132) versus treatment of physician's choice (TPC) in Patients With Previously Untreated, Locally Advanced, Inoperable or Metastatic Triple-Negative Breast Cancer Whose Tumors Do Not Express PD-L1 or in Patients Previously Treated With Anti-PD-(L)1 Agents in the Early Setting Whose Tumors Do Express PD-L1. As a consequence, sections 4.1, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted

15.3.36. Secukinumab – COSENTYX (CAP) – EMA/VR/0000326984

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Extension of indication to include treatment of polymyalgia rheumatica in adults who have had an inadequate response to glucocorticoids or who experience a relapse during glucocorticoid taper for COSENTYX, based on the week 52 primary analysis results from study CAIN457C22301 as well as supportive safety data from the Phase 3 study CAIN457R12301 (GCAptAIN) in giant cell arteritis (GCA) patients. Study CAIN457C22301 is a randomized, parallel-group, double-blind, placebo-controlled, multicenter Phase 3 trial to evaluate efficacy and safety of secukinumab administered subcutaneously versus placebo, in combination with a glucocorticoid taper regimen, in patients with polymyalgia rheumatica (PMR). 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 13.0 of the RMP has also been submitted. In addition, the MAH is taking this opportunity to implement updates regarding polysorbate 80 in the PI following the guidance on excipients, and to introduce minor editorial changes to the PI.

15.3.37. Serplulimab – HETRONIFLY (CAP) – EMA/VR/0000290021

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include HETRONIFLY in combination with carboplatin and nab-paclitaxel is indicated for the first-line treatment of adult patients with unresectable, locally advanced or metastatic squamous non-small cell lung carcinoma based on final results from study HLX10-004-NSCLC303; this is a randomized, double-blind, multi-center, phase III pivotal study, was conducted to compare the clinical efficacy and safety of serplulimab combined with chemotherapy (carboplatin and nab-paclitaxel) versus placebo combined with chemotherapy (carboplatin and nab-paclitaxel). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP Version 1.3 has been submitted.

15.3.38. Somapacitan – SOGROYA (CAP) – EMA/VR/0000264734

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Dennis Lex

Scope: Grouped extension of indication application to include treatment of children born small for gestational age (SGA), Noonan syndrome (NS) and idiopathic short stature (ISS) for SOGROYA, based on interim results from the pivotal, confirmatory phase 3 study NN8640-4467 supported by the phase 3 study NN8640-4469 and the phase 2 study NN8640-4245. Study 4467 is a study comparing the effect and safety of once weekly dosing of somapacitan with daily Norditropin as well as evaluating long-term safety of somapacitan in a basket study design in children with short stature either born small for gestational age or with Turner syndrome, Noonan syndrome, or idiopathic short stature. Study 4469 is a study evaluating the safety and efficacy of once-weekly dosing of somapacitan in a basket study design in paediatric participants with short stature either born small for gestational age or with turner syndrome, Noonan syndrome or idiopathic short stature. Study 4245 is a dose-finding trial evaluating the effect and safety of once-weekly treatment of somapacitan compared to daily Norditropin in children with short stature born small for gestational age with no catch-up growth by 2 years of age or older. 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 4.0 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.4. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.39. Sotatercept – WINREVAIR (CAP) – EMA/VR/0000315667

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Update of sections 4.4, 4.8, and 5.1 of the SmPC in order to update efficacy and safety information based on the final results from the study MK-7962-005 (HYPERION). MK-7962-005 (HYPERION) is a Phase 3, randomized, double-blind, placebo-controlled study designed to evaluate the effect of sotatercept in participants who had received the diagnosis less than 1 year earlier, had an intermediate or high risk of death, and were receiving double or triple background therapy. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.40. Tirzepatide – MOUNJARO (CAP) – EMA/VR/0000310637

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, myocardial infarction, or stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease for MOUNJARO, based on final results from study I8F-MC-GPGN (SURPASS-CVOT). SURPASS-CVOT was a Phase 3, event-driven, multicentre, international, randomized, double-blind, active-comparator, parallel-group study to assess the effect of tirzepatide versus dulaglutide on major adverse cardiovascular events in participants with type 2 diabetes. As a consequence, sections 4.1, 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 minor editorial and formatting changes to the PI.

15.3.41. Trastuzumab – ZERCEPAC (CAP) – EMA/X/0000321364

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Dirk Mentzer

Scope: Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (600 mg) and a new route of administration (subcutaneous use).

15.3.42. Trastuzumab deruxtecan – ENHERTU (CAP) – EMA/VR/0000326482

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include treatment of adult patients with HER2-positive breast cancer (IHC3+ or ISH+) who have residual invasive disease after neoadjuvant HER2 targeted treatment for ENHERTU, based on interim results from study DS8201-A-U305 (DESTINY-Breast05); this is a phase 3, multicenter, randomized, open-label, active-controlled study of trastuzumab deruxtecan (T-DXd) versus trastuzumab emtansine (T-DM1) in subjects with high-risk HER2-positive primary breast cancer who have residual invasive disease in breast or axillary lymph nodes following neoadjuvant 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 10.2 of the RMP has also been submitted.

15.3.43. Upadacitinib – RINVOQ (CAP) – EMA/VR/0000312506

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Extension of indication to include the treatment of severe alopecia areata (AA) in adult and adolescents 12 years and older for RINVOQ, based on interim results from 2 pivotal, Phase 3 studies (M23-716 Study 1 and Study 2); those are randomized, double blind, placebo-controlled, multi-center studies of Upadacitinib evaluating the efficacy and safety of Upadacitinib 15 mg QD and 30 mg QD versus placebo for the treatment of severe

AA in subjects who are at least 12 years of age. 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 Annex II are updated in accordance. Version 18.0 of the RMP has also been submitted. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.44. Upadacitinib – RINVOQ (CAP) – EMA/VR/0000325958

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Extension of indication to include the treatment of non-segmental vitiligo in adults and adolescents 12 years and older who are candidates for systemic therapy, for RINVOQ, based on results from the two replicate Phase 3 studies M19-044: study 1 (R&D/25/1342) and study 2 (R&D/25/1343), as well as from integrated long-term safety data. Study 1 and study 2 are Phase 3, global, randomized, double-blind, placebo-controlled multi-center studies that evaluate the safety and efficacy of upadacitinib in adult and adolescent patients with non-segmental vitiligo. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC have been updated. The Package Leaflet has been updated in accordance. Version 19.0 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. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.45. Ustekinumab – USRENTY (CAP) – EMA/VR/0000325350

Applicant: Biosimilar Collaborations Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: C.2.a (Type IB): To update sections 4.1, 4.5, 4.8 and 5.2 of the SmPC to reflect the removal of the wording "or have medical contraindications to such therapies" from the therapeutic indication for Crohn's disease, the brief update of interaction data, the update of safety data, and the addition of CYP450 interaction information, following assessment of the same changes for the reference product Stelara;

Q.IV.2.a (Type II): To add 45 mg solution for injection in pre-filled pen (EU/1/25/1973/00x) and 90 mg solution for injection in pre-filled pen (EU/1/25/1973/00x);

Version 1.1 of RMP (dated 21-Jan-2026) for which data lock point is 31-Oct-2025 has been included.

15.3.46. Ustekinumab – STELARA (CAP) – EMA/VR/0000316205

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include treatment of ulcerative colitis in paediatric patients from the age of 2 years and older for STELARA, based on results from study CNTO1275PUC3001; this is a Phase 3 Study of the Efficacy, Safety and Pharmacokinetics of Ustekinumab as Open-label Intravenous Induction Treatment Followed by Randomized Double-blind Subcutaneous Ustekinumab Maintenance in Pediatric Participants (2 to <18 Years of Age) with Moderately to Severely Active Ulcerative Colitis. 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 32.2 of the RMP has also been submitted.

16. Annex I - Periodic safety update reports (PSURs)

Based on the assessment of the following PSURs, PRAC concluded that the benefit-risk balance of the medicine(s) mentioned below remains favourable in the approved indication(s) and adopted a recommendation to maintain the current terms of the marketing authorisation(s) together with the assessment report. As per the agreed criteria, the procedures listed below were finalised at the PRAC level without further plenary discussion.

The next PSURs should be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal, unless changes apply as stated in the outcome of the relevant PSUR/PSUSA procedure(s).

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

16.1.1. Alemtuzumab – LEMTRADA (CAP) – EMA/PSUR/0000321520

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00010055/202509)

16.1.2. Atogepant – AQUIPTA (CAP) – EMA/PSUR/0000321517

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00000100/202509)

16.1.3. Brolucizumab – BEOVU (CAP) – EMA/PSUR/0000321518

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010829/202510)

16.1.4. Chenodeoxycholic acid – CHENODEOXYCHOLIC ACID LEADIANT (CAP) – EMA/PSUR/0000321503

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010590/202510)

16.1.5. Dibotermin alfa – INDUCTOS (CAP) – EMA/PSUR/0000321514

Applicant: Medtronic Biopharma B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001034/202509)

16.1.6. Etrasimod – VELSIPITY (CAP) – EMA/PSUR/0000321519

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00000273/202510)

16.1.7. Futibatinib – LYTGOBI (CAP) – EMA/PSUR/0000321515

Applicant: Taiho Pharma Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00000068/202509)

16.1.8. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) – EMA/PSUR/0000321507

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010678/202510)

16.1.9. Histamine dihydrochloride – CEPLENE (CAP) – EMA/PSUR/0000321522

Applicant: Laboratoires Delbert

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00001610/202510)

16.1.10. Inavolisib – ITOVEBI (CAP) – EMA/PSUR/0000321509

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011164/202510)

16.1.11. Lasmiditan – RAYVOW (CAP) – EMA/PSUR/0000321508

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Jana Pecherova

Scope: Evaluation of a PSUSA procedure (PSUSA/00011011/202510)

16.1.12. Macitentan / Tadalafil – YUVANCI (CAP) – EMA/PSUR/0000321504

Applicant: Janssen Cilag International

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00011090/202510)

16.1.13. Maralixibat – LIVMARLI (CAP) – EMA/PSUR/0000321513

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011032/202509)

16.1.14. Marstacimab – HYMPAVZI (CAP) – EMA/PSUR/0000321516

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011101/202510)

16.1.15. Mirikizumab – OMVOH (CAP) – EMA/PSUR/0000321511

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000049/202509)

16.1.16. Nemolizumab – NEMLUVIO (CAP) – EMA/PSUR/0000321530

Applicant: Galderma International

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011111/202509)

16.1.17. Olipudase alfa – XENPOZYME (CAP) – EMA/PSUR/0000321501

Applicant: Sanofi B.V.

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00011003/202509)

16.1.18. Selumetinib – KOSELUGO (CAP) – EMA/PSUR/0000321505

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010936/202510)

16.1.19. Vilobelimab – GOHIBIC (CAP) – EMA/PSUR/0000321533

Applicant: InflaRx GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011103/202510)

16.2. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)

16.2.1. Choriogonadotropin alfa – OVITRELLE (CAP); NAP – EMA/PSUR/0000321521

Applicants: Merck Europe B.V., various

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000736/202509)

16.2.2. Midazolam – BUCCOLAM (CAP); NAP – EMA/PSUR/0000321529

Applicants: Neuraxpharm Pharmaceuticals S.L., various

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010118/202509)

16.2.3. Sodium oxybate – XYREM (CAP); NAP – EMA/PSUR/0000321502

Applicants: UCB Pharma, various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010612/202510)

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

16.3.1. Allergen for therapy: dermatophagoides pteronyssinus / dermatophagoides farina (oromucosal use, products authorised via mutually recognition procedure and decentralised procedure) – EMA/PSUR/0000321532

Applicants: various

PRAC Lead: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010582/202509)

16.3.2. Bivalirudin – EMA/PSUR/0000321527

Applicants: various

PRAC Lead: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00000421/202509)

16.3.3. Lactitol – EMA/PSUR/0000321534

Applicants: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00001819/202509)

16.3.4. Lisinopril, lisinopril / hydrochlorothiazide – EMA/PSUR/0000321531

Applicants: various

PRAC Lead: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010532/202509)

16.3.5. Progesterone – EMA/PSUR/0000321526

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00002540/202509)

16.3.6. Silver sulfadiazine – EMA/PSUR/0000321525

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00002702/202509)

16.3.7. Terizidone – EMA/PSUR/0000321528

Applicants: various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00002904/202509)

16.4. Follow-up to PSUR/PSUSA procedures

None

16.5. Variation procedure(s) resulting from PSUSA evaluation

None

16.6. Expedited summary safety reviews[20]

None

[20] 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

17. Annex I – Post-authorisation safety studies (PASS)

Based on the assessment of the following PASS protocol(s), result(s), interim result(s) or feasibility study(ies), and following endorsement of the comments received, PRAC adopted the conclusion of the Rapporteurs on their assessment for the medicines listed below without further plenary discussion.

17.1. Protocols of PASS imposed in the marketing authorisation(s)[21]

17.1.1. Volanesorsen – WAYLIVRA (CAP) – EMA/PASS/0000334506

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Dennis Lex

Scope: PASS amendment (PASS 107o): PASS and Product Registry to further characterise the safety and effectiveness of WAYLIVRA in patients with Familial Chylomicronaemia Syndrome (FCS) under real-world conditions

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[22]

17.2.1. Abaloparatide – ELADYNOS (CAP) – EMA/PAM/0000281538

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Karin Erneholm

Scope: Protocol amendment for Study EUPAS1000000613 (MEA 001: European non-interventional post-authorization safety study (PASS) to evaluate cardiovascular (CV) events in patients newly exposed to abaloparatide or teriparatide)

17.2.2. Tofacitinib – XELJANZ (CAP) – EMA/PAM/0000294280

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Xeljanz Submission of A3921321 study (RMP category 3 study; MEA) interim report & protocol amendment (version 8.0) "A Post-Authorisation Safety Study of the Utilisation and Prescribing Patterns of Xeljanz (tofacitinib) in the European Union Using Secondary Data Sources"

17.3. Results of PASS imposed in the marketing authorisation(s)[23]

None

[21] In accordance with Article 107n of Directive 2001/83/EC
[22] 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
[23] In accordance with Article 107p-q of Directive 2001/83/EC

17.4. Results of PASS non-imposed in the marketing authorisation(s)[24]

17.4.1. Conestat alfa – RUCONEST (CAP) – EMA/VR/0000326016

Applicant: Pharming Group N.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of the final report from study PHARM/EU/aRMM/01 listed as a category 3 study in the RMP. This is a non-imposed non-interventional PASS concerning additional risk minimization measures for Ruconest – European survey of educational materials. The RMP version 22.0 has also been submitted.

17.4.2. COVID-19 mRNA vaccine – COMIRNATY (CAP) – EMA/VR/0000332196

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the final report from study C4591009 listed as a category 3 study in the RMP. This is an observational PASS designed to assess safety events of interest (including myocarditis and pericarditis) among recipients of original monovalent Pfizer-BioNTech COVID-19 Vaccine, using data from administrative claims and electronic health records from data research partners participating in the Sentinel System.

17.4.3. Emicizumab – HEMLIBRA (CAP) – EMA/VR/0000302494

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final report from study MO40685 (PedNet) listed as a category 3 study in the RMP. This is a non-interventional, secondary data use post-authorization safety study (PASS) relying on data collected as part of the PedNet Registry. The RMP version 6.0 has also been submitted.

17.4.4. Enfortumab vedotin – PADCEV (CAP) – EMA/VR/0000333033

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final report from study ISN: 7465-PV-0002 listed as a category 3 study in the RMP. This is a non-interventional PASS to assess patients', or their caregivers', awareness and understanding of the content of the Padcev Patient Card (PC) related to the risk of skin reactions and reported behaviours to minimise the risk. The RMP version 5.2 has also been submitted.

17.4.5. Eslicarbazepine acetate – ZEBINIX (CAP) – EMA/VR/0000332409

Applicant: Bial Portela & Ca S.A.

[24] 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: Dennis Lex

Scope: Submission of the final report from the post authorisations safety study EURAP (BIA-2093-402) listed as a category 3 study in the RMP. This is an international, prospective observational registry designed to assess the risks associated with antiepileptic drug exposure during pregnancy. The updated RMP version 23.0 has also been submitted. Risk information has been updated based on clinical evidence, including clinical trials and post-marketing data, together with a comprehensive review of the published literature.

17.4.6. Linaclotide – CONSTELLA (CAP) – EMA/VR/0000281586

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Dennis Lex

Scope: Submission of the final report from study EVM-18888 (P21-481) listed as a category 3 study in the RMP. The study, titled "Linaclotide Safety Study for the Assessment of Diarrhoea Complications and Associated Risk Factors in Selected European Populations with IBS-C," is an observational safety study. It assesses the risk of severe complications of diarrhoea (SCD) during treatment with linaclotide, as well as other risk factors among patients with IBS-C in the UK, Sweden, and Spain. The RMP version 11.2 has also been submitted.

17.4.7. Ofatumumab – KESIMPTA (CAP) – EMA/VR/0000315689

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Update of section 4.6 'pregnancy' of the SmPC based on the final reports from Kesimpta Pregnancy Registry and the PRegnancy outcomes Intensive Monitoring (PRIM) study.

17.4.8. Ropeginterferon alfa-2b – BESREMI (CAP) – EMA/VR/0000332690

Applicant: Aop Orphan Pharmaceuticals GmbH

PRAC Rapporteur: Carla Torre

Scope: Submission of the final report from the post-authorisation safety study (PASS) EUPAS29462, listed as a category 3 study in the RMP. This is a multicenter, non-interventional, observational and non-imposed post-authorisation safety study of ropeginterferon alfa-2b in polycythaemia vera patients. The RMP version 4.0 has also been submitted.

17.4.9. Tacrolimus – ADVAGRAF (CAP); MODIGRAF (CAP); NAP – EMA/VR/0000315125

Applicants: Astellas Pharma Europe B.V., various

PRAC Rapporteur: Eamon O Murchu

Scope: Submission of the final report from noninterventional post-authorization safety study (NIPASS) listed as a category 3 study in the RMP. This is a feasibility assessment of conducting a NIPASS of outcomes associated with the use of tacrolimus around conception,

or during pregnancy or lactation using data from available secondary use data sources to replicate the Transplant Pregnancy Registry International (TPRI) study. The RMP version 6.0 has also been submitted.

17.5. Interim results and other post-authorisation measures for imposed and non-imposed studies

17.5.1. Abatacept – ORENCIA (CAP) – EMA/PAM/0000334018

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Interim study results for Study IM101240: Observational Registry of Abatacept in Patients with Juvenile Idiopathic Arthritis.

17.5.2. Abrocitinib – CIBINQO (CAP) – EMA/PAM/0000333269

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Petar Mas

Scope: Submission of the first progress report for the PASS B7451120, a prospective active surveillance study to monitor growth, development, and maturation among adolescents with atopic dermatitis exposed to abrocitinib.

17.5.3. Atogepant – AQUIPTA (CAP) – EMA/PAM/0000334196

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Submission of the third interim report for Study P22-392: Atogepant pregnancy exposure registry

17.5.4. Atogepant – AQUIPTA (CAP) – EMA/PAM/0000334182

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Third Interim report and Updated Protocol Submission - Study P22-419 Category 3 PASS: Observational study to assess pregnancy outcomes following exposure to atogepant

17.5.5. Diroximel fumarate – VUMERITY (CAP) – EMA/PAM/0000334226

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Dennis Lex

Scope: Third annual interim report for cat. 3 PASS 272MS401 (A prospective observational pregnancy exposure registry to characterise how DRF may affect pregnancy and infant outcomes).

17.5.6. Fenfluramine – FINTEPLA (CAP) – EMA/PAM/0000326084

Applicant: UCB Pharma

PRAC Rapporteur: Dennis Lex

Scope: P46 RWE1609 Final Clinical Study Report of non-interventional retrospective cohort study using US claims and fact-of-death to evaluate mortality rates and associated risk factors among patients diagnosed with Dravet Syndrome and Lennox-Gastaut Syndrome.

17.5.7. Fenfluramine – FINTEPLA (CAP) – EMA/PAM/0000327550

Applicant: UCB Pharma

PRAC Rapporteur: Dennis Lex

Scope: P46 Study RWE1608: non-interventional retrospective cohort analysis using US Komodo claims data to evaluate the impact of Fintepla initiation among LGS patients.

17.5.8. Fenfluramine – FINTEPLA (CAP) – EMA/PAM/0000323622

Applicant: UCB Pharma

PRAC Rapporteur: Dennis Lex

Scope: P46 EP0241 Final Clinical Study Report for non-interventional retrospective cohort study using national pharmacy database to evaluate the real-world use of fenfluramine (Fintepla) for Dravet syndrome, Lennox-Gastaut syndrome, and other epilepsies in the United States.

17.5.9. Inotersen – TEGSEDI (CAP) – EMA/PAM/0000326086

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Fourth annual report on A Prospective, Non-Interventional, Long-Term, Multinational Cohort Safety Study of Patients with Hereditary Transthyretin Amyloidosis with Polyneuropathy
(hATTR-PN) .

17.5.10. Iptacopan – FABHALTA (CAP) – EMA/PAM/0000331969

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Lina Seibokiene

Scope: PAM [MEA] - First Interim report of Post-authorization safety study of iptacopan in adult patients with paroxysmal nocturnal hemoglobinuria (PNH) using data from the non-interventional IPIG PNH Registry

17.5.11. Iptacopan – FABHALTA (CAP) – EMA/PAM/0000331978

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Lina Seibokiene

Scope: PAM [MEA] -2nd Interim report of safety and eGFR data from all patients with recurrent complement 3 glomerulopathy (C3G) enrolled in the C3G EAP/MAP

17.5.12. Lasmiditan – RAYVOW (CAP) – EMA/PAM/0000332938

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Jana Pecherova

Scope: Interim study results for Observational Cohort Study of Lasmiditan Exposure and Motor Vehicle Accidents in the United States

17.5.13. Naldemedine – RIZMOIC (CAP) – EMA/PAM/0000320323

Applicant: Shionogi B.V.

PRAC Rapporteur: Eamon O Murchu

Scope: 4th Annual Progress Report with interim report with study results for Naldemedine: An Observational Post-Authorisation Safety Study (PASS) of Patients with Chronic Opioid Use for Non-Cancer Pain and Cancer Pain who have Opioid-Induced Constipation (OIC)

17.5.14. Risdiplam – EVRYSDI (CAP) – EMA/PAM/0000310307

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: 4th annual progress report for Evrysdi non-interventional pregnancy surveillance Study BN42833

17.5.15. Rurioctocog alfa pegol – ADYNOVI (CAP) – EMA/PAM/0000326983

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Bianca Mulder

Scope: 5th Interim report of study PASS TAK-660-403: Evaluation of long-term safety of Adynovi/Adynovate (Antihaemophilic Factor [Recombinant] PEGylated, rurioctocog alfa pegol) in patients with haemophilia A

17.5.16. Ustekinumab – STELARA (CAP) – EMA/PAM/0000310166

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Second interim report for an Observational Post-authorization Safety Study To Describe The Safety Of Ustekinumab and Other Biologic Treatments in a Cohort of Patients With Ulcerative Colitis or Crohn's Disease Using Compulsory Swedish Nationwide Healthcare Registers and the Independent Swedish National Quality Register for Inflammatory Bowel Disease (SWIBREG; PCSIMM002807); former MEA 047.

17.6. New Scientific Advice

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

17.7. Ongoing Scientific Advice

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

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

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

18. Annex I – Renewals of the marketing authorisation, conditional renewals and annual reassessments

Based on the review of the available pharmacovigilance data for the medicine(s) listed below and the CHMP Rapporteur's assessment report, PRAC considered that either the renewal of the marketing authorisation procedure could be concluded - and supported the renewal of their marketing authorisations for an unlimited or additional period, as applicable - or no amendments to the specific obligations of the marketing authorisation under exceptional circumstances for the medicines listed below were recommended. As per the agreed criteria, the procedures were finalised at the PRAC level without further plenary discussion.

18.1. Annual reassessments of the marketing authorisation

18.1.1. Glucarpidase – VORAXAZE (CAP) – EMA/S/0000322329

Applicant: Serb

PRAC Rapporteur: Dennis Lex

Scope: Annual reassessment of the marketing authorisation

18.1.2. Pegzilarginase – LOARGYS (CAP) – EMA/S/0000326830

Applicant: Immedica Pharma AB

PRAC Rapporteur: Dennis Lex

Scope: Annual reassessment of the marketing authorisation

18.1.3. Susoctocog alfa – OBIZUR (CAP) – EMA/S/0000324538

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Annual reassessment of the marketing authorisation

18.1.4. Tabelecleucel – EBVALLO (CAP) – EMA/S/0000326533

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Avapritinib – AYVAKYT (CAP) – EMA/R/0000335342

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.2. Dorocubicel / Allogeneic umbilical cord-derived CD34- cells, non-expanded – ZEMCELPRO (CAP) – EMA/R/0000333327

Applicant: Cordex Biologics International Limited

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.2.3. Elafibranor – IQIRVO (CAP) – EMA/R/0000335590

Applicant: Ipsen Pharma

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

18.2.4. Epcoritamab – TEPKINLY (CAP) – EMA/R/0000334812

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Conditional renewal of the marketing authorisation

18.2.5. Larotrectinib – VITRAKVI (CAP) – EMA/R/0000335017

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

18.2.6. Odronextamab – ORDSPONO (CAP) – EMA/R/0000333139

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Veronika Macurova

Scope: Conditional renewal of the marketing authorisation

18.2.7. Tafasitamab – MINJUVI (CAP) – EMA/R/0000334308

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Adalimumab – LIBMYRIS (CAP) – EMA/R/0000326540

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Karin Bolin

Scope: 5-year renewal of the marketing authorisation

18.3.2. Adalimumab – HUKYNDRA (CAP) – EMA/R/0000326487

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Karin Bolin

Scope: 5-year renewal of the marketing authorisation

18.3.3. Diroximel fumarate – VUMERITY (CAP) – EMA/R/0000327345

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Dennis Lex

Scope: 5-year renewal of the marketing authorisation

18.3.4. Pegcetacoplan – ASPAVELI (CAP) – EMA/R/0000326756

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: 5-year renewal of the marketing authorisation

18.3.5. Pneumococcal polysaccharide conjugate vaccine (15 valent, adsorbed) – VAXNEUVANCE (CAP) – EMA/R/0000326976

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: 5-year renewal of the marketing authorisation

18.3.6. Ripretinib – QINLOCK (CAP) – EMA/R/0000326982

Applicant: Deciphera Pharmaceuticals (Netherlands) B.V.

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: 5-year renewal of the marketing authorisation

18.3.7. Rivaroxaban – RIVAROXABAN VIATRIS (CAP) – EMA/R/0000327079

Applicant: Viatris Limited

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.8. Sacituzumab govitecan – TRODELVY (CAP) – EMA/R/0000326788

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

18.3.9. Sugammadex – SUGAMMADEX MYLAN (CAP) – EMA/R/0000327067

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Terhi Lehtinen

Scope: 5-year renewal of the marketing authorisation

18.3.10. Zanubrutinib – BRUKINSA (CAP) – EMA/R/0000326587

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

19. Annex II – List of participants

including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the May 2026 PRAC meeting, which was held in-person.

An asterisk (*) after the role, in the second column, signals that the member/alternate attended remotely. Additional experts participated in (part of) the meeting, either in person or remotely.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Ulla Wändel Liminga	Chair	Sweden	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Jan Neuhauser	Member*	Austria	No interests declared	
Sonja Radowan	Alternate*	Austria	No interests declared	
Jean-Michel Dogné	Member	Belgium	No restrictions applicable to this meeting	
Jo Robays	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva	Member*	Bulgaria	No interests declared	
Stanislav Stoilov	Alternate	Bulgaria	No interests declared	
Petar Mas	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi	Alternate*	Croatia	No interests declared	
Panagiotis Psaras	Member	Cyprus	No interests declared	
Elena Kaisis	Alternate*	Cyprus	No interests declared	
Eva Jirsová	Member	Czechia	No interests declared	
Veronika Macurova	Alternate	Czechia	No interests declared	
Marie Louise Schougaard Christiansen	Member	Denmark	No interests declared	
Karin Erneholm	Alternate*	Denmark	No interests declared	
Maia Uusküla	Member	Estonia	No interests declared	
Terhi Lehtinen	Member	Finland	No interests declared	
Kimmo Jaakkola	Alternate*	Finland	No interests declared	
Tiphaine Vaillant	Member	France	No interests declared	
Zoubida Amimour	Alternate	France	No participation in	5.2.1. EMA/VR/0000288444

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			discussion, final deliberations and voting on:	15.3.4. EMA/VR/0000327005 15.3.27. EMA/VR/0000319172 17.5.1. EMA/PAM/0000334018
Dennis Lex	Member	Germany	No interests declared	
Dirk Mentzer	Alternate	Germany	No interests declared	
Georgia Gkegka	Member*	Greece	No interests declared	
Maria Poulianiti	Alternate*	Greece	No participation in discussion, final deliberations and voting on:	4.1.1. Alprazolam (NAP); amitriptyline hydrochloride / medazepam (NAP); amitriptyline / chlordiazepoxide (NAP); bromazepam (NAP); bromazepam / propantheline bromide (NAP); brotizolam (NAP); chlordiazepoxide (NAP); chlordiazepoxide / clidinium bromide (NAP); cinolazepam (NAP); clidinium bromide / diazepam (NAP); clobazam (NAP); cyclobarbital calcium / diazepam (NAP);clonazepam (NAP); clorazepate (NAP); clotiazepam (NAP); cloxazolam

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				(NAP); delorazepam (NAP); diazepam (NAP); diazepam / gamma-amino-beta-hydroxybutyric acid (NAP); diazepam / isopropamide iodide (NAP); diazepam / octatropine methylbromide (NAP); diazepam / otilonium bromide (NAP); diazepam / sulpiride (NAP); diazepam / sulpiride / pyridoxine hydrochloride (NAP); estazolam (NAP); ethyl loflazepate (NAP); etizolam (NAP); flunitrazepam (NAP); flurazepam (NAP); ketazolam (NAP); loprazolam (NAP); lorazepam (NAP); lormetazepam (NAP); medazepam (NAP); mexazolam (NAP); midazolam - BUCCOLAM (CAP), NAP; nitrazepam (NAP); nordazepam (NAP); oxazepam (NAP); pinazepam (NAP); prazepam (NAP); remimazolam – BYFAVO (CAP),

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				NAP; temazepam (NAP); tofisopam (NAP); triazolam (NAP); trimebutine maleate / medazepam (NAP) 14.1.1. Dapagliflozin – EDISTRIDE (CAP); DAPAGLIFLOZIN VIATRIS (CAP); FORXIGA (CAP), NAP; dapagliflozin / metformin – EBYMECT (CAP), XIGDUO (CAP), NAP; dapagliflozin / , saxagliptin – QTERN (CAP); dapagliflozin/sitagliptin (NAP)
Julia Pallos	Member	Hungary	No participation in discussion, final deliberations and voting on:	5.2.1. EMA/VR/0000288444 5.3.4. EMA/VR/0000327005 5.3.28. EMA/VR/0000319172 7.5.1. EMA/PAM/0000334018
Melinda Palfi	Alternate*	Hungary	No interests declared	
Guðrún Stefánsdóttir	Member	Iceland	No restrictions applicable to this meeting	
Rhea Fitzgerald	Member	Ireland	No interests declared	
Eamon O Murchu	Alternate	Ireland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Amelia Cupelli	Member	Italy	No interests declared	
Zane Neikena	Member	Latvia	No interests declared	
Diana Litenboka	Alternate*	Latvia	No interests declared	
Rugile Pilviniene	Member	Lithuania	No restrictions applicable to this meeting	
Lina Seibokiene	Alternate	Lithuania	No interests declared	
Anne-Cecile Vuillemin	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No restrictions applicable to this meeting	
Liana Martirosyan	Member	Netherlands	No interests declared	
Bianca Mulder	Alternate	Netherlands	No restrictions applicable to this meeting	
David Olsen	Member	Norway	No participation in discussion, final deliberations and voting on:	15.3.14. EMA/VR/0000326847 18.2.5. EMA/R/0000335017
Pernille Harg	Alternate	Norway	No interests declared	
Katarzyna Ziolkowska	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins	Member	Portugal	No interests declared	
Carla Torre	Alternate	Portugal	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Roxana Dondera	Member	Romania	No interests declared	
Roxana Stefania Udrescu	Alternate*	Romania	No interests declared	
Miroslava Gocova	Member	Slovakia	No interests declared	
Jana Pecherova	Alternate	Slovakia	No interests declared	
Polona Golmajer	Member	Slovenia	No interests declared	
Maria del Pilar Rayon	Member	Spain	No interests declared	
Maria Martinez Gonzalez	Alternate	Spain	No interests declared	
Mari Thorn	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin	Alternate*	Sweden	No restrictions applicable to this meeting	
Annalisa Capuano	Member*	Independent scientific expert	No restrictions applicable to this meeting	
Milou-Daniel Drici	Member	Independent scientific expert	No restrictions applicable to this meeting	
Maria Teresa Herdeiro	Member	Independent scientific expert	No restrictions applicable to this meeting	
Patricia McGettigan	Member	Independent scientific expert	No restrictions applicable to this meeting	
Hedvig Marie Egeland Nordeng	Member	Independent scientific expert	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Anette Kirstine Stark	Member	Independent scientific expert	No restrictions applicable to this meeting	
Roberto Frontini	Member	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	14.1.1. Dapagliflozin – EDISTRIDE (CAP); DAPAGLIFLOZIN VIATRIS (CAP); FORXIGA (CAP), NAP; dapagliflozin / metformin – EBYMECT (CAP), XIGDUO (CAP), NAP; dapagliflozin / saxagliptin – QTERN (CAP); dapagliflozin/sitagliptin (NAP)
Martin Votava	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Yiannoula Koulla	Member*	Patients' Organisation Representative	No interests declared	
Michal Rataj	Alternate	Patients' Organisation Representative	No interests declared	
Els Beghein	Expert	Belgium	No interests declared	
Laurence de Fays	Expert	Belgium	No interests declared	
Marta Romano	Expert	Belgium	No restrictions applicable to this meeting	
Martine Sabbe	Expert	Belgium	No interests declared	
Chloé Wyndham-Thomas	Expert	Belgium	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Jana Kopecka	Expert	Czech Republic	No interests declared	
Jana Sipkova	Expert	Czech Republic	No interests declared	
Michaela Skorepova	Expert	Czech Republic	No interests declared	
Cecilie Louise Pedersen	Expert	Denmark	No participation in discussion, final deliberations and voting on:	15.3.38. EMA/VR/0000264734 6.1.3. EMA/PSUR/0000321510
Moritz Sander	Expert	Denmark	No restrictions applicable to this meeting	
Ummahan Cakin Vural	Expert	Denmark	No restrictions applicable to this meeting	
Thomas Berbain	Expert	France	No interests declared	
Cecile Choquet	Expert	France	No interests declared	
Marion Perrin	Expert	France	No interests declared	
Youssef Shaim	Expert	France	No restrictions applicable to this meeting	
Dario Ortiz	Expert	Germany	No interests declared	
Christopher Schulze	Expert	Germany	No interests declared	
Laura Zein	Expert	Germany	No interests declared	
Kevin Keohane	Expert	Ireland	No interests declared	
Ruth Kieran	Expert	Ireland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Grainne Kirwan	Expert	Ireland	No restrictions applicable to this meeting	
Melanie Murphy	Expert	Ireland	No restrictions applicable to this meeting	
Bernice Aronsson	Expert	Sweden	No interests declared	
Helena Back	Expert	Sweden	No interests declared	
Charlotte Backman	Expert	Sweden	No interests declared	
Annie George Chandy	Expert	Sweden	No interests declared	
Henrik Dahllöf	Expert	Sweden	No interests declared	
Charlotta Ekstrand	Expert	Sweden	No interests declared	
Rolf Gedeborg	Expert	Sweden	No restrictions applicable to this meeting	
Jenny Jönsson	Expert	Sweden	No restrictions applicable to this meeting	
Matti Karvanen	Expert	Sweden	No restrictions applicable to this meeting	
Emilia Lekholm	Expert	Sweden	No participation in discussion, final deliberations and voting on:	16.1.16. EMA/PSUR/0000 321530
Elin Magnusdottir	Expert	Sweden	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Muzaffer Özalp	Expert	Sweden	No interests declared	
Anna Schölin	Expert	Sweden	No interests declared	
Charlotte Söderberg Nyhem	Expert	Sweden	No interests declared	
Jonas Tallkvist	Expert	Sweden	No interests declared	
A representative from the European Commission attended the meeting				
Observers from Health Canada (Canada) attended the meeting.				
Meeting run with support from relevant EMA staff				

Experts were evaluated against the agenda topics or activities they participated in.

20. Annex III - List of acronyms and abbreviations

For a list of acronyms and abbreviations used in the PRAC minutes, see:

List of abbreviations used in EMA human medicines scientific committees and CMDh documents, and in relation to EMA's regulatory activities

21. Explanatory notes

The Notes give a brief explanation of relevant minute's items and should be read in conjunction with the minutes.

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

(Items 2 and 3 of the PRAC minutes)

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, 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 minutes)

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 minutes)

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 minutes)

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 minutes)

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 minutes)

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

Article 58 of Regulation (EC) No 726/2004 (EU-M4all)

Article 58 (EU-M4all) procedure 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).

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