10 February 2026
EMA/PRAC/21905/2026
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 24-27 November 2025

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 Chair opened the 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 Chair welcomed the new member(s) and alternate(s) and thanked the departing members/alternates 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 24-27 November 2025

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 27-30 October 2025

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 27-30 October 2025 were published on the EMA website on 18 December 2025 (EMA/PRAC/375420/2025).

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

3.2.1. Levamisole hydrochloride (NAP) – EMA/REF/0000293746

Applicants: various

PRAC Rapporteur: Roxana Dondera, PRAC Co-rapporteur: Barbara Kovacic Bytyqi

Scope: Review of the benefit-risk balance following notification by Romania of a referral under Article 31 of Directive 2001/83/EC, based on pharmacovigilance data

Background

A referral procedure under Article 31 of Directive 2001/83/EC is ongoing for levamisole-containing medicines. For further background, see PRAC minutes September 2025.

Summary of recommendation(s)/conclusions

- PRAC adopted a list of questions to be addressed by the Scientific Advisory Group (SAG) on vaccines and therapies for infectious diseases, as well as a list of outstanding issues (LoOI) for the MAHs, together with a revised timetable for the procedure. For further details, see Levamisole-containing medicinal products - referral | European Medicines Agency (EMA).

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

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

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. Axicabtagene ciloleucel – YESCARTA (CAP)

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Karin Erneholm

Scope: Signal of increased risk of brain oedema in primary mediastinal large B-cell lymphoma (PMBCL) patients

EPITT 20224 – New signal

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 increased risk of brain oedema in PMBCL patients was identified by EMA, based on information received from the MAH's safety database and other databases and registries. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from the MAH's safety database and other databases and registries, PRAC agreed that further evaluation on the signal of increased risk of brain oedema in PMBCL patients is warranted and that the review should be extended to include both CAR-T cell therapies approved for this indication.

Summary of recommendation(s)

- The MAHs for Yescarta (axicabtagene ciloleucel) and Breyanzi (lisocabtagene maraleucel) should submit to EMA, by 5 February 2026, a cumulative review of the signal of brain oedema in PMBCL patients, and discuss a proposal for amending the product information and/or additional RMMs (i.e. the HCP educational materials), and/or a direct healthcare professional communication (DHPC) and a communication plan, as warranted.

[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

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

4.1.2. Venlafaxine (NAP)

Applicant(s): various

PRAC Rapporteur: Karin Bolin

Scope: Signal of cardiotoxicity

EPITT 20230 – New signal

Background

Venlafaxine is a serotonin-norepinephrine reuptake inhibitor (SNRI) indicated for treatment of depression, prevention of relapse and prevention of recurrence of depression, anxiety or generalized anxiety disorder (including long-term treatment), social anxiety disorder (including long-term treatment) and panic disorder (including long-term treatment).

During routine signal detection activities, a signal of cardiotoxicity was identified by the MAH Zentiva, based on a literature article[3]. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from case reports in EudraVigilance and the literature, PRAC agreed that further evaluation on the signal of cardiotoxicity is warranted. The EMA will additionally explore the possibility to conduct a study using real-world evidence to complement the assessment.

PRAC appointed Karin Bolin as Rapporteur for the signal.

Summary of recommendation(s)

- The MAH Viatris Limited for venlafaxine-containing medicinal products should submit to EMA, by 13 April 2026, a cumulative review of the signal, including an analysis of all case reports of cardiomyopathy and heart failure, and a proposal for amending the product information and/or the RMP, as warranted.
- 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. Desogestrel (NAP), etonogestrel (NAP)

Applicant(s): various

PRAC Rapporteur: Karin Bolin

Scope: Signal of meningioma

EPITT 20167 – Follow-up to May 2025

[3] Batusha Sopi B, Yonekawa K, Russmann S, et al. Cardiotoxicity Associated with Venlafaxine-Defining Features in a Series of Five Cases and a Call for Proactive Monitoring. J Clin Med. 2025 Apr 18;14(8):2792

Background

For background information, see PRAC minutes May 2025.

The MAH replied to the request for information on the signal of meningioma and the responses were assessed by the Rapporteur.

Discussion

Having considered the results of the study by *Roland et al, 2025*[4] as well as a plausible mechanism, a causal association between desogestrel and meningioma is considered possible. However, further analysis is needed before a final conclusion can be made by PRAC.

Summary of recommendation(s)

- The study authors of *Roland et al, 2025* are requested to submit to EMA, within 90 days, responses to a list of questions: perform a sensitivity analysis and clarify some data and statistical analyses included in the supplement, as well as discuss on potential inconsistencies which may impede the validity of the study results.
- A 60-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.2.2. Valproate (NAP) and related substances[5]

Applicant(s): various

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of neurodevelopmental disorders with paternal exposure

EPITT 20191 – Follow-up to July 2025

Background

For background information, see PRAC minutes July 2025.

The MAH Sanofi replied to the request for information on the signal of neurodevelopmental disorders with paternal exposure and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence from the epidemiological studies and the responses submitted by the MAH Sanofi, PRAC agreed to have an additional request for supplementary information to the MAH before concluding on this signal. In addition, PRAC will address a list of questions to the *Botton et al, 2025*[6] study authors.

Summary of recommendation(s)

- The MAH Sanofi as the innovator of valproate should submit to EMA, by 11 March 2026, a detailed discussion of the results of the studies by *Botton et al, 2025* and by *Olstad et*

[4] Roland N, Kolla E, Baricault B, et al. Oral contraceptives with progestogens desogestrel or levonorgestrel and risk of intracranial meningioma: national case-control study. BMJ. 2025 Jun 11;389:e083981. doi: 10.1136/bmj-2024-083981. PMID: 40500141; PMCID: PMC12153057.
[5] Valproic acid, sodium valproate, valproate semisodium, valpromide
[6] Botton J, Rios P, Drouin J, et al. R. Paternal exposure to valproate during spermatogenesis and risk of neurodevelopmental disorders in children: national study based on the French EPI-MÈRES Register. EPI-PHARE (ANSM-Cnam). Saint-Denis, 6 November 2025

al, 2025[7] and any other relevant literature or non-clinical data, as well as a discussion for amending the product information and/or the additional RMMs in view of the overall available evidence, as warranted.

- The study authors of *Botton et al, 2025* study are requested to submit to EMA, by 11 March 2026, responses to a list of questions to clarify parts of the performed analyses.
- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

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/See also Annex I 15.1. / None

5.1.1. Acoziborole - (Art 58[8] MAA) - EMEA/H/W/006686

Scope (pre D-120 phase, accelerated assessment): Treatment of first and second-stage human African trypanosomiases (HAT) due to Trypanosoma brucei gambiense

5.1.2. Aficamten - (CAP MAA) - EMEA/H/C/006228

Scope (pre D-210 phase): Treatment of symptomatic obstructive hypertrophic cardiomyopathy (oHCM) in adult patients

5.1.3. Copper (^{64}Cu) oxodotreotide - (CAP MAA) - EMEA/H/C/006608, Orphan

Applicant: Cis Bio International

Scope (pre D-180 phase): Positron emission tomography (PET) for localization of somatostatin receptor positive neuroendocrine neoplasms (NENs).

5.1.4. Influenza and COVID-19 vaccine - (CAP MAA) - EMEA/H/C/006472

Scope (pre D-180 phase): Immunisation for the prevention of diseases associated with

[7] Olstad EW, Nordeng HME, Bjørk MH, Selmer K, Gervin K. Paternal valproate use and impact of shared genetic susceptibility on child neurodevelopment. Sci Rep. 2025 Nov 7;15(1):39033

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

seasonal influenza viruses and SARS-CoV-2

5.1.5. Levodopa / Carbidopa - (CAP MAA) - EMEA/H/C/006429

Scope (pre D-180 phase): Treatment of motor fluctuations in patients with Parkinson's disease

5.1.6. Mavorixafor - (CAP MAA) - EMEA/H/C/006496, Orphan

Applicant: X4 Pharmaceuticals (Austria) GmbH

Scope (pre D-180 phase): Treatment of WHIM syndrome

5.1.7. Nadofaragene firadenovec - (CAP MAA) - EMEA/H/C/005856

ATMPScope (pre D-180 phase): Treatment of adult patients with high-grade (HG), Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC).

5.1.8. Paltusotine - (CAP MAA) - EMEA/H/C/006636, Orphan

Applicant: Crinetics Pharmaceuticals Europe GmbH

Scope (pre D-180 phase): Maintenance treatment in adult patients with acromegaly

5.1.9. Pertuzumab - (CAP MAA) - EMEA/H/C/006583

Scope (pre D-180 phase): Treatment of breast cancer

5.1.10. Remibrutinib - (CAP MAA) - EMEA/H/C/006313

Scope (pre D-180 phase): Treatment of chronic spontaneous urticaria in patients with inadequate response to H1 antihistamine

5.1.11. Tovorafenib - (CAP MAA) - EMEA/H/C/006140, Orphan

Applicant: Ipsen Pharma

Scope (pre D-180 phase): Treatment of paediatric low-grade glioma (LGG)

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

See also Annex I 15.2.

5.2.1. Darbepoetin alfa – ARANESP (CAP) – EMA/VR/0000267359

Applicants: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 10.0 in order to remove the safety concern and risk minimisation measures regarding the 'Incorrect Use of the Pre-filled Pen Device Associated with Adverse Reactions, Including Underdose and Drug Dose Omission'. The Annex II is updated accordingly.

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 Aranesp, a centrally authorised medicine containing darbepoetin alfa, to update the RMP to reflect the update on the safety concern and risk minimisation measures regarding the 'Incorrect Use of the Pre-filled Pen Device Associated with Adverse Reactions, Including Underdose and Drug Dose Omission'. 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. For further background, see PRAC minutes July 2025 and PRAC minutes September 2025.

Summary of advice

- The RMP version 10.0 for Aranesp (darbepoetin alfa) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.
- PRAC agreed with the removal of the safety concern (important potential risk) and risk minimisation measures (demonstration device, associated training checklist, and poster-size IFU) regarding 'Incorrect Use of the Pre-filled Pen Device Associated with Adverse Reactions, Including Underdose and Drug Dose Omission' from the RMP and Annex II is updated accordingly.

5.2.2. Emtricitabine / Rilpivirine / Tenofovir disoproxil – EVIPLERA (CAP) – EMA/VR/0000287296

Applicants: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of two variations:

C.I.11.b: Submission of an updated RMP version 16.1 in order to propose the removal of 'Missing information' (Safety in pregnancy) and the removal of a Category 3 Additional Pharmacovigilance Activity (Antiretroviral Pregnancy Registry [APR]).

C.I.11.b: Submission of an updated RMP version 16.1 in order to propose the removal of Specific Adverse Reaction Follow-up Questionnaires related to bone and renal risks.

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 Eviplera, a centrally authorised medicine containing emtricitabine/rilpivirine/tenofovir disoproxil, to update the RMP to reflect the removal of the missing information 'safety in pregnancy' along with the APR study, and of the Specific follow-up questionnaires related to bone and renal risks. 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. For further background, see PRAC minutes October 2025[9].

Summary of advice

- The RMP version 17.0 for Eviplera (emtricitabine/rilpivirine/tenofovir disoproxil) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.
- PRAC agreed to remove the 'renal toxicity' and 'bone events due to proximal renal tubulopathy/loss of bone mineral density (BMD)' from the safety specification and the related follow-up questionnaires and data collection, as the risks are sufficiently characterized and have been integrated in the routine practice as these will be reported in future PSURs with focus on published studies. In addition, PRAC agreed to remove 'safety in pregnancy' as missing information from the RMP and, consequently, to delete the category 3 study APR. The committee also decided to remove 'safety in lactation' as a safety concern from the RMP, noting that any significant new information on breastfeeding will be included in future PSURs.

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

See Annex I 15.3.

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. Dostarlimab – JEMPERLI (CAP) – EMA/PSUR/0000288247

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010931/202504)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Jemperli, a centrally authorised medicine containing dostarlimab 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 Jemperli (dostarlimab) in the approved indication(s) remains unchanged.

[9] Held on 29 September – 02 October 2025

- Nevertheless, the product information should be updated to amend the warning regarding immune-related rash and to add Stevens-Johnson syndrome as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAH should present a comprehensive review of lichen disorders based on data from all relevant sources and discuss whether any amendments to the product information are warranted. In addition, the MAH should present a comprehensive review on the risk of immune-related adverse reactions and flares of the pre-existing autoimmune disease following dostarlimab/immune checkpoint inhibitors therapy and discuss the need for amendment to the product information. Finally, the MAH should provide a causality assessment of the association between dostarlimab and hemophagocytic lymphohistiocytosis (HLH) and discuss 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.

6.1.2. Fezolinetant – VEOZA (CAP) – EMA/PSUR/0000288230

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000231/202505)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Veoza, a centrally authorised medicine containing fezolinetant 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 Veoza (fezolinetant) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to remove information about incidence rates of alanine aminotransferase (ALT)/aspartate aminotransferase (AST) elevations calculated from pooled data of clinical trials from the description of selected adverse reaction. Therefore, the current terms of the marketing authorisation(s) should be varied[11].
- In the next PSUR, the MAH should present interval and cumulative data from clinical trials, post-marketing cases and literature concerning the risk of drug-induced liver injury (DILI) and discuss in this context whether the current product information on the recommended time points for liver function testing during treatment with fezolinetant remains sufficient to further minimise the risk of DILI, as warranted.

[10] 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
[11] Update of SmPC section 4.8. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

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.

6.1.3. Loncastuximab tesirine – ZYNLONTA (CAP) – EMA/PSUR/0000288255

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00011027/202504)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Zynlonta, a centrally authorised medicine containing loncastuximab tesirine 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 Zynlonta (loncastuximab tesirine) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding capillary leak syndrome and to add cutaneous collagenous vasculopathy as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAH should monitor cases suggestive of capillary leak syndrome, acute kidney injury and of tumour lysis syndrome.

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.

6.1.4. Mannitol – BRONCHITOL (CAP) – EMA/PSUR/0000288227

Applicant: Pharmaxis Europe Limited

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00009226/202504)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Bronchitol, a centrally authorised medicine containing mannitol 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 Bronchitol (mannitol) in the approved indication(s) remains unchanged.

[12] 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

- Nevertheless, the product information should be updated to remove the additional risk minimisation measures regarding the risk of bronchospasm, haemoptysis and cough related sequelae from Annex II-D 'Conditions or restrictions with regard to the safe and effective use of medicinal product'. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- At the next regulatory opportunity or at the latest by the next PSUR data lock point, the MAH should remove from the RMP the follow-up questionnaires (FUQ) for the events of haemoptysis and bronchospasms, as well as haemoptysis, bronchospasm, cough, increase risk of respiratory or systemic infection as important risks, and patients who have had significant haemoptysis in last 3 months and patients with <30% predicted FEV1 as missing information from the list of safety concerns.

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. rADAMTS13 – ADZYNMA (CAP) – EMA/PSUR/0000288290

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00011077/202505)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Adzynma, a centrally authorised medicine containing rADAMTS13 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 Adzynma (rADAMTS13) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide a review of cases of neutralizing antibodies formation and discuss the analytical method used to detect neutralising recombinant ADAMTS13 antibodies.

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.

6.1.6. Selpercatinib – RETSEVMO (CAP) – EMA/PSUR/0000288253

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010917/202505)

[13] Update of Annex II-D. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Retsevmo, a centrally authorised medicine containing selpercatinib 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 Retsevmo (Selpercatinib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include Stevens-Johnson syndrome (SJS) as a warning and an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[14].
- In the next PSUR, the MAH should provide a review of new cases of acute kidney injury with a time-to-onset of ≤28 days, of blood CPK increase as well as of the important potential risk of liver injury with a discussion of new cases of drug-induced liver injury. Regarding toxic epidermal necrolysis (TEN), the MAH should provide an update on whether more details are available for the literature case (*Shiyu and Xianmei 2025*) and discuss whether new TEN cases have been identified.

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.

6.1.7. Tirzepatide – MOUNJARO (CAP) – EMA/PSUR/0000288292

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011019/202505)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Mounjaro, a centrally authorised medicine containing tirzepatide 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 Mounjaro (tirzepatide) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide a cumulative review of tirzepatide and its (potential) interaction with levothyroxine, discussing relevant cases from clinical trials and post-marketing data as well as scientific literature and update the product information, as warranted. In addition, considering the plausible mechanism of action for starvation ketoacidosis, the MAH should continue monitoring malnutrition and

[14] 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

starvation ketoacidosis, discussing any new relevant information from spontaneous cases with at least possible causality or from unblinded trials.

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.

6.1.8. Tocilizumab - AVTOZMA (CAP); ROACTEMRA (CAP); TOFIDENCE (CAP); TYENNE (CAP) – EMA/PSUR/0000288251

Applicants: Celltrion Healthcare Hungary Kft., Fresenius Kabi Deutschland GmbH, Roche Registration GmbH, STADA Arzneimittel AG

PRAC Lead: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00002980/202504)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Avtozma, RoActemra, Tofidence and Tyenne, centrally authorised medicines containing tocilizumab and issued a recommendation on its marketing authorisations.

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Avtozma, RoActemra, Tofidence and Tyenne (tocilizumab) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, all MAHs should closely monitor cases of pyoderma gangrenosum and present new cases. Moreover, the MAH Roche should monitor new cases of hypersensitivity reactions and the MAHs Fresenius Kabi, Celltrion and STADA Arzneimittel AG should present a cumulative review of cases of hypersensitivity reactions and discuss them in future PSURs.
- In addition, PRAC considered that possible underlying reasons (root-cause) for the hypersensitivity reactions reported following Tyenne (tocilizumab) administration should be further evaluated, and requested the MAH Fresenius Kabi to submit a quality investigation focusing on changes in quality since the initial marketing authorisation application approval as part of a post-authorisation measure.

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 also Annex I 16.2.

6.2.1. Telmisartan – KINZALMONO (CAP); MICARDIS (CAP); PRITOR (CAP); NAP; Telmisartan / Hydrochlorothiazide - KINZALKOMB (SRD[15]); PRITORPLUS (SRD[16]) – EMA/PSUR/0000288281

Applicants: Bayer AG, Boehringer Ingelheim International GmbH, various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00002882/202503)

Background

Telmisartan is a specific angiotensin II receptor (type AT1) antagonist, indicated for the treatment of essential hypertension in adults and reduction of cardiovascular morbidity in adults with manifest atherothrombotic cardiovascular disease or type 2 diabetes mellitus with documented target organ damage. Hydrochlorothiazide is a thiazide diuretic. The fixed dose combination telmisartan/hydrochlorothiazide is indicated in patients whose blood pressure is not adequately controlled on telmisartan or hydrochlorothiazide alone.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of products containing telmisartan and telmisartan/hydrochlorotiazide and issued a recommendation on their 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 telmisartan and telmisartan/hydrochlorothiazide-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add dizziness as undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisations should be varied[17].
- In the next PSUR, all MAHs should continue monitoring cases of sprue-like enteropathy, provide any new evidence emerging during the reporting interval, and discuss the need for updates to the product information, as warranted. In addition, all MAHs should provide a comprehensive summary of cumulative and interval cases of headache, including a causality assessment and a discussion on the need to revise the product information, as warranted.

The frequency of PSUR submission should be revised from three-yearly to five-yearly and the next PSUR should be submitted to EMA within 90 days of the data lock point. The EURD list provided for under Article 107c(7) of Directive 2001/83/EC is updated accordingly.

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

See also Annex I 16.3.

[15] European Commission decision for the withdrawal of the marketing authorisation, at the holder's request: 26.09.2025
[16] European Commission decision for the withdrawal of the marketing authorisation, at the holder's request: 1.10.2025
[17] 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

6.3.1. Captopril (NAP) – EMA/PSUR/0000288214

Applicants: various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00000535/202504)

Background

Captopril is an inhibitor of angiotensin-I converting enzyme (ACE), indicated for the treatment of hypertension, myocardial infarction and macroproteinuric diabetic nephropathy in patients with type I diabetes, as well for the treatment of chronic heart failure with reduction of systolic ventricular function in combination with diuretics and, when appropriate, digitalis and beta-blockers.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing captopril and issued a recommendation on their 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 captopril-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning on angioedema to state that severe angioedema may develop after months or years of long-term treatment with an ACE inhibitor. In addition, the product information should be updated to add a warning on insulin autoimmune syndrome and angioedema, as well as to add insulin autoimmune syndrome as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[18].
- In the next PSUR, in case any new significant safety information regarding angioedema is identified, all MAHs should assess whether additional regulatory actions are warranted. In addition, all MAHs should provide cumulative reviews of cases of psoriasis, cutis laxa and malignancies related to captopril treatment, based on relevant data sources, and evaluate any new significant information on this matter. Moreover, the MAHs should monitor cases of drug rash with eosinophilia and systemic symptoms (DRESS), toxic epidermal necrolysis (TEN) and linear IgA disease and discuss any new safety information identified.

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.

6.3.2. Cefditoren (NAP) – EMA/PSUR/0000288221

Applicants: various

PRAC Lead: Maria del Pilar Rayon

[18] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

Scope: Evaluation of a PSUSA procedure (PSUSA/00000592/202503)

Background

Cefditoren pivoxil is a cephalosporin antibiotic for oral use, a prodrug of cefditoren, and it is indicated for the treatment of infections from cefditoren-susceptible strains. Specifically, it is indicated for the treatment of different infection location.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing cefditoren and issued a recommendation on their 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 cefditoren-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add warnings on acute generalised exanthematous pustulosis (AGEP) and on the interference with neonatal screening tests. In addition, the product information should be updated to add AGEP, pseudomembranous colitis and tubulointerstitial nephritis as undesirable effects with frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[19].
- In the next PSUR, all MAHs should provide cumulative reviews of cases of hypoglycaemia accompanying hypocarnitinaemia, hepatitis cholestatic and haematochezia. In addition, all MAHs should provide a cumulative review of cases of convulsions/seizures and related events and discuss whether any further updates to the product information are warranted.

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.

6.3.3. Cytarabine (NAP) – EMA/PSUR/0000288257

Applicants: various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00000911/202503)

Background

Cytarabine is an antineoplastic agent indicated for the induction of remission, consolidation and maintenance of remission of acute non-lymphatic leukaemia, induction of remission and consolidation of remission of acute lymphatic leukaemia and intrathecal prophylaxis and treatment of leukemic infiltrations of the central nervous system. It is also indicated for the treatment of non-Hodgkin's lymphoma (NHL) of intermediate and high malignancy in adulthood and in children, acute and chronic myeloid leukaemia, diffuse lymphoma, blast cell

[19] Update of SmPC sections 4.4, 4.6 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

crisis, diffuse large b-cell lymphoma, leukaemia secondary, leukemic infiltration brain, leukaemia relapse, and solid tumour, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing cytarabine and issued a recommendation on their 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 cytarabine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add neutrophilic eccrine hidradenitis and auricular erythema as undesirable effects with frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[20].
- In the next PSUR, all MAHs should maintain monitoring of cases of hypotension/vascular shock and include preferred term 'cytarabine syndrome' in the search strategies.

The frequency of PSUR submission should be revised from two-yearly to five-yearly and the next PSUR should be submitted to EMA within 90 days of the data lock point. The EURD list provided for under Article 107c(7) of Directive 2001/83/EC is updated accordingly.

6.3.4. Isotretinoin (oral formulations) (NAP) – EMA/PSUR/0000288240

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00010488/202505)

Background

Isotretinoin is a retinoid (vitamin A-derivative) and it is indicated for the oral treatment of severe forms of acne.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing isotretinoin and issued a recommendation on their 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 isotretinoin-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add anal fissure as an undesirable effect with a frequency 'not known'. In addition, the product information should be updated to include acute generalised exanthematous pustulosis (AGEP) as a warning and undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[21].

[20] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position
[21] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

- In the next PSUR, the MAHs should provide cumulative reviews of cases of transient headache and neurologic deficit with cerebrospinal fluid lymphocytosis (HaNDL syndrome) and all cases of headache/migraine that could be characterized as an HaNDL syndrome, including data from clinical trials, observational study data and literature data, and discuss whether an update of the product information is warranted. The MAHs should also continue to follow-up pregnancy cases and present them as part of the evaluation of the important identified risks in the next PSUR.

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.

6.3.5. Linezolid (NAP) – EMA/PSUR/0000288225

Applicants: various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00001888/202504)

Background

Linezolid is an antibiotic indicated for the treatment of infections, including cases with concurrent bacteraemia, when suspected or known to be caused by susceptible strains of anaerobic or aerobic gram-positive microorganisms: nosocomial pneumonia, community-acquired pneumonia, skin and soft tissue infections, enterococcal infections, including those caused by vancomycin-resistant *Enterococcus faecium* and *Enterococcus faecalis*.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing linezolid and issued a recommendation on their 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 linezolid-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add hypoglycaemia and black hairy tongue as undesirable effects with frequencies 'uncommon' and 'rare', respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[22].
- In the next PSUR, the MAHs should provide cumulative reviews of cases of hallucination and monitor the following safety topics: purpuric drug eruption, events of drug resistance, aplasia pure red cell, interstitial nephritis and posterior reversible encephalopathy syndrome (PRES), drug reaction with eosinophilia and systemic symptoms (DRESS), and interaction with warfarin, risk of hepatobiliary disorders and QT prolongation.

[22] Update of SmPC section XX. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

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.

6.3.6. Nefopam (NAP) – EMA/PSUR/0000288226

Applicants: various

PRAC Lead: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00002131/202503)

Background

Nefopam is a non-morphinic analgesic and it is indicated as solution for injection for the symptomatic treatment of acute painful conditions, whereas nefopam oral formulations are indicated for relief of acute and chronic pain, including post-operative pain, dental pain, musculoskeletal pain, acute traumatic pain and cancer pain.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing nefopam and issued a recommendation on their 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 nefopam-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning on drug dependence and to add drug dependence as undesirable effect with a frequency 'rare'. Therefore, the current terms of the marketing authorisation(s) should be varied[23].
- In the next PSUR, all MAHs should provide cumulative analyses of cases of drug-drug interaction between nefopam and serotonin-norepinephrine reuptake inhibitors (SNRI) (including venlafaxine), and between nefopam and selective serotonin reuptake inhibitors (SSRI) (including sertraline), including data from literature.

The frequency of PSUR submission should be revised from three-yearly to five-yearly and the next PSUR should be submitted to EMA within 90 days of the data lock point. The EURD list provided for under Article 107c(7) of Directive 2001/83/EC is updated accordingly.

6.3.7. Piritramide (NAP) – EMA/PSUR/0000288223

Applicants: various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00002437/202503)

Background

Piritramide is a synthetic opioid used in the treatment of severe pain.

[23] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing piritramide and issued a recommendation on their 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 piritramide-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated in order to further minimise the risk of opioid use disorder (OUD), including the addition of a new black box warning about the risk of dependence and addiction in the package leaflet. The PI should also be updated to reflect the drug-drug interaction with gabapentinoids and to amend the information about the detection of piritramide in the colostrum. Therefore, the current terms of the marketing authorisation(s) should be varied[24].
- In the next PSUR, the MAH(s) should provide a more detailed review on all cases of medication error received during the reporting interval, including a discussion on the cases of incorrect route of administration. In addition, the MAH(s) should provide a cumulative review of cases of drug interaction between baclofen administered intrathecally and piritramide.
- The MAH(s) should update the product information regarding the concomitant use of benzodiazepines through an appropriate regulatory procedure.

The frequency of PSUR submission should be revised from fourteen-yearly to five-yearly and the next PSUR should be submitted to EMA within 90 days of the data lock point. The EURD list provided for under Article 107c(7) of Directive 2001/83/EC is updated accordingly.

6.3.8. Simvastatin (NAP) – EMA/PSUR/0000288235

Applicants: various

PRAC Lead: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00002709/202504)

Background

Simvastatin is an HMG-CoA reductase inhibitor indicated for the treatment of primary hypercholesterolaemia or mixed dyslipidaemia, homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid-lowering treatments and for the reduction of cardiovascular mortality and morbidity in patients with manifest atherosclerotic cardiovascular disease or diabetes mellitus.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing simvastatin and issued a recommendation on their marketing authorisation(s).

Summary of recommendation(s) and conclusions

[24] Update of SmPC sections 4.2, 4.4, 4.5, 4.6 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

- Based on the review of the data on safety and efficacy, the benefit-risk balance of simvastatin-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add information regarding drug-drug interactions between simvastatin and palbociclib, and simvastatin and ribociclib. Therefore, the current terms of the marketing authorisation(s) should be varied[25].
- In the next PSUR, the MAHs should provide a cumulative review of cases of microscopic colitis, and to discuss whether an update of product information is warranted. The MAHs should also monitor cases of osteoporosis and serious ocular events, and present any new information in the next PSURs, and provide a review of cases of acute generalised exanthematous pustulosis.

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.

6.4. Follow-up to PSUR/PSUSA procedures

See Annex I 16.4.

6.5. Variation procedure(s) resulting from PSUSA evaluation

See also Annex I 16.5.

6.5.1. Semaglutide – OZEMPIC (CAP); RYBELSUS (CAP) – EMA/VR/0000292593

Applicants: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Update of section 4.8 of the SmPC in order to add Dysaesthesia to the list of adverse drug reactions (ADRs) for Ozempic and Rybelsus following PRAC request for cumulative review of "Altered skin sensation" for semaglutide PSUR (EMEA/H/C/PSUSA/00010671/202405); the Package Leaflet is updated accordingly.

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 cumulative review of cases of dysaesthesia and to assess the need to update the product information for Ozempic and Rybelsus (semaglutide). 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.

[25] Update of SmPC section 4.5. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

Summary of recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed that the product information[26] of Ozempic (semaglutide) should be updated to add 'dysaesthesia' as an undesirable effect with a frequency 'not known'. In addition, the product information[27] of Rybelsus (semaglutide) should be amended to mention that there were no imbalances of dysaesthesia events with lower doses of Rybelsus in phase 3a trials, however, events have been reported in the post- marketing experience.

6.6. Expedited summary safety reviews[28]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[29]

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 for Leqembi (lecanemab), the MAH submitted on 16 September 2025 a PASS protocol version 2.0 to the EMA. For further background, see PRAC minutes July 2025.

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 2.0, 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 registry-based study on the existing registry data source should be supported by an adequate feasibility assessment. Furthermore, the

[26] Update of SmPC section 4.8. The package leaflet is updated accordingly
[27] Update of SmPC section 4.8. The package leaflet is updated accordingly

[28] 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
[29] In accordance with Article 107n of Directive 2001/83/EC

MAH should amend the study objectives as per PRAC's request, as well as clarify and provide more information related to the follow-up period, sample size, data source, data collection, data capture and limitations of the study, including a statistical analysis plan. The MAH should also provide a discussion on the evaluation of compliance and effectiveness of risk minimisation measures.

- The MAH should submit a revised PASS protocol within 60 days to EMA. A 60 days-assessment timetable will be followed.

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

See Annex I 17.2.

7.3. Results of PASS imposed in the marketing authorisation(s)[31]

See also Annex I 17.3.

7.3.1. Deferasirox – EXJADE (CAP) – EMA/VR/0000280855

Applicants: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section D of Annex II of the PI based on the submission of the final report from study CICL670E2422, listed as an imposed PASS in the Annex II. This is an observational study that evaluated the safety of deferasirox in the treatment of pediatric patients with non-transfusion-dependent iron overload. The RMP version 23.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

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 purpose of the present submission is to fulfil an Annex II Post-Authorization Measure with the EMA, ANX-038, requiring a post-authorization safety study (PASS) as a condition of the marketing authorization. The submission provides the final results from the non-interventional (observational) Study E2422.

In order to fulfil this condition, the MAH submitted on 20 June 2025 a final report for study CICL670E2422 conducted to assess the long-term safety of deferasirox in the treatment of paediatric patients with non-transfusion-dependent iron overload.

PRAC discussed the final study results in addition to the MAH's responses to the request for supplementary information (RSI). For further background, see PRAC minutes September 2025.

Summary of recommendation(s) and conclusions

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

- Based on the review of the final report of the non-interventional PASS entitled 'an observational, multi-center study to evaluate the safety of deferasirox in the treatment of paediatric patients with non-transfusion dependent iron overload', PRAC considered that the benefit-risk balance of Exjade (deferasirox) remains unchanged. As a consequence, PRAC recommended that the terms of the marketing authorisation(s) for Exjade (deferasirox) should be varied to update the product information[32] to reflect the conclusions of the observational study and to remove the PASS from the Annex II 'conditions or restrictions with regard to the safe and effective use of the medicinal product'. Consequently, PRAC agreed to remove the product from the additional monitoring list, and to update the RMP accordingly.

7.4. Results of PASS non-imposed in the marketing authorisation(s)[33]

See also Annex I 17.4.

7.4.1. Erenumab – AIMOVIG (CAP) – EMA/VR/0000267640

Applicants: Novartis Europharm Limited

PRAC Rapporteur: Terhi Lehtinen

Scope: Submission of the final study report for the non-interventional (NIS) study CAMG334A2023; this is a non-interventional study to examine patient characteristics and drug utilization patterns in migraine patients treated with prophylactic drugs in Nordic countries, listed as a category 3 PASS in the RMP. The RMP version 5.0 has also been submitted.

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 stated in the RMP of Aimovig (erenumab), the MAH conducted a non-imposed non-interventional PASS (CAMG334A2023) to examine patient characteristics and drug utilization patterns in migraine patients treated with prophylactic drugs. The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI). For further background, see PRAC minutes July 2025.

Summary of advice

- Based on the available data, the MAH's responses to the RSI and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be recommended for approval.
- PRAC agreed to remove the study from the pharmacovigilance plan in the RMP. . PRAC concluded that the evaluation of the cardiovascular outcomes in patients with preexisting cardiovascular risks or use in pregnant women would not be feasible in a non-interventional PASS setting, and thus the routine pharmacovigilance including signal detection and PSURs are sufficient measures for monitoring these issues.

[32] Update of SmPC sections 4.4, 4.8 and 5.1, and Annex II-D.
[33] 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. Interim results and other post-authorisation measures for imposed and non-imposed studies

See Annex I 17.5.

7.6. New Scientific Advice

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

7.7. Ongoing Scientific Advice

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

7.8. 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.

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 CHMP or EMA

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.1.1. Ciprofloxacin (intravenous and oral use) (NAP); Moxifloxacin (intravenous and oral use) (NAP) - FR/H/xxxx/WS/485

Applicant(s): Bayer HealthCare S.A.S. (Iziflox, Ciflox)

PRAC Lead: Zoubida Amimour

Scope: PRAC consultation on a worksharing variation procedure (FR/H/xxxx/WS/485) to update the product information in order to add information on acute myocardial ischemia with or without myocardial infarction as part of a hypersensitivity reaction (Kounis syndrome), at request of France.

Background

Ciprofloxacin and moxifloxacin are fluoroquinolones antibiotics, indicated for the treatment of various infections.

In the context of the evaluation of a worksharing variation procedure to update the product information in order to add information on acute myocardial ischemia with or without myocardial infarction as part of a hypersensitivity reaction (Kounis syndrome), France requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC agreed that the product information for the ciprofloxacin-containing (intravenous and oral use) and moxifloxacin-

containing (intravenous and oral use) medicinal products should be updated to include Kounis syndrome as a warning and an adverse event with a frequency 'not known'[34]. In addition, PRAC agreed that this recommendation also applies to all ciprofloxacin-containing medicinal products for intravenous and oral use and all moxifloxacin-containing medicinal products for intravenous and oral use.

11.1.2. Ketoprofen (NAP) - FR/H/xxxx/WS/558

Applicant(s): Sanofi Winthrop Industrie (Profemigr, Toprec, Profenid, Bi-Profenid)

PRAC Lead: Tiphaine Vaillant

Scope: PRAC consultation on a worksharing variation procedure (FR/H/xxxx/WS/558) to update the product information regarding foetal death secondary to cardiopulmonary and/or renal toxicity after nonsteroidal anti-inflammatory drugs (NSAID) exposure after the second trimester of pregnancy and the risk of formation of intestinal diaphragm-like strictures, at request of France.

Background

Ketoprofen is a NSAID used as an analgesic, anti-inflammatory and anti-pyretic for various conditions, as warranted.

In the context of the evaluation of a worksharing variation procedure to update the product information regarding foetal death secondary to cardiopulmonary and/or renal toxicity after NSAID exposure after the second trimester of pregnancy and the risk of formation of intestinal diaphragm-like strictures, France requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC concluded that there is insufficient data for ketoprofen-containing products to warrant an update of the product information (section 4.8 of the SmPC and section 4 of PL) to add the effect 'formation of intestinal diaphragm-like strictures'. It has been noted that this effect could be considered as a consequence of gastrointestinal toxicity on the intestine lumen and mucosal integrity, caused by chronic NSAIDs use; gastrointestinal toxicity is well-known toxicity of NSAIDs and is already labelled across the class. In addition, PRAC concluded that, considering that new data have not emerged since the previous update as per the EMA/CMDh/642745/2022 which already appropriately describes the advice for monitoring and the periods at risks for cardiopulmonary and renal toxicity, there is no rationale for further revisions regarding foetal death. Moreover, the proposed revision would not be changing the overall recommendation for use in pregnancy for the patients and clinicians.

11.1.3. Levofloxacin (intravenous and oral use) (NAP) - DE/H/5119/001-003/II/117/G

Applicant(s): Sanofi-Aventis Deutschland GmbH (Tavanic)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a variation procedure (DE/H/5119/001-003/II/117/G) to update the product information regarding cerebellar syndrome and Guillain-Barré syndrome

[34] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly.

following the conclusions of PSUSA/00010767/202310, at request of Germany.

Background

Levofloxacin is a fluoroquinolone antibiotic, indicated for the treatment of various infections.

In the context of the evaluation of a type II variation procedure to update the product information regarding cerebellar syndrome and Guillain-Barré syndrome, Germany requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC considered that the currently available evidence is insufficient to establish a causal relationship between levofloxacin and cerebellar syndrome as well as Guillan-Barré Syndrome. As a consequence, PRAC did not support an update of the product information of levofloxacin-containing medicinal products (intravenous and oral use) to reflect cerebellar syndrome and Guillain-Barré syndrome at this point in time. PRAC therefore maintained the request made in the context of PSUSA procedure PSUSA/00010767/202310, for all MAHs of levofloxacin-containing medicinal products (intravenous and oral use) to closely monitor cerebellar syndrome and Guillain-Barré syndrome, and present the results of this monitoring in the next PSUR (PSUSA/00010767/202610, DLP 01/10/2026, submission date 30/12/2026) together, if appropriate, with proposals for corresponding updates of the list of safety concerns and/or the product information.

11.1.4. Tramadol (NAP) - DE/H/xxxx/WS/2290; DE/H/0639/001-004/II/040

Applicants: Ethypharm, Mylan Germany GmbH, Viatris Healthcare GmbH

PRAC Lead: Martin Huber

Scope: PRAC consultation on two worksharing variation procedures (DE/H/xxxx/WS/2290 and DE/H/0639/001-004/II/040) to update the product information to include a warning on the use of prolonged-/modified-release opioids for acute post-operative pain owing to increased risk of persistent post-operative opioid use (PPOU) and opioid-induced ventilatory impairment (OIVI), at request of Germany.

Background

Tramadol is a centrally acting opioid agonist and serotonin/norepinephrine reuptake inhibitor (SNRI) used for the management of moderate to severe pain.

In the context of the evaluation of a type II variation procedure to update the product information to include a warning on the use of prolonged-/modified-release opioids for acute post-operative pain owing to increased risk of PPOU and OIVI, Germany requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC discussed the update as proposed by the MAHs to include a warning not to use prolonged-/modified-release opioids for acute post-operative pain owing to an increased risk of PPOU and OIVI, and considered that these changes are not justified. The current EU product information (PI) already includes comprehensive warnings on dependence/opioid use disorder (OUD) and

central nervous system (CNS)/respiratory depression, and no new relevant data were provided that would necessitate an SmPC update.

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

12.1.2. The Chair thanked Anna Marekova for her contribution as a member representing Slovakia. Vote by proxy

Annalisa Capuano gave a proxy to Maria Teresa Herdeiro and Yiannoula Koulla gave a proxy to Panagiotis Psaras – both 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

12.3.1. Scientific Advice Working Party (SAWP) - SAWP composition - re-examination exercise

The EMA Secretariat presented details on the requirements, procedural aspects, application forms and timelines related to the SAWP composition. PRAC members are invited to express their interest for the PRAC joint members to represent their Committee at SAWP by 30 January 2026. The full SAWP composition will subsequently be proposed to and adopted by the CHMP.

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2026

PRAC lead: Ulla Wändel Liminga, Liana Martirosyan

The EMA Secretariat presented to PRAC the final draft PRAC workplan for 2026. PRAC members were invited to send their final comments or suggestions on the draft work plan before its adoption at the PRAC January 2026 meeting.

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.1. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead:

12.10.2. The EMA Secretariat and the PRAC Lead presented to PRAC an update on the GPAG activities, as well as the proposed objectives and deliverables included in the GPAG work plan for 2026. PRAC endorsed the GPAG PRAC work plan for 2026. PSURs repository

None

12.10.3. 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 December 2025, 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 December 2025, the updated EURD list was adopted by CHMP and CMDh at their December 2025 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)

12.10.4. Revisions of the Questions and Answers for assessors on Periodic safety update reports (PSUSA), PSUSA assessment report template and Explanatory Note to Good Pharmacovigilance Practice (GVP) Module VII

PRAC lead: Ulla Wändel Liminga

At the ORGAM meeting held on 10 December 2025, the EMA Secretariat presented to PRAC the outcome of the drafting group on best practice guidance on PSUSA Assessment, set up in April 2025. The EMA Secretariat presented to PRAC the key revisions to the explanatory note to GVP Module VII, the PSUSA assessment report template and the questions & answers document on PSUSA for assessors. PRAC members were invited to send their comments in writing to these 3 documents by 16 January 2026.

12.11. Signal management

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

PRAC lead: The EMA Secretariat presented to PRAC an update on the in-person session of the SMART Methods group including an update on the activities of the group's 2022-2025 workplan , as well as an update of the UMC-EMA collaborative workshop that took place in 2025. 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. Draft Good Pharmacovigilance Practice (GVP) Module V and RMP template rev 3.0

PRAC lead: Ulla Wändel Liminga

At the ORGAM meeting held on 10 December 2025, the EMA Secretariat presented to PRAC an update on the progress of the drafting group regarding the revision 3.0 of the GVP Module V and the RMP template. The purpose of this revision is to provide updated risk management recommendations for ATMPs and to reflect the experience gained in assessing RMPs since the previous revision in 2017. The EMA Secretariat provided an overview of the main changes and invited PRAC members to review and comment on the draft document .

12.14.2. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

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

At the ORGAM meeting held on 10 December 2025, the EMA Secretariat presented to PRAC an update on RWE and DARWIN EU activities, including data partners and the criteria for DARWIN EU study prioritisation. Moreover, the EMA Secretariat presented a list of ongoing and planned DARWIN EU studies, as well as an assessment of the impact of these studies in the regulatory framework. PRAC noted the information.

12.21.2. Lactose used as excipient in medicinal products – revised information for the labelling and package leaflet

12.21.3. Dominique Masset, the NcWP member and ExcpDG co-chair, presented to PRAC the revised information for the labelling and package leaflet regarding the lactose used as an excipient in the medicinal products. PRAC was specifically informed on the precautionary threshold of zero and its implication for the labelling and assessment, in order to have a harmonisation of information on the risks associated with lactose of bovine origin throughout the EU, thereby enhancing the safety of patients with cow's milk protein allergies. PRAC noted the information.Patient Registries activities - update

At the ORGAM meeting held on 10 December 2025, the EMA Secretariat provided to PRAC an update on the patient registry initiative, outlining upcoming activities and priorities for 2026. These include developing new guidance on data and evidence, promoting knowledge dissemination and capacity building, strengthening training and stakeholder engagement, and supporting the European medicines regulatory network in matters related to data and study designs. PRAC members interested in contributing further to these activities were invited to contact the EMA Secretariat .

13. Any other business

14. Annex I – Signals assessment and prioritisation[35]

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[36].

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Ponatinib – ICLUSIG (CAP)

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Signal of congenital megacolon, maternal exposure during pregnancy

EPITT 20231 – New signal

14.2. New signals detected from other sources

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. Furosemide - (CAP MAA) - EMEA/H/C/006617, PUMA[37]

Scope (pre D-180 phase): Treatment of all conditions requiring diuresis due to mechanical obstruction or venous insufficiency.

15.1.2. Insulin aspart - (CAP MAA) - EMEA/H/C/006187

Scope (pre D-180 phase): Treatment of diabetes mellitus

[35] 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

[36] 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

[37] Paediatric use marketing authorisation(s)

15.1.3. Insulin lispro - (CAP MAA) - EMEA/H/C/006158

Scope (pre D-180 phase): Treatment of diabetes mellitus

15.1.4. Tocilizumab - (CAP MAA) - EMEA/H/C/006416

Scope (pre D-180 phase): Treatment of rheumatoid arthritis and other immunological conditions

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. Adalimumab – HEFIYA (CAP); HYRIMOZ (CAP) – EMA/VR/0000295410

Applicants: Sandoz GmbH

PRAC Rapporteur: Karin Bolin

Scope: C.I.11.z - to update the Risk Management Plan (RMP) for Hyrimoz and Hefiya (duplicate of Hyrimoz) to align it with the originator's (Humira) RMP.

15.2.2. Denosumab – XGEVA (CAP) – EMA/VR/0000272344

Applicants: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of an updated RMP version 37.0 in order to modify and update the list of safety concerns based on previously completed post-authorization safety studies, including registry study 20101102 and the long-term safety follow-up study 20140114.

15.2.3. Epcoritamab – TEPKINLY (CAP) – EMA/VR/0000296114

Applicants: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Submission of an updated RMP version 3.0 in order to amend the important identified risk of serious infections to now encompass progressive multifocal leukoencephalopathy (PML).

15.2.4. Fingolimod – FINGOLIMOD MYLAN (CAP); NAP – EMA/VR/0000280709

Applicants: Mylan Pharmaceuticals Limited, various

PRAC Rapporteur: Tiphaine Vaillant

Scope: C.I.11.z - to implement changes to the Risk Management Plans for Fingolimod Mylan and Mulfiyna, following relevant updates to the Risk Management Plan of the innovator product Gilenya (Novartis Europharm Limited, EMEA/H/C/002202).

15.2.5. Latanoprost / Netarsudil – ROCLANDA (CAP); netarsudil – RHOKIINSA (CAP) – EMA/VR/0000290523

Applicants: Santen Oy

PRAC Rapporteur: Maria del Pilar Rayon

Scope: C.I.11.z (Type IB) – To update the RMP by removing the PASS study from the RMP, as agreed during the MEA 001.6 (EMA/PAM/0000272898) procedure.

15.2.6. Mepolizumab – NUCALA (CAP) – EMA/VR/0000291438

Applicants: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of an updated RMP version 15 following procedure EMA/CHMP/PRAC/525630/2024.

15.2.7. Ocrelizumab – OCREVUS (CAP) – EMA/VR/0000296075

Applicants: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of an updated RMP version 14.0 in order to amend the study description (primary and secondary endpoints) of Category 3 Post-Authorisation Safety Study WA40404 (O'HAND) to align with the latest study protocol version 6.0. In addition, the MAH proposes to postpone the milestone date for the final CSR of this study.

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

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

15.3.1. Aflibercept – EYLEA (CAP) – EMA/VR/0000264981

Applicants: Bayer AG

PRAC Rapporteur: Zoubida Amimour

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

C.I.6: Extension of indication to include the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch, central and hemiretinal retinal vein occlusion, RVO) for EYLEA, based on results from study 22153 (QUASAR); this is a randomized, double-masked, active-controlled Phase 3 study of the efficacy and safety of aflibercept 8 mg in macular edema secondary to retinal vein occlusion. 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 accordingly. The RMP version 36.1 has also been submitted.

C.I.4: Update of section 4.2 of the SmPC in order to change posology recommendations of the approved indications neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME) based on the results from study 22153 (QUASAR) and post-hoc analysis of the pivotal studies 20968 (PULSAR), 21091 (PHOTON) and Phase II study 21086 (CANDELA).

15.3.2. Amivantamab – RYBREVANT (CAP) – EMA/X/0000268898

Applicants: Janssen Cilag International

PRAC Rapporteur: Dirk Mentzer

Scope: Extension application to add a new strength of 2400 mg and 3520 mg (solution for injection) grouped with the following variations:

C.I.4: Update of sections 4.2, 4.4, 4.8, 5.1, 5.2, 6.5 and 6.6 in order to include the Q3W dosing regimen based on data from relevant cohorts from the Phase 2 bridging study PALOMA-2 (NSC2002) and supported by data from the Phase 1 PALOMA study (NSC1003). The Package Leaflet and Labelling are updated accordingly. The RMP version 7.1 has also been submitted.

C.I.4: Update of sections 4.2, 4.4, 4.8, 5.1, 5.2, 6.5 and 6.6 in order to introduce a new Q4W dosing regimen based on data from the PALOMA-2 study (NSC2002) and supported by data from the Phase 1 PALOMA study (NSC1003). The Package Leaflet and Labelling are updated accordingly. The RMP version 7.1 has also been submitted.

15.3.3. Apalutamide – ERLEADA (CAP) – EMA/VR/0000296280

Applicants: Janssen Cilag International

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of sections 4.2, and 5.2 of the SmPC in order to introduce a dose recommendation for apalutamide in patients with severe hepatic impairment based on the results from Study 56021927PCR1026 listed as a category 3 study in the RMP; this is an open-label, single-dose, multi-center, non-randomized Phase 1 PK study of apalutamide in participants who either had severe hepatic impairment (Child-Pugh Class C) or healthy participants with Normal hepatic function ; the Package Leaflet is updated accordingly. The RMP version 8.2 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI.

15.3.4. Asciminib – SCEMBLIX (CAP) – EMA/X/0000256688

Applicants: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: Extension application to introduce a new strength (100 mg film-coated tablets) grouped with a type II variation (C.I.6.a) to add a new indication (treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) harbouring the T315I mutation), based on final results from study CABL001X2101 and study CABL001A2004. Study CABL001X2101 is a Phase I, multicenter, open-label, dose escalation FIH study to define the MTD/RDEs, to characterize safety and tolerability, and to

assess the PK profile and preliminary evidence of efficacy of asciminib given as single agent or in combination with either nilotinib or imatinib or dasatinib in patients with Ph+ CML or Ph+ ALL.

Study CABL001A2004 assessed the real-world effectiveness of asciminib and treatment patterns in patients with Chronic Myeloid Leukemia with T315I mutation. As a consequence, sections 1, 2, 3, 4, 5, 6 and 8 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 3.0 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection.

15.3.5. Avelumab – BAVENCIO (CAP) – EMA/VR/0000261861

Applicants: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add "Gastritis" to the list of adverse drug reactions (ADRs) with frequency "Not known" based on postmarketing data and literature. The Package Leaflet is updated accordingly. The RMP version 9.1 has also been submitted.

15.3.6. Axicabtagene ciloleucel – YESCARTA (CAP) – EMA/VR/0000301490

Applicants: Kite Pharma EU B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the final report from study KTE-C19-105 (ZUMA-5) to fulfil additional pharmacovigilance activities (Category 3) requirements listed in RMP. This is a phase 2 multicenter study of axicabtagene ciloleucel in subjects with relapsed/refractory indolent non-Hodgkin lymphoma. The RMP version 11.3 has also been submitted.

15.3.7. Baricitinib – OLUMIANT (CAP) – EMA/X/0000257923

Applicants: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new pharmaceutical form (oral suspension) associated with a new strength (2 mg/ml).

15.3.8. Blinatumomab – BLINCYTO (CAP) – EMA/VR/0000286935

Applicants: Amgen Europe B.V.

PRAC Rapporteur: Veronika Macurova

Scope: Update of sections 4.4, 4.8 of the SmPC in order to add a new warning on Haemophagocytic lymphohistiocytosis (HLH)/Immune effector-cell-associated haemophagocytic lymphohistiocytosis-like syndrome (IEC-HS) following the evolving understanding of cytokine release syndrome and HLH/IEC-HS; the Package Leaflet is updated accordingly. The RMP version 20.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI.

15.3.9. Budesonide – JORVEZA (CAP) – EMA/X/0000257468

Applicants: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (0.2 mg/ml oral suspension). The new presentation is indicated for paediatric patients 2 to 17 years of age.

15.3.10. Cangrelor – KENGREXAL (CAP) – EMA/VR/0000295860

Applicants: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.2 and 4.5 of the SmPC with regards to the transitioning scheme to the oral therapy with P2Y12 inhibitors based on the 2023 European Society of Cardiology guidelines for the management of Acute Coronary Syndrome, and based on new evidence from post-marketing clinical studies (PK/PD, real-world safety and efficacy). The Package Leaflet is updated accordingly. The RMP version 6.1 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4.

15.3.11. Capivasertib – TRUQAP (CAP) – EMA/VR/0000293735

Applicants: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Extension of indication to include include Truqap in combination with abiraterone for the treatment of metastatic castration-sensitive prostate cancer characterized by PTEN deficient tumours based on non-clinical and clinical dataset, including interim results from the pivotal study D361BC00001 (CAPItello-281); this is a Phase III double-blind, randomised, placebo-controlled study assessing the efficacy and safety of capivasertib + abiraterone versus placebo + abiraterone as treatment for patients with de novo metastatic hormone-sensitive prostate cancer (mHSPC) characterised by PTEN deficiency; As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.12. COVID-19 mRNA vaccine – KOSTAIVE (CAP) – EMA/VR/0000284897

Applicants: Seqirus Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Update of sections 4.5, 4.8 and 5.1 of the SmPC in order to add information based on final results from study ARCT-2303-01 listed as a category 3 study in the RMP; this is a Phase 3 observer-blind, randomized controlled study to evaluate the immunogenicity, reactogenicity, and safety of Kostaive administered concomitantly with quadrivalent influenza vaccines in adults. The Package Leaflet is updated accordingly. The RMP version 1.1 has also

been submitted. In addition, the MAH is taking the opportunity to implement editorial changes to the PI.

15.3.13. Dabrafenib – TAFINLAR (CAP); Trametinib – MEKINIST (CAP) – EMA/VR/0000278305

Applicants: Novartis Europharm Limited

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include treatment of differentiated thyroid cancer (DTC) for TAFINLAR and MEKINIST based on primary analysis from pivotal study CDRB436J12301. This is a randomized, double-blind, placebo-controlled Phase 3 study to evaluate the efficacy and safety of dabrafenib plus trametinib in previously treated patients with locally advanced or metastatic, radio-active iodine refractory BRAF V600E mutation-positive differentiated thyroid cancer. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 14.0 and Version 22.0 of the RMPs for Tafinlar and Mekinist, respectively, have also been submitted.

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

Applicants: 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.

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

Applicants: 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.

15.3.16. Fosnetupitant / Netupitant / Palonosetron – AKYNZEO (CAP) – EMA/X/0000258060

Applicants: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Extension application to introduce a new pharmaceutical form (300 mg / 0.5 ml oral suspension).

15.3.17. Gadopiclenol – ELUCIREM (CAP); VUEWAY (CAP) – EMA/VR/0000249008

Applicants: Bracco Imaging S.p.A., Guerbet

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of new population (0 to 2 years of age patients) for ELUCIREM / VUEWAY, based on final results from study GDX-44-015; this is a phase II clinical study concerning gadopiclenol pharmacokinetics, safety and efficacy in pediatric patients < 2 years of age undergoing contrast-enhanced MRI; extension of indication is also supported with the non-clinical data. 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 0.4 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to remove Annex IV from the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

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

Applicants: 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).

15.3.19. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0121

Applicant: Janssen Cilag International

PRAC Rapporteur: Karin Bolin

Scope: Extension of indication to include treatment of paediatric ulcerative colitis for SIMPONI, based on results from study CNTO148UCO3003; this is a Phase 3 Randomized, Open-label Study to Assess the Efficacy, Safety, and Pharmacokinetics of Golimumab Treatment, a Human anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Paediatric Participants with Moderately to Severely Active Ulcerative Colitis; As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. Version 28.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is updated in accordance with the latest EMA excipients guideline and aligned with the latest QRD template version 10.4.

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

Applicants: 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.

15.3.21. Inebilizumab – UPLIZNA (CAP) – EMA/VR/0000257358

Applicants: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: A grouped application consisting of:

C.I.6 (Extension of indication): Extension of indication to include add-on to standard therapy for the treatment of adult patients with generalised myasthenia gravis (gMG) for Uplizna, based on primary analysis results from Study MINT (VIB0551.P3.S1); this is a pivotal phase 3 multicentre, randomised, double-blind, placebo-controlled, parallel-cohort study to evaluate the efficacy and safety of inebilizumab in adults subjects with myasthenia gravis. As a consequence, sections 4.1, 4.2, 4.4 ,4.5, 4.6, 4.8, 5.1, 5.2, and 7 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.4.

A.6: Update of the ATC code of inebilizumab to L04AG10 in line with the 2024 ATC INDEX.

15.3.22. Influenza vaccine (live, nasal) – FLUENZ (CAP) – EMA/VR/0000302352

Applicants: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to introduce self-administration instructions based on postmarketing data and literature. The Package Leaflet and Labelling updated accordingly. The RMP version 13.1 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4.

15.3.23. Leuprorelin – CAMCEVI (CAP) – EMA/X/0000258054

Applicants: Accord Healthcare S.L.U.

PRAC Rapporteur: Amelia Cupelli

Scope: Extension application to add a new strength of 21 mg for leuprorelin prolonged-release suspension for injection pre-filled syringe, for subcutaneous (SC) administration.

15.3.24. Lomitapide – LOJUXTA (CAP) – EMA/X/0000258068

Applicants: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to add a new strength of 2 mg hard capsules.

This application is grouped with

- type II variation (C.I.6.a): an Extension of Indication to include treatment of paediatric patients aged 5 years and older with homozygous familial hypercholesterolaemia (HoFH) for LOJUXTA, based on final results from the pivotal paediatric study APH-19; this is a phase 3, single-arm, open-label, international, multi-centre study to evaluate the efficacy and safety of lomitapide in paediatric patients with homozygous familial hypercholesterolaemia (HOFH) on stable lipid-lowering therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Annex II and Package Leaflet are updated accordingly. The RMP version 7.1 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4.

- 3 x type IB variations (C.I.7.b): to delete the 30 mg, 40 mg and 60 mg strengths from the Lojuxta marketing authorisation (EU/1/13/851/004 - 006).

15.3.25. Nivolumab – OPDIVO (CAP) – EMA/VR/0000288087

Applicants: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Update of sections 4.1 and 4.2 of the SmPC following procedure EMEA/H/C/003985/X/0144. In addition, the MAH took the opportunity to update sections 4.4, 4.8, and 5.1 of the SmPC to align it with the new indications and to implement editorial changes to the PI. The Package Leaflet is updated in accordance. The RMP version 46.0 has also been submitted.

15.3.26. Nivolumab – OPDIVO (CAP) – EMA/VR/0000278256

Applicants: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of the final report for the final Overall Survival analysis from the post authorisation efficacy study (PAES) CA209577 listed as an obligation in the Annex II of the Product Information. This is a randomized, multicenter, double-blind phase 3 study of adjuvant nivolumab in subjects with resected oesophageal cancer or gastroesophageal cancer who have received chemoradiotherapy followed by surgery. The Annex II and the RMP (version 45.0) are updated accordingly.

15.3.27. Omaveloxolone – SKYCLARYS (CAP) – EMA/VR/0000296476

Applicants: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of section 5.3 of the SmPC in order to update preclinical information based on results from study RTA-P-21070: this is a 104-week once daily oral gavage toxicity and toxicokinetic study with RTA 408 in rats. The RMP version 2.0 has also been submitted.

15.3.28. Pembrolizumab – KEYTRUDA (CAP) – EMA/VR/0000293815

Applicants: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include in combination with paclitaxel, with or without bevacizumab, the treatment of platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal carcinoma in adults whose tumours express PD-L1 with a CPS ≥ 1 and who have received one or two prior systemic treatment regimens for KEYTRUDA, based on interim results from study PB96V01MK3475 (KEYNOTE-B96); this is a Phase 3, randomized, double-blind study of pembrolizumab in combination with paclitaxel with or without bevacizumab for the treatment of platinum-resistant recurrent ovarian cancer. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 50.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.

15.3.29. Pneumococcal polysaccharide conjugate vaccine (21-valent) – CAPVAXIVE (CAP) – EMA/VR/0000294070

Applicants: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include treatment of children and adolescents 2 to less than 18 years of age for CAPVAXIVE, based on final results from study V116-013 (P013V116); this is a phase 3, randomized, double-blind study to evaluate the safety, tolerability, and immunogenicity of V116 in children and adolescents with increased risk of pneumococcal disease; As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.

15.3.30. Recombinant respiratory syncytial virus pre-fusion F protein, adjuvanted with AS01E – AREXVY (CAP) – EMA/VR/0000276225

Applicants: GlaxoSmithKline Biologicals

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in adults 18 years of age and older for AREXVY, based on results from study 222253 (RSV OA=ADJ-025); this is a Phase 3b, open-label study to evaluate the non-inferiority of the immune response and to evaluate the safety of the RSVPreF3 OA investigational vaccine in adults 18-49 years of age at increased risk of respiratory syncytial virus disease, compared to older adults ≥60 years of age. As a consequence, sections 4.1, 4.6, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 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.

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

Applicants: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

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.

15.3.32. Tafamidis – VYNDAQEL (CAP) – EMA/X/0000287968

Applicants: Pfizer Europe MA EEIG

PRAC Rapporteur: Zoubida Amimour

Scope: Extension application to introduce a new pharmaceutical form (61 mg film-coated tablet). The RMP (version 10.1) is updated in accordance.

15.3.33. Tirzepatide – MOUNJARO (CAP) – EMA/VR/0000281937

Applicants: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adolescents and children aged 10 years and above with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise for MOUNJARO, based on final results from study I8F-MC-GPGV (SURPASS-PEDS); this is a study to evaluate efficacy, safety, and pharmacokinetics/pharmacodynamics of tirzepatide compared to placebo in paediatric and adolescent participants with type 2 diabetes mellitus inadequately controlled with metformin, or basal insulin, or both. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.1 of the RMP has also been submitted.

15.3.34. Tofersen – QALSODY (CAP) – EMA/VR/0000296462

Applicants: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.8, 5.1, and 5.2 of the SmPC to numerically update the summary of safety profile and description of selected adverse reactions, as well as, to update clinical efficacy and pharmacokinetic information based on final integrated analysis from Study 233AS101 and Study 233AS102. Submission of the final results of Study 233AS102 is listed as a specific obligation in the Annex II and a category 2 study in the RMP. Study 233AAS102 was an open label extension study to assess the long-term safety, tolerability, pharmacokinetics, and effect on disease progression of tofersen administered to previously treated adults with amyotrophic lateral sclerosis caused by superoxide dismutase 1 mutation. The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to update the Annex II.

15.3.35. Trastuzumab deruxtecan – ENHERTU (CAP) – EMA/VR/0000293327

Applicants: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include treatment of adult patients with unresectable or metastatic HER2-positive (IHC3+) solid tumours who have received prior treatment and who have no satisfactory alternative treatment options for Enhertu, based on pooled pop-PK analysis and interim results from study D967VC00001 (DESTINY-PanTumor02); this is a Phase II, Multicenter, Open-label Study to Evaluate the Efficacy and Safety of Trastuzumab Deruxtecan (T-DXd, DS-8201a) for the Treatment of Selected HER2-expressing Tumors; 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 9.2 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce editorial changes to the PI.

15.3.36. Ustekinumab – OTULFI (CAP) – EMA/VR/0000296289

Applicants: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Quality

15.3.37. Vamorolone – AGAMREE (CAP) – EMA/VR/0000293535

Applicants: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include treatment of 2 to <4 year olds for AGAMREE, based on final results from study VBP15-006; this is a phase II open-label, multiple dose study to assess the safety, tolerability, pharmacokinetics, pharmacodynamics, and exploratory efficacy of vamorolone in boys ages 2 to <4 years and 7 to <18 years with Duchenne Muscular Dystrophy (DMD) and an updated paediatric extrapolation report referencing 4 to

<7-year-old subjects with DMD from Study VBP15-004, compared to the 2 to <4-year-old population from Study VBP15-006. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to make some editorial corrections to SmPC.

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. Abaloparatide – ELADYNOS (CAP) – EMA/PSUR/0000288287

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00011029/202504)

16.1.2. Alogliptin – VIPIDIA (CAP); alogliptin / metformin VIPDOMET (CAP); alogliptin / pioglitazone INCRESYNC (CAP) – EMA/PSUR/0000288265

Applicant: Takeda Pharma A/S

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010061/202504)

16.1.3. Andexanet alfa – ONDEXXYA (CAP) – EMA/PSUR/0000288243

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010764/202504)

16.1.4. Asciminib – SCEMBLIX (CAP) – EMA/PSUR/0000288288

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00011008/202504)

16.1.5. Aztreonam / Avibactam – EMBLAVEO (CAP) – EMA/PSUR/0000288268

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure (PSUSA/00011055/202504)

16.1.6. Capivasertib – TRUQAP (CAP) – EMA/PSUR/0000288286

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011061/202505)

16.1.7. Capmatinib – TABRECTA (CAP) – EMA/PSUR/0000288242

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00011022/202505)

16.1.8. Chikungunya vaccine (live) – IXCHIQ (CAP) – EMA/PSUR/0000288260

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011058/202505)

16.1.9. Conestat alfa – RUCONEST (CAP) – EMA/PSUR/0000288246

Applicant: Pharming Group N.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000873/202504)

16.1.10. Delamanid – DELTYBA (CAP) – EMA/PSUR/0000288248

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00010213/202504)

16.1.11. Diphtheria / tetanus / pertussis antigens (pertussis toxoid, filamentous haemagglutinin) (acellular, component) / hepatitis b (rDNA) / poliomyelitis (inactivated) / *Haemophilus* type B conjugate vaccines (adsorbed) – HEXACIMA (CAP); HEXYON (CAP) – EMA/PSUR/0000288217

Applicant: Sanofi Winthrop Industrie

PRAC Lead: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010091/202504)

16.1.12. Durvalumab – IMFINZI (CAP) – EMA/PSUR/0000288249

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010723/202504)

16.1.13. Efbemalenograstim alfa – RYZNEUTA (CAP) – EMA/PSUR/0000288213

Applicant: Evive Biotechnology Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000286/202505)

16.1.14. Ertapenem – INVANZ (CAP) – EMA/PSUR/0000288215

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00001256/202503)

16.1.15. Estrogens conjugated / Bazedoxifene – DUAVIVE (CAP) – EMA/PSUR/0000288280

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010321/202504)

16.1.16. Exagamglogene autotemcel – CASGEVY (CAP) – EMA/PSUR/0000288219

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000244/202505)

16.1.17. Febuxostat – ADENURIC (CAP) – EMA/PSUR/0000288258

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00001353/202504)

16.1.18. Florbetapir (^{18}F) – AMYVID (CAP) – EMA/PSUR/0000288236

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010032/202504)

16.1.19. Insulin glargine - ABASAGLAR (CAP); LANTUS (CAP); SEMGLEE (CAP); TOUJEO (CAP) – EMA/PSUR/0000288220

Applicants: Biosimilar Collaborations Ireland Limited, Eli Lilly Nederland B.V., Sanofi-Aventis Deutschland GmbH

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001751/202504)

16.1.20. Ivosidenib – TIBSOVO (CAP) – EMA/PSUR/0000288259

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011048/202505)

16.1.21. Linzagolix choline – YSELTY (CAP) – EMA/PSUR/0000288245

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010998/202505)

16.1.22. Mavacamten – CAMZYOS (CAP) – EMA/PSUR/0000288218

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00000074/202504)

16.1.23. Mirvetuximab soravtansine – ELAHERE (CAP) – EMA/PSUR/0000288269

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00011097/202505)

16.1.24. Niraparib / Abiraterone acetate – AKEEGA (CAP) – EMA/PSUR/0000288266

Applicant: Janssen Cilag International

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00011051/202504)

16.1.25. Nirsevimab – BEYFORTUS (CAP) – EMA/PSUR/0000288237

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00011026/202504)

16.1.26. Parathyroid hormone – NATPAR (CAP) – EMA/PSUR/0000288231

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00010591/202504)

16.1.27. Potassium citrate / Potassium hydrogen carbonate – SIBNAYAL (CAP) – EMA/PSUR/0000288250

Applicant: Advicenne

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010932/202504)

16.1.28. Ramucirumab – CYRAMZA (CAP) – EMA/PSUR/0000288229

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010323/202504)

16.1.29. RdESAT-6 / rCFP-10 – SIILTIBCY (CAP) – EMA/PSUR/0000288289

Applicant: Serum Life Science Europe GmbH

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011104/202505)

16.1.30. Recombinant vesicular stomatitis virus (strain indiana) with A deletion of the envelope glycoprotein, replaced with the Zaire Eebolavirus (strain kikwit-1995) surface glycoprotein – ERVEBO (CAP) – EMA/PSUR/0000288234

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010834/202505)

16.1.31. Remdesivir – VEKLURY (CAP) – EMA/PSUR/0000288244

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00010840/202505)

16.1.32. Repotrectinib – AUGTYRO (CAP) – EMA/PSUR/0000288264

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00011102/202505)

16.1.33. Ripretinib – QINLOCK (CAP) – EMA/PSUR/0000288238

Applicant: Deciphera Pharmaceuticals (Netherlands) B.V.

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00010962/202505)

16.1.34. Sacituzumab govitecan – TRODELVY (CAP) – EMA/PSUR/0000288232

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010959/202504)

16.1.35. Siltuximab – SYLVANT (CAP) – EMA/PSUR/0000288233

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010254/202504)

16.1.36. Tofersen – QALSODY (CAP) – EMA/PSUR/0000288271

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00011064/202504)

16.1.37. Tremelimumab – IMJUDO (CAP) – EMA/PSUR/0000288263

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011038/202504)

16.1.38. Vamorolone – AGAMREE (CAP) – EMA/PSUR/0000288222

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00000223/202504)

16.1.39. Volanesorsen – WAYLIVRA (CAP) – EMA/PSUR/0000288252

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010762/202505)

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

16.2.1. Cetrorelix - CETROTIDE (CAP); NAP – EMA/PSUR/0000288224

Applicants: Merck Europe B.V., various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000633/202504)

16.2.2. Fesoterodine – TOVIAZ (CAP); NAP – EMA/PSUR/0000288254

Applicants: Pfizer Europe MA EEIG, various

PRAC Lead: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00001387/202504)

16.2.3. Olanzapine - ZALASTA (CAP); ZYPADHERA (CAP); ZYPREXA (CAP); ZYPREXA VELOTAB (CAP); NAP – EMA/PSUR/0000288282

Applicants: Cheplapharm Registration GmbH, KRKA tovarna zdravil d.d. Novo mesto, various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010540/202503)

16.2.4. Tacrolimus (topical formulations) - PROTOPIC (CAP); NAP – EMA/PSUR/0000288228

Applicants: LEO PHARMA A/S, various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00002840/202503)

16.2.5. Telmisartan / Amlodipine - TWYNSTA (CAP); NAP – EMA/PSUR/0000288216

Applicants: Boehringer Ingelheim International GmbH, various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000180/202503)

16.2.6. Zonisamide - ZONEGRAN (CAP); NAP – EMA/PSUR/0000288293

Applicants: Amdipharm Limited, various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00003152/202503)

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

16.3.1. Carvedilol / ivabradine (NAP) – EMA/PSUR/0000288241

Applicants: various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010883/202504)

16.3.2. Ethinylestradiol / levonorgestrel (NAP) – EMA/PSUR/0000288262

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00001309/202504)

16.3.3. Ivermectin (systemic use) (NAP) – EMA/PSUR/0000288278

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00010377/202504)

16.3.4. Ofloxacin (systemic use) (NAP) – EMA/PSUR/0000288261

Applicants: various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00002203/202504)

16.3.5. Reboxetine (NAP) – EMA/PSUR/0000288277

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00002615/202504)

16.3.6. Sulprostone (NAP) – EMA/PSUR/0000288256

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00002828/202504)

16.3.7. Triamcinolone (intraocular formulations) (NAP) – EMA/PSUR/0000288267

Applicants: various

PRAC Lead: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010292/202503)

16.4. Follow-up to PSUR/PSUSA procedures

16.4.1. Dolutegravir – TIVICAY (CAP) – EMA/PAM/0000268716

Applicants: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Responses to request for supplementary information on PAM/LEG submission for Tivicay, Dovato, Triumeq regarding diabetes and hypertension evaluation.

16.4.2. Dolutegravir / Abacavir / Lamivudine – TRIUMEQ (CAP) – EMA/PAM/0000268721

Applicants: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Responses to request for supplementary information on PAM/LEG submission for Tivicay, Dovato, Triumeq regarding diabetes and hypertension evaluation.

16.4.3. Dolutegravir / Lamivudine – DOVATO (CAP) – EMA/PAM/0000268725

Applicants: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: Responses to request for supplementary information on PAM/LEG submission for Tivicay, Dovato, Triumeq regarding diabetes and hypertension evaluation.

16.5. Variation procedure(s) resulting from PSUSA evaluation

16.5.1. Vortioxetine – BRINTELLIX (CAP) – EMA/VR/0000296460

Applicants: H. Lundbeck A/S

PRAC Rapporteur: Jo Robays

Scope: Update of section 4.6 of the SmPC in order to update information regarding lactation, following the PRAC Assessment Report for PSUSA/00010052/20240. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

16.6. Expedited summary safety reviews[38]

None

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)[39]

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

Applicants: 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.

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[40]

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

Applicants: 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.

17.2.2. Inavolisib – ITOVEBI (CAP) – EMA/PAM/0000301716

Applicants: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: PASS Protocol GO46271: Evaluating safety in insulin-requiring diabetic receiving inavolisib plus endrocrine therapy-based regiments in the real world.

Action: For adoption

17.2.3. Nemolizumab – NEMLUVIO (CAP) – EMA/PAM/0000269409

Applicants: Galderma International

[38] 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
[39] In accordance with Article 107n of Directive 2001/83/EC
[40] 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 Rapporteur: Liana Martirosyan

Scope: First study protocol for a non-imposed non-interventional PASS to evaluate fetal and infant outcomes following maternal exposure to nemolizumab for treatment of moderate to severe Atopic dermatitis or Prurigo nodularis during pregnancy.

17.3. Results of PASS imposed in the marketing authorisation(s)[41]

17.3.1. Sodium valproate (NAP) – EMA/PASS/0000287665

Applicants: various

PRAC Rapporteur: Liana Martirosyan

Scope: valproate PASS results [107q]: Final study results for Drug Utilisation Study extension of valproate and related substances, in Europe, using databases.

17.4. Results of PASS non-imposed in the marketing authorisation(s)[42]

17.4.1. Conestat alfa – RUCONEST (CAP) – EMA/VR/0000263304

Applicants: Pharming Group N.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of the final report from Ruconest EU registry listed as a category 3 study in the RMP. This is a non-imposed non-interventional PASS (phase IV) of C1 inhibitor Treatment Registry to assess the Safety and Immunological Profile of Ruconest in the treatment of HAE Attacks.

17.4.2. Elosulfase alfa – VIMIZIM (CAP) – EMA/VR/0000268096

Applicants: Biomarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.6, 4.8 and 5.1 of the SmPC based on final results from Morquio A Registry Study (MARS, Study 110-504) listed as a category 1 study in the RMP; this is an observational registry study to evaluate long-term safety and effectiveness of elosulfase alfa. The RMP version 7.0 has also been submitted. In addition, the MAH took the opportunity to update Annex II and to update the PI in accordance with the latest EMA excipients guideline.

17.4.3. Fenfluramine – FINTEPLA (CAP) – EMA/VR/0000296039

Applicants: UCB Pharma

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report for study EP0220 listed as a category 3 study in the RMP. This is a non-interventional study to assess the effectiveness of risk minimization

[41] In accordance with Article 107p-q of Directive 2001/83/EC
[42] 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

measures in approved indications for fenfluramine hydrochloride. The RMP version 5.1 has been updated accordingly.

17.4.4. Tofacitinib – XELJANZ (CAP) – EMA/VR/0000296333

Applicants: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the final report from RWE study A3921427 listed as a category 3 study (PASS) in the RMP. This is an observational study of effectiveness and safety of recombinant zoster vaccine (Shingrix) in moderately to severely active ulcerative colitis or rheumatoid arthritis patients treated with tofacitinib (Xeljanz) in real-world clinical care settings.

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

17.5.1. Adalimumab – HUMIRA (CAP) – EMA/PAM/0000293837

Applicants: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Karin Bolin

Scope: Eighth Annual Interim Report of Study No. P11-292 Registry: Paediatric Crohn's disease registry: A long-Term Non-Interventional Registry to Assess Safety and Effectiveness of Humira (Adalimumab) in Paediatric Patients with Moderately to Severely Active Crohn's Disease (CD).

17.5.2. Botulinum toxin type A – NUCEIVA (CAP) – EMA/PAM/0000301773

Applicants: Evolus Pharma B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Non-Interventional Post-Authorisation Safety Study of NUCEIVA for the Treatment of Moderate-to-Severe Glabellar Lines (Study EV-010) - Annual update

17.5.3. Brexucabtagene autoleucel – TECARTUS (CAP) – EMA/PAM/0000267756

Applicants: Kite Pharma EU B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Second Annual Interim Safety Report for the Category 1 (ANX) Non-interventional Post Authorisation Efficacy and Safety Study (PAES/PASS) for Tecartus (Study KT-EU-472-6036) for the MCL indication

17.5.4. Cannabidiol – EPIDYOLEX (CAP) – EMA/PAM/0000301780

Applicants: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: A Prospective, Observational Cohort Study to Assess Long-Term Safety in Patients Prescribed Epidyolex with a Focus on Drug-induced Liver Injury (Study GWEP21042) - Annual update

17.5.5. Ciltacabtagene autoleucel – CARVYKTI (CAP) – EMA/PAM/0000301551

Applicants: Janssen Cilag International, ATMP

PRAC Rapporteur: Jo Robays

Scope: Third Interim Report for Study 68284528MMY4004 - An Observational Post-authorization Safety Study to Evaluate the Safety of Multiple Myeloma Patients Treated with Ciltacabtagene Autoleucel (CARVYKTI)

17.5.6. Ciltacabtagene autoleucel – CARVYKTI (CAP) – EMA/PAM/0000304040

Applicants: Janssen Cilag International, ATMP

PRAC Rapporteur: Jo Robays

Scope: First Interim Report for Study 68284528MMY4009 – A Post-authorization Safety Study to Evaluate the Safety of Multiple Myeloma Patients Treated with Ciltacabtagene Autoleucel (CARVYKTI)

17.5.7. Dinutuximab beta – QARZIBA (CAP) – EMA/PAM/0000303342

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: An interim report for the non-interventional post-authorisation safety study (PASS)

titled: A Patient Registry of Patients with High-Risk Neuroblastoma Being Treated with the Monoclonal Antibody Dinutuximab Beta” (EUSA DB 0001)

17.5.8. Ganaxolone – ZTALMY (CAP) – EMA/PAM/0000301696

Applicants: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Study LLF001 (Candid observational study) - Interim report at milestone = after 100 participants completed the 1st year visit.

17.5.9. Infliximab – REMSIMA (CAP) – EMA/PAM/0000301635

Applicants: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Following EMA/PAM/0000245463, MAH presents the 3-year interim report for Study CT-P13 4.8. An observational, prospective cohort study to evaluate safety of Remsima SC patients with Rheumatoid Arthritis, Ankylosing Spondylitis, Psoriatic Arthritis and Psoriasis

17.5.10. Mavacamten – CAMZYOS (CAP) – EMA/PAM/0000293843

Applicants: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Interim study results for the Cat 3 PASS Study CV027012 (DISCOVER-HCM): Deliver Insights on Safety in Hypertrophic Cardiomyopathy and Observe Endpoints in Real-world. This is an observational, multicenter registry of prospectively enrolled adult patients with symptomatic (New York Heart Association [NYHA] functional class II-IV) obstructive hypertrophic cardiomyopathy (oHCM) in the United States (US) and Puerto Rico and left ventricular ejection fraction (LVEF) ≥ 55% at enrollment. The registry aims to recruit an estimated 65 sites in the US and Puerto Rico to enroll at least 550 patients with oHCM including at least 350 patients initiating treatment with mavacamten at enrollment, once it is available. Enrollment is estimated to require two years.

17.5.11. Naltrexone hydrochloride / Bupropion hydrochloride – MYSIMBA (CAP) – EMA/PAM/0000292603

Applicants: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Study NB-451: Interim report of Drug Utilisation and Safety Study (Study NB-451) for Mysimba/ Contrave in Europe and the United States.

17.5.12. Ropeginterferon alfa-2b – BESREMI (CAP) – EMA/PAM/0000295680

Applicants: Aop Orphan Pharmaceuticals GmbH

PRAC Rapporteur: Carla Torre

Scope: Submission of an interim study report of EUPAS29462: a Prospective, multicentre, non-interventional, observational, post-authorisation safety study of Ropeginterferon alfa-2b in polycythaemia vera patients.

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

Applicants: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

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

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. Asfotase alfa – STRENSIQ (CAP) – EMA/S/0000293951

Applicants: Alexion Europe

PRAC Rapporteur: Eamon O Murchu

Scope: Annual reassessment of the marketing authorisation

18.1.2. Cerliponase alfa – BRINEURA (CAP) – EMA/S/0000290075

Applicants: Biomarin International Limited

PRAC Rapporteur: Mari Thorn

Scope: Annual reassessment of the marketing authorisation

18.1.3. Eladocagene exuparvovec – UPSTAZA (CAP) – EMA/S/0000293355

Applicants: PTC Therapeutics International Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Annual reassessment of the marketing authorisation

18.1.4. Mecasermin – INCRELEX (CAP) – EMA/S/0000293938

Applicants: Esteve Pharmaceuticals S.A.

PRAC Rapporteur: Terhi Lehtinen

Scope: Annual reassessment of the marketing authorisation

18.1.5. Vestronidase alfa – MEPSEVII (CAP) – EMA/S/0000289610

Applicants: Ultragenyx Germany GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Delamanid – DELTYBA (CAP) – EMA/R/0000293774

Applicants: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Conditional renewal of the marketing authorisation

18.2.2. Exagamglogene autotemcel – CASGEVY (CAP) – EMA/R/0000290395

Applicants: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.3. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted, prepared in cell cultures) – INCELLIPAN (CAP) – EMA/R/0000302072

Applicants: Seqirus Netherlands B.V.

PRAC Rapporteur: Karin Bolin

Scope: Conditional renewal of the marketing authorisation

18.2.4. Parathyroid hormone – NATPAR (CAP) – EMA/R/0000301520

Applicants: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Rhea Fitzgerald

Scope: Conditional renewal of the marketing authorisation

18.2.5. Pemigatinib – PEMAZYRE (CAP) – EMA/R/0000302406

Applicants: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Adalimumab – YUFLYMA (CAP) – EMA/R/0000295845

Applicants: Celltrion Healthcare Hungary Kft. Kft.

PRAC Rapporteur: Karin Bolin

Scope: 5-year renewal of the marketing authorisation

18.3.2. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence – STRIMVELIS (CAP) – EMA/R/0000290462

Applicants: Fondazione Telethon Ets

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

18.3.3. Berotralstat – ORLADEYO (CAP) – EMA/R/0000282356

Applicants: Biocryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: 5-year renewal of the marketing authorisation

18.3.4. Evinacumab – EVKEEZA (CAP) – EMA/R/0000293523

Applicants: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.5. Ponesimod – PONVORY (CAP) – EMA/R/0000292277

Applicants: Laboratoires Juvise Pharmaceuticals

PRAC Rapporteur: Karin Erneholm

Scope: 5-year renewal of the marketing authorisation

18.3.6. Satralizumab – ENSPRYNG (CAP) – EMA/R/0000293585

Applicants: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

18.3.7. Thiotepa – THIOTEPA RIEMSER (CAP) – EMA/R/0000282361

Applicants: Esteve Pharmaceuticals GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.8. Tirbanibulin – KLISYRI (CAP) – EMA/R/0000293300

Applicants: Almirall S.A.

PRAC Rapporteur: Anna Mareková

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 December PRAC meeting, which was held in-person. Participants marked with "a" attended the plenary session while those marked with "b" attended the ORGAM. 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 [a,b]	Chair	Sweden	No interests declared	
Jan Neuhauser [a]	Member*	Austria	No interests declared	
Sonja Radowan [a]	Alternate*	Austria	No interests declared	
Jean-Michel Dogné [a,b]	Member	Belgium	No restrictions applicable to this meeting	
Jo Robays [a,b]	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva [a,b]	Member	Bulgaria	No interests declared	
Petar Mas [a]	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi [a,b]	Alternate	Croatia	No interests declared	
Panagiotis Psaras [a,b]	Member	Cyprus	No interests declared	
Elena Kaisis [a]	Alternate*	Cyprus	No interests declared	
Eva Jirsová [a]	Member	Czechia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Veronika Macurova [a,b]	Alternate	Czechia	No interests declared	
Marie Louise Schougaard Christiansen [a,b]	Member	Denmark	No interests declared	
Karin Erneholm [a,b]	Alternate	Denmark	No interests declared	
Maia Uusküla [a]	Member	Estonia	No interests declared	
Krõõt Aab [a]	Alternate*	Estonia	No interests declared	
Terhi Lehtinen [a,b]	Member	Finland	No interests declared	
Kimmo Jaakkola [a,b]	Alternate*	Finland	No interests declared	
Tiphaine Vaillant [a,b]	Member	France	No interests declared	
Zoubida Amimour [a,b]	Alternate	France	No participation in discussion, final deliberations and voting on:	15.3.25. EMA/VR/00002 88087 15.3.26. EMA/VR/00002 78256 16.1.22. EMA/PSUR/000 0288218 16.1.32. EMA/PSUR/000 0288264 17.5.10. EMA/PAM/0000 293843
Martin Huber [a,b]	Member*	Germany	No interests declared	
Dirk Mentzer [a]	Alternate	Germany	No interests declared	
Georgia Gkegka [a,b]	Member	Greece	No interests declared	
Maria Poulianiti [a,b]	Alternate	Greece	No participation in discussion, final deliberations	4.2.2. Valproate (NAP) and related substances 6.3.5. EMA/PSUR/000 0288225

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			and voting on:	
Julia Pallos [a,b]	Member	Hungary	No participation in discussion, final deliberations and voting on:	15.3.25. EMA/VR/000028087 15.3.26. EMA/VR/000027826 16.1.22. EMA/PSUR/0000288218 16.1.33. EMA/PSUR/0000288264 17.5.10. EMA/PAM/0000293843
Melinda Palfi [a]	Alternate*	Hungary	No interests declared	
Guðrún Stefánsdóttir [a,b]	Member	Iceland	No participation in discussion, final deliberations and voting on:	5.2.1. EMA/VR/000026735 9 15.2.2. EMA/VR/000027234 4 15.3.8. EMA/VR/000028693 5 15.3.21. EMA/VR/000025735 8
Rhea Fitzgerald [a,b]	Member	Ireland	No interests declared	
Eamon O Murchu [a,b]	Alternate	Ireland	No interests declared	
Amelia Cupelli [a,b]	Member	Italy	No interests declared	
Zane Neikena [a]	Member	Latvia	No interests declared	
Diana Litenboka [a]	Alternate*	Latvia	No interests declared	
Rugile Pilviniene [a,b]	Member	Lithuania	No restrictions applicable to this meeting	
Lina Seibokiene [a]	Alternate	Lithuania	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Magdalena Wielowieyska [a],[b]	Alternate	Luxembourg	No participation in discussion, final deliberations and voting on:	6.1.5. EMA/PSUR/0000288290 16.1.2. EMA/PSUR/0000288265 16.1.26. EMA/PSUR/0000288231 18.2.4. EMA/R/0000301520
John Joseph Borg	Member	Malta	No restrictions applicable to this meeting	
Liana Martirosyan [a],[b]	Member (Vice-Chair)	Netherlands	No interests declared	
Bianca Mulder [a]	Alternate	Netherlands	No interests declared	
David Olsen [a],[b]	Member	Norway	No participation in discussion, final deliberations and voting on:	6.2.1. EMA/PSUR/0000288281 15.3.1. EMA/VR/0000264981 16.3.2. EMA/PSUR/0000288262
Pernille Harg [a]	Alternate	Norway	No interests declared	
Adam Przybylkowski [a]	Member	Poland	No restrictions applicable to this meeting	
Ana Sofia Diniz Martins [a],[b]	Member	Portugal	No interests declared	
Carla Torre [a]	Alternate	Portugal	No restrictions applicable to this meeting	
Roxana Dondera [a],[b]	Member	Romania	No interests declared	
Irina Sandu [a]	Alternate*	Romania	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Anna Mareková [a]	Member	Slovakia	No interests declared	
Miroslava Gocova [a]	Alternate*	Slovakia	No interests declared	
Jana Pecherova[b]	Alternate*	Slovakia	No restrictions applicable to this meeting	
Polona Golmajer [a,b]	Member	Slovenia	No interests declared	
Maria del Pilar Rayon [a,b]	Member	Spain	No interests declared	
Maria Martinez Gonzalez [a]	Alternate	Spain	No interests declared	
Mari Thorn [a,b]	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin [a,b]	Alternate*	Sweden	No restrictions applicable to this meeting	
Milou-Daniel Drici [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Maria Teresa Herdeiro [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Patricia McGettigan [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Hedvig Marie Egeland Nordeng [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark [a]	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
Roberto Frontini [a,b]	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Martin Votava [a,b]	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Yiannoula Koulla [a,b]	Member*	Patients' Organisation Representative	No interests declared	
Harald Bernsteiner [a]	Expert	Austria	No interests declared	
Laurence de Fays[b]	Expert	Belgium	No interests declared	
Dominik Dautović [a]	Expert	Croatia	No interests declared	
Behija Hudina [a]	Expert	Croatia	No restrictions applicable to this meeting	
Nina Lalić [a]	Expert	Croatia	No restrictions applicable to this meeting	
Ivana Ljubičić [a]	Expert	Croatia	No interests declared	
Lora Pavlinović [a]	Expert	Croatia	No interests declared	
Lidija Prka [a]	Expert	Croatia	No interests declared	
Jana Kopecka [a]	Expert	Czech Republic	No interests declared	
Lucie Skálová [a]	Expert	Czech Republic	No interests declared	
Michaela Skorepova [a]	Expert	Czech Republic	No interests declared	
Ummahan Cakin [a]	Expert	Denmark	No restrictions applicable to this meeting	
Nicklas Hasselblad Lundstrøm [a]	Expert*	Denmark	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Signe Hertz Hansen [a]	Expert	Denmark	No interests declared	
Marian Hjortlund Allon[b]	Expert	Denmark	No interests declared	
Aviaja Højegaard Ammentorp [a]	Expert	Denmark	No interests declared	
Cecilie Louise Pedersen [a,b]	Expert	Denmark	No participation in final deliberations and voting on:	6.5.1. EMA/VR/00002 92593 15.3.31. EMA/VR/00002 64734 16.5.1. EMA/VR/00002 96460
Helle Gerda Olsen [a]	Expert	Denmark	No interests declared	
Moritz Sander [a]	Expert	Denmark	No restrictions applicable to this meeting	
Aynur Sert [a]	Expert	Denmark	No interests declared	
Per Sindahl [a]	Expert	Denmark	No interests declared	
Jean-Baptiste Bienvenu [a]	Expert	France	No interests declared	
Jeremie Botton [a]	Expert	France	No restrictions applicable to this meeting	
Benjamin Burrus [a]	Expert	France	No interests declared	
Cecile Choquet [a]	Expert	France	No interests declared	
Pauline Dayani [a]	Expert	France	No interests declared	
Camille De-Kervasdoue [a]	Expert	France	No interests declared	
Rosemary Dray-Spira [a]	Expert	France	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Dina Habib-Hanawy [a]	Expert	France	No interests declared	
Fatiha Karam [a]	Expert	France	No interests declared	
Guillaume Martinant De Preneuf [a]	Expert	France	No interests declared	
Dominique Masset [a]	Expert	France	No interests declared	
Emilie Vittaz [a]	Expert	France	No interests declared	
Dennis Lex [a,b]	Expert	Germany	No interests declared	
Laura Zein [a]	Expert	Germany	No interests declared	
Negar Babae [a]	Expert	Netherlands	No interests declared	
Esther de Vries [a]	Expert	Netherlands	No interests declared	
Marianne Klanker [a]	Expert	Netherlands	No interests declared	
Margje Monster-Simons [a]	Expert	Netherlands	No restrictions applicable to this meeting	
Hester Peltenburg [a]	Expert	Netherlands	No interests declared	
Joyce van der Heijden [a]	Expert	Netherlands	No interests declared	
Fokaline Vroom [a]	Expert	Netherlands	No interests declared	
Ruxandra-Ana Moldoveanu [a]	Expert	Romania	No interests declared	
Iulia-Maria Stanescu [a]	Expert	Romania	No restrictions applicable to this meeting	
Roxana Stefania Udrescu [a]	Expert	Romania	No interests declared	
Anna Mareková [b]	Expert	Slovakia	No interests declared	
Helena Back [a]	Expert	Sweden	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Charlotte Backman [a,b]	Expert	Sweden	No interests declared	
Rolf Gedeborg [a]	Expert	Sweden	No restrictions applicable to this meeting	
Asa Lindh [a]	Expert	Sweden	No interests declared	
Anna Schölin [a]	Expert	Sweden	No interests declared	
Gerardo Priotto [a]	Expert	WHO	No interests declared	
A representative from the European Commission attended the meeting				
Observers from Health Canada (Canada) and MHLW/PMDA (Japan) 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.

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