31 August 2026
EMA/PRAC/186037/2026
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 08-11 June 2026

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

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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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1. Introduction

1.1. Welcome and declarations of interest of members, alternates and experts

The Chairperson opened the 08-11 June 2026 meeting by welcoming all participants. The meeting was held remotely.

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

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

The Chair welcomed the new member(s) and alternate(s).

1.2. Agenda of the meeting on 08-11 June 2026

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

1.3. Minutes of the previous meeting on 04-07 May 2026

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

Post-meeting note: the PRAC minutes of the meeting held on 04-07 May 2026 were published on the EMA website on 30 June 2026 (EMA/PRAC/128532/2026).

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing Procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

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

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

See also Annex I 14.1.

4.1.1. Abemaciclib – VERZENIOS (CAP); palbociclib – IBRANCE (CAP); ribociclib – KISQALI (CAP)

Applicant: Eli Lilly Nederland B.V. (Verzenios), Novartis Europharm Limited (Kisqali), Pfizer Europe MA EEIG (Ibrance)

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

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

EPITT 20271 – New signal

Lead Member State(s): DK, PT

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 PML was identified by EMA, based on cases retrieved from EudraVigilance and literature (3 cases for abemaciclib and 5 cases for palbociclib). Four of these cases were of high diagnostic certainty and therefore a signal was confirmed. Denmark and Portugal 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 on a potential class signal of PML with CDK4/6 inhibitors, PRAC has agreed that further review of available data is warranted.

PRAC appointed Marie Louise Schougaard Christiansen as Rapporteur for the signal.

Summary of recommendation(s)

- The MAHs for Ibrance (palbociclib), Verzenios (abemaciclib) and Kisqali (ribociclib), should submit to EMA, by 26 august 2026, a cumulative review of all cases with MedDRA preferred terms 'Progressive Multifocal Leukoencephalopathy', 'Human polyomavirus infection', 'JC virus CSF test positive', 'JC virus granule cell neuronopathy', 'JC polyomavirus test positive', 'Encephalitis viral', 'Demyelination', 'JC virus infection' associated with ribociclib, palbociclib and abemaciclib as suspect drugs. The MAHs should perform a detailed analysis of all the identified cases, including a causality assessment preferably using the WHO-UMC causality assessment criteria. The cumulative review should include a review of the published literature, data from spontaneous reports and study reports from both the EudraVigilance database and MAHs' safety databases, as well as a discussion on possible biological plausibility and mechanism of this association, including any preclinical or clinical data on the impact of abemaciclib, palbociclib and ribociclib on lymphocyte counts. The MAHs should also discuss the need for any potential amendment to the product information (PI) and/or the risk management plan (RMP) and make accordingly a proposal for the changes to the relevant sections within this discussion, taking into consideration the strategy proposed by *Segec et al*[3].
- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.2. Atezolizumab – TECENTRIQ (CAP); avelumab – BAVENCIO (CAP); cemiplimab - LIBTAYO (CAP); dostarlimab – JEMPERLI (CAP); durvalumab – IMFINZI (CAP); ipilimumab – YERVOY (CAP); nivolumab – OPDIVO (CAP); nivolumab / relatlimab – OPDUALAG (CAP); pembrolizumab – KEYTRUDA (CAP); retifanlimab – ZYNYZ (CAP); serplulimab - HETRONIFLY (CAP); sugemalimab – CEJEMLY (CAP);

[3] Segec A, Keller-Stanislawski B, Vermeer NS, Macchiarulo C, Straus SM, Hidalgo-Simon A, et al. Strategy in Regulatory Decision-Making for Management of Progressive Multifocal Leukoencephalopathy. Clin Pharmacol Ther. 2015;98(5):502-5.

Applicants: Accord Healthcare S.L.U. (Hetronifly), AstraZeneca AB (Imfinzi, Imjudo), Beone Medicines Ireland Limited (Tevimbra); Bristol-Myers Squibb Pharma (Opdivo), Bristol-Myers Squibb Pharma EEIG (Opdualag, Yervoy), Cstone Pharmaceuticals Ireland Limited (Cejemly), Incyte Biosciences Distribution B.V. (Zynyz), Merck Europe B.V. (Bavencio), Merck Sharp & Dohme B.V. (Keytruda), Glaxosmithkline Trading Services Limited (Jemperli), Regeneron Ireland U.C. (Libtayo), Roche Registration GmbH (Tecentriq), Topalliance Biosciences Europe Limited (Loqtorzi)

PRAC Rapporteur: Bianca Mulder

Scope: Signal of acquired haemophilia

EPITT 20279 – New signal

Lead Member States: DE, DK, HR, NL, NO, PT, AT

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 acquired haemophilia was identified by EMA, based on cases retrieved from EudraVigilance and literature (12 for nivolumab, 14 for pembrolizumab, 4 cases for atezolizumab and 1 case for ipilimumab). The Netherlands, Portugal, Denmark, Croatia, Norway, Germany and Austria 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 has agreed that further review of available data is warranted.

PRAC appointed Bianca Mulder as Rapporteur for the signal.

Summary of recommendation(s)

- The MAHs for Opdivo (nivolumab) and Opdualag (nivolumab/relatlimab), Tecentriq (atezolizumab), Bavencio (avelumab), Libtayo (cemiplimab), Jemperli (dostarlimab), Imfinzi (durvalumab), Yervoy (ipilimumab), Keytruda (pembrolizumab), Zynyz (retifanlimab), Hetronifly (serplumimab), Cejemly (sugemalimab), Tevimbra (tislelizumab), Loqtorzi (toripalimab) and Imjudo (tremelimumab) should submit by 26 August 2026 a cumulative review of all cases of acquired haemophilia A, including a review of the published literature, data from spontaneous reports and reports from studies including all cases in EudraVigilance database, as well as a discussion on possible biological plausibility and mechanism of this association. The MAHs should also discuss the need for any potential amendment to the product information (PI) and/ or the risk management plan (RMP) and make accordingly a proposal for the changes to the relevant sections within this discussion.
- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.3. Osimertinib - TAGRISSO (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Signal of pulmonary alveolar haemorrhage

EPITT 20284 – New signal

Lead Member State: NL

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 pulmonary alveolar haemorrhage was identified by EMA, based on 11 cases retrieved from EudraVigilance and literature.

Discussion

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

Summary of recommendation(s)

- The MAH for Tagrisso (osimertinib) should submit to EMA, within the PSUR with data lock point 12 November 2026, a cumulative review of all cases of pulmonary alveolar haemorrhage associated with osimertinib as suspect drug. This analysis should include a review of the published literature, data from spontaneous reports and reports from studies including all cases in EudraVigilance database, as well as a discussion on possible biological plausibility and mechanism of this association. The MAH should also discuss the need for any potential amendment to the product information (PI) and/ or the risk management plan (RMP) and make accordingly a proposal for the changes to the relevant sections within this discussion.
- PRAC will assess the cumulative review within the PSUR procedure PSUSA/00010472/202611.

4.2. Signals follow-up and prioritisation

4.2.1. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/SDA/005

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Signal of angioedema

EPITT 20237 – Follow-up to January 2026

Background

For background information, see PRAC minutes January 2026.

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

Discussion

Having considered the available evidence in EudraVigilance, including the submitted cumulative review and additional data on time to onset, PRAC agreed that there is sufficient evidence to support a potential association between darolutamide and angioedema and that the product information should be updated to add angioedema (including laryngeal oedema, lip swelling, swelling face, and swollen tongue) as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAH for Nubeqa (darolutamide) should submit to EMA, within 2 months, a variation to update the product information[4].

4.2.2. Gemcitabine (NAP)

Applicant(s): various

PRAC Lead: Jenny Jönsson

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

EPITT 20256 – Follow-up to March 2026

Background

For background information, see PRAC minutes March 2026.

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

Discussion

Having considered all the available evidence, including data from EudraVigilance and the literature, including the responses provided by the MAHs, PRAC agreed that there is sufficient evidence to support a potential association between gemcitabine and DRESS and that the product information should be updated to add DRESS as a warning and as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAHs for gemcitabine should submit to the national competent authorities (NCAs), within 2 months, a variation to update the product information[5].

4.2.3. Valproate (NAP) and related substances[6]

Applicant(s): various

PRAC Lead: Liana Martirosyan

Scope: Signal of neurodevelopmental disorders with paternal exposure

[4] Update of SmPC section 4.8. The package leaflet is updated accordingly.
[5] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly.
[6] valproic acid, sodium valproate, magnesium valproate, valproate semisodium, valpromide

EPITT 20191 – Follow-up to December 2025

Background

For background information, see PRAC minutes December 2025[7].

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

Discussion

Taking into account the available evidence in the literature, PRAC considered uncertainty remains regarding the risk of NDD after paternal exposure to valproate during the spermatogenic risk window and therefore this should remain an important potential risk. PRAC agreed to maintain the precautionary measures in the product information and additional risk minimisation measures. The final report of the PASS TANGO study will be awaited before considering any major changes to the current risk minimisation measures in place considering the inconsistent results in the currently available studies. However, PRAC considered an update of the product information is warranted, as the current product information only describes the results of the paternal PASS whereas other available (epidemiological) studies have shown variable results. PRAC considered important to reflect this in the product information for transparency, to ensure that HCPs and patients have access to accurate and up-to-date information, and to acknowledge the totality of available evidence on this potential risk. The aRMMs (HCP guide, Patient Guide for male patients) should be updated in line with the proposed PI updates. No update of the patient card was considered necessary, as the information provided on this card remains valid and appropriate.

Summary of recommendation(s)

- The MAHs for valproate-containing products should submit to the national competent authorities (NCAs), within 2 months, a variation to update the product information[8].

4.2.4. Vortioxetine - BRINTELLIX (CAP) - EMEA/H/C/002717/SDA/011

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Jo Robays

Scope: Signal of acute pancreatitis

EPITT 20234 – Follow-up to January 2026

Background

For background information, see PRAC minutes January 2026.

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

Discussion

Having considered the available evidence in EudraVigilance and the response from the MAH, PRAC has concluded that the current evidence is insufficient to establish a causal relationship

[7] Held on 24-27 November 2025
[8] Update of SmPC sections 4.4 and 4.6. The package leaflet is updated accordingly.

between vortioxetine and pancreatitis to further warrant an update to the product information and/or risk management plan at present.

Summary of recommendation(s)

- The MAHs for vortioxetine-containing products should continue to monitor these events as part of routine pharmacovigilance.

4.2.5. X-ray contrast agents: Iobitridol (NAP); Iodixanol (NAP); Iohexol (NAP); Iomeprol (NAP); Iopamidol (NAP); Iopromide (NAP); Ioversol (NAP); Ioxitalamic acid (NAP)

Applicants: various

PRAC Lead: Pernille Harg

Scope: Signal of fixed drug eruption

EPITT 20229 - Follow-up to January 2026

Background

For background information, see PRAC minutes January 2026.

The MAHs replied to the request for information on the signal of fixed drug eruption and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance and the literature, including the cumulative review submitted by the MAHs, PRAC has agreed that there is sufficient evidence to establish a causal association between iomeprol, iodixanol, ioversol, iopromide, iopamidol, iohexol, iobitridol and ioxitalamic acid and fixed drug eruption. Therefore, PRAC agreed that the product information should be updated to add fixed drug eruption as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAHs for iomeprol, iodixanol, ioversol, iopromide, iopamidol, iohexol, iobitridol and ioxitalamic acid-containing products should submit to the national competent authorities (NCAs), within 2 months, a variation to update the product information[9]. Taking into account the already existing wording in some nationally authorised products the text may need to be adapted by MAHs to individual products.

4.2.6. Zolbetuximab - VYLOY (CAP) - EMEA/H/C/005868/SDA/002

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Signal of protein-losing gastroenteropathy

EPITT 20236 – Follow-up to January 2026

Background

For background information, see PRAC minutes January 2026.

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

The MAH replied to the request for information on the signal of protein-losing gastroenteropathy and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance and literature, including the cumulative review submitted by the MAH, PRAC agreed that there is sufficient evidence to support a potential association between zolbetuximab and protein-losing gastroenteropathy and that the product information should be updated to add gastritis and protein-losing gastroenteropathy as undesirable effects with frequency 'uncommon' and 'not known', respectively.

Summary of recommendation(s)

- The MAH should submit to EMA, within 2 months, a variation to update the product information[10].

4.3. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

5.1.1. Glepaglutide - (CAP MAA) - EMEA/H/C/005855

Scope (pre D-180 phase): Treatment of adults with short bowel syndrome

5.1.2. RABIES VIRUS (INACTIVATED) STRAIN WISTAR (PM/WI 38-1503-3M) - (CAP MAA) - EMEA/H/C/006602

Scope (pre D-180 phase): Pre-exposure and post-exposure prophylaxis against rabies in all age groups

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

See also Annex 15.2

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

5.2.1. Loncastuximab tesirine – ZYNLONTA (CAP) – EMA/VR/0000337919

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Jirsová

Scope: Submission of an updated RMP version 3.1 in order to remove the Category 3 study ADCT-402-107 (LOTIS-10). This is a phase 1b, open-label, non-randomized, dose-escalation hepatic impairment (HI) study to determine the recommended dosing regimen of loncastuximab tesirine in patients with moderate and severe HI, with assessment of safety and pharmacokinetics.

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 Zynlonta, a centrally authorised medicine containing loncastuximab tesirine, to update the RMP to reflect the removal of the category 3 study ADCT-402-107 (LOTIS-10). PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

S**ummary of advice**

- The RMP for Zynlonta (loncastuximab tesirine) in the context of the variation procedure under evaluation by PRAC and CHMP is considered acceptable.
- PRAC agreed with the removal of the category 3 study Lotis -10 as an additional pharmacovigilance from the RMP and to maintain risk management through routine pharmacovigilance through PSURs.

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

See also Annex 15.3

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

Applicant: 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.

Background

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

CHMP is evaluating variation for Skyclarys, a centrally authorised product containing omaveloxolone, to update preclinical information based on results from study RTA-P-21070.

PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

Summary of advice

- The RMP version 2.0 for Skyclarys (omaveloxolone) in the context of the variation under evaluation by CHMP is considered acceptable.
- PRAC agreed with the inclusion of 'malignancy' as important potential risk in the RMP, however did not support the proposed targeted follow-up questionnaires to address this safety concern. Regarding the pharmacovigilance plan, PRAC supported the MAH's proposal to develop a new separate non-interventional, retrospective study to characterize and contextualize the risk of malignancy among omaveloxolone-exposed and -unexposed patients with Friedreich ataxia, considering that the MAH has committed to submit a feasibility assessment of the proposed study, including further details on study design and methodological framework. Finally, PRAC agreed that routine risk minimization measures are sufficient to adequately manage the safety risks of the medicinal product.

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 16.1

6.1.1. Acalabrutinib – CALQUENCE (CAP) – EMA/PSUR/0000327904

Applicant: AstraZeneca AB

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00010887/202510)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Calquence, a centrally authorised medicine containing acalabrutinib 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 Calquence (acalabrutinib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include oedema peripheral as an undesirable effect with a frequency 'very common'. Therefore, the current terms of the marketing authorisation(s) should be varied[11].

[11] 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

- In the next PSUR, the MAH should continue to monitor and provide cumulative data on ventricular arrhythmias, cardiac failure and myocardial infarction, as separate analysis, from clinical trials and (long-term) extension studies. Additionally, the MAH should provide a cumulative analysis of Stevens-Johnson syndrome (SJS) reports from all relevant sources, with a proposal for updating product information if 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.

6.1.2. Avacopan – TAVNEOS (CAP) – EMA/PSUR/0000327958

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010967/202509)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tavneos, a centrally authorised medicine containing avacopan 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 Tavneos (avacopan) in the approved indication(s) remains unchanged. This conclusion is without prejudice to the ongoing article 20 referral procedure (EMA/REF/0000325221).
- Nevertheless, the product information should be updated to amend existing information on the use in patients with renal impairment and on the risk of liver injury. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In view of the totality of the new liver safety related data, PRAC also considered that there is a need to further communicate on the updated recommendations. Therefore, PRAC endorsed a DHPC, together with a communication plan, to inform healthcare professionals on the introduction of a strengthened liver monitoring advice, as well as new stopping rules.
- In the next PSUR, the MAH should ensure consistent reporting of fatal cases, discuss the potential higher risk of developing serious liver-related undesirable effects by Japanese patients and possible mechanism(s) for this observed geographical difference, and evaluate the effectiveness of the new liver monitoring recommendations.
- The MAH should address all relevant information related to the important identified risk of liver injury in the next RMP update to be submitted at the latest by 24 July 2026.

The frequency of PSUR submission should be revised from three-yearly to 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.

[12] Update of SmPC sections 4.2, 4.4 and 5.2. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

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

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Dirk Mentzer

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

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Ixchiq, a centrally authorised medicine containing chikungunya vaccine (live) 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 Ixchiq (chikungunya vaccine (live)) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a restriction of the indication to individuals 'at a high risk of acquiring chikungunya infection' and to amend the warning regarding use of chikungunya vaccine (live). Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- PRAC also considered that there is a need to further communicate on the restriction of the indication, thus PRAC endorsed a DHPC to be circulated in the Member States where the product is currently on the market to inform healthcare professionals of the updated recommendations, together with a communication plan.
- In the next PSUR, the MAH should provide complete case-level causality assessments using the WHO - Adverse Event Following Immunization (AEFI) algorithm, including discussion of temporal relationship and potential risk factors, and consistently address serious individual case safety reports (ICSRs) with fatal outcome. Additionally, the MAH should list all co-administrations with other vaccines and to discuss the potential influence of the co-vaccination on the reported event(s), as well as to address 'thrombotic microangiopathy and multiorgan injury' as a monitored safety topic in PSURs.

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. Mercaptamine – PROCYSBI (CAP); Mercaptamine bitartrate – CYSTAGON (CAP) – EMA/PSUR/0000327901

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Evaluation of a PSUSA procedure (PSUSA/00010573/202510)

Background

[13] Update of SmPC sections 4.1 and 4.4. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Procysbi and Cystagon, centrally authorised medicines containing mercaptamine 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 Procysbi and Cystagon (mercaptamine) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAHs should continue monitoring of psychiatric disorders and fibrosing colonopathy, and provide detailed assessments of all pregnancy cases, including exposure duration, concomitant medications, potential abortion causes, and live-birth follow-up. The MAHs should also thoroughly evaluate reported sub-ileus/constipation cases. In addition, the MAH of Procysbi should provide all cases related to gastrostomy tube obstruction, specifically for PTs 'device occlusion', 'product administration error (tube blockage)', and 'complication associated with device (tube blockage)'.
- The MAH of Procysbi should update the RMP in line with GVP Module V Rev.2, at the next regulatory opportunity, removing the well-characterised important identified risk 'leukopenia' from the summary 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. Palopegteriparatide – YORVIPATH (CAP) – EMA/PSUR/0000327865

Applicant: Ascendis Pharma Bone Diseases A/S

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure (PSUSA/00000173/202511)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Yorvipath, a centrally authorised medicine containing palopegteriparatide 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 Yorvipath (palopegteriparatide) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include hypersensitivity and anaphylactic reaction as undesirable effects with frequency 'uncommon' and 'not known', respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[14].

[14] 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

- In the next PSUR, the MAH should further monitor cases reporting anaphylactic reactions.

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

6.1.6. Pegcetacoplan – ASPAVELI (CAP) – EMA/PSUR/0000327907

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010974/202511)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Aspaveli, a centrally authorised medicine containing pegcetacoplan 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 Aspaveli (pegcetacoplan) 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 further characterise off-label use including any new related safety concerns, closely monitor reported cases involving biopsy findings and potential renal effects, prospectively and retrospectively, particularly in C3G or IC-MPGN patients.
- At the next regulatory opportunity affecting the RMP, the MAH should remove 'controlled distribution' as additional risk minimisation measure (aRMM) from the RMP, while the patient card, SmPC and package leaflet, RMP Annex 6 and Annex II should be updated to reflect vaccination and revaccination requirements against encapsulated bacteria in line with national guidelines. The healthcare professional guide and patient/caregiver guide should no longer address the important potential risk of intravascular haemolysis (IVH) after drug discontinuation in paroxysmal nocturnal haemoglobinuria (PNH) patients. The MAH should rigorously follow up biopsy findings and potential renal effects in patients with C3G or IC-MPGN, introduce a dedicated follow-up questionnaire in the RMP, and assess whether ongoing studies and possible protocol updates could provide further data on polyethylene glycol (PEG) accumulation.

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. Ranibizumab – BYOOVIZ (CAP); EPRUVY (CAP); LUCENTIS (CAP); RANIVISIO (CAP); RIMMYRAH (CAP); XIMLUCI (CAP) – EMA/PSUR/0000327906

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00002609/202510)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Byooviz, Epruvy, Lucentis, Ranivisio, Rimmyrah, Ximluci, centrally authorised medicines containing ranibizumab 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 Byooviz, Epruvy, Lucentis, Ranivisio, Rimmyrah, Ximluci (ranibizumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include retinal vasculitis and retinal occlusive vasculitis as undesirable effects with frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[15].

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. Zanubrutinib – BRUKINSA (CAP) – EMA/PSUR/0000327900

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010960/202511)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Brukinsa, a centrally authorised medicine containing zanubrutinib 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 Brukinsa (zanubrutinib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include nausea as an undesirable effect with frequency 'very common' in monotherapy and 'common' in combination with obinutuzumab. Therefore, the current terms of the marketing authorisation(s) should be varied[16].
- In the next PSUR, the MAH should provide cumulative reviews of risks of syncope and acute kidney injury (AKI), discussing whether updates to the product information are warranted.

[15] 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
[16] 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

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. Methotrexate - JYLAMVO (CAP); NORDIMET (CAP), NAP – EMA/PSUR/0000327873

Applicants: Nordic Group B.V. (Nordimet), Oresund Pharma ApS (Jylamvo), various

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00002014/202510)

Background

Methotrexate is a folic acid analogue that belongs to the therapeutic classes of antimetabolites and immunosuppressants. It is indicated as a chemotherapeutic agent and also, in low doses, used in the treatment of certain autoimmune diseases.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Jylamvo and Nordimet, centrally authorised medicines containing methotrexate and nationally authorised medicines containing methotrexate 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 methotrexate-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include epidermal necrosis as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[17].
- In the next PSUR, the MAH(s) should apply established causality assessment guidelines (e.g. WHO Uppsala monitoring centre (UMC)), report overdose and medication error cases separately by formulation and (non-)EEA region and continue evaluating the effectiveness of Article 31 risk minimisation measures for once-weekly dosing in inflammatory diseases. Furthermore, the MAHs should ensure adequate reporting of reproductive toxicity, include geographical distribution for skin cancer cases, provide updates or statements on recognised risks where applicable (only for the MAHs Easymed, Laboratorios Gebro Pharma and Oresund Pharma), and submit a cumulative review of electrolyte disturbance with a proposed term and system organ class (SOC) allocation. Finally, MAHs should comment on limiting PSUR safety concerns to a core list covering important identified risks for all and non-oncological indications, one important potential risk of skin cancer including malignant melanoma, and no missing information.
- The MAH Pfizer Limited should submit, within 3 months, a worksharing variation, (Germany acting as Rapporteur), that comprehensively reviews and discusses the

[17] 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

pharmacokinetic interactions between methotrexate and anticonvulsants (i.e., levetiracetam, phenytoin, valproate and carbamazepine), including consequences for both methotrexate and the specific anticonvulsant. The review should assess whether product information updates or specific clinical measures are warranted, distinguishing between low-dose (inflammatory diseases) and high-dose (haemato-oncological indications) of methotrexate.

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

See also Annex I 16.3.

6.3.1. A-tocopheril, a-tocopherol, vitamin E – EMA/PSUR/0000327898

Applicants: various

PRAC Rapporteur: Roxana Stefania Udrescu

Scope: Evaluation of a PSUSA procedure (PSUSA/00003186/202511)

Background

Vitamin E is a lipid-soluble vitamin that acts as an antioxidant and also has a role in heme biosynthesis, steroid metabolism, and collagen formation. Alpha-tocopherol is the most biologically active form. Vitamin E is indicated in adults and children for the treatment of malabsorption disorders: cystic fibrosis, abetalipoproteinemia, chronic cholestasis, hepato-biliary tract disease with malabsorption syndromes, pancreatic impairment, elemental enteral feeding.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing a-tocopheril, a-tocopherol, vitamin E 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 A-tocopheril, a-tocopherol, vitamin E-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning about the increased risk of haemorrhagic events in patients with vitamin K deficiency or on concomitant anticoagulant treatment with vitamin K antagonists, to add the interaction between vitamin E and vitamin K antagonists, as well as a recommendation for vitamin E overdose management. Therefore, the current terms of the marketing authorisation(s) should be varied[18].
- In the next PSUR, the MAH(s) should include in the list of safety concerns the risk of coagulation disorders leading to haemorrhagic events in patients with vitamin K

[18] Update of SmPC sections 4.4, 4.5 and 4.9. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

deficiency or on treatment with vitamin K antagonists as an important identified risk and use in pregnancy as missing 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.

6.3.2. Bisoprolol – EMA/PSUR/0000327936

Applicants: various

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00000419/202509)

Background

Bisoprolol is a beta-blocker and is indicated for the treatment of hypertension, coronary heart disease and stable chronic heart failure in combination with angiotensin-converting-enzyme (ACE) inhibitors, diuretics and cardiac glycosides. Furthermore, bisoprolol by Merck and Sandoz is also indicated for hyperkinetic heart syndrome and bisoprolol by Sandoz is indicated for ventricular extra systoles.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing bisoprolol 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 bisoprolol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning regarding the risk of severe hypoglycaemia with the concomitant use of beta-blockers and sulfonylureas. Therefore, the current terms of the marketing authorisation(s) should be varied[19].
- In the next PSUR, the MAHs should closely monitor cases of Torsade de pointes, elevated antinuclear antibodies (ANA)/lupus diseases, hyperkalaemia, tinnitus, and interaction with dabigatran and should provide comprehensive reviews of cases of severe cutaneous reactions (SCARs).

The frequency of PSUR submission should be revised from five-yearly to six-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.

6.3.3. Bisoprolol / perindopril – EMA/PSUR/0000327893

Applicants: various

PRAC Rapporteur: Jana Pecherova

[19] Update of SmPC sections 4.4 and 4.5. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

Scope: Evaluation of a PSUSA procedure (PSUSA/00010462/202510)

Background

Bisoprolol/perindopril is a fixed-dose combination of bisoprolol, a beta-blocker, combined with perindopril, an angiotensin converting enzyme (ACE) inhibitor. It is indicated as substitution therapy for treatment of hypertension and/or stable coronary artery disease (in patients with a history of myocardial infarction and/or revascularization) and/or stable chronic heart failure (only for strengths 5mg/5mg and 10mg/5mg) with reduced systolic left ventricular function in adult patients adequately controlled with bisoprolol and perindopril given concurrently at the same dose level.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing bisoprolol/perindopril 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 bisoprolol/perindopril-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning regarding the risk of severe hypoglycaemia with the concomitant use of bisoprolol/perindopril and sulfonylureas. Therefore, the current terms of the marketing authorisation(s) should be varied[20].

The frequency of PSUR submission should be revised from five-yearly to seven-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. Carbidopa / levodopa – EMA/PSUR/0000327864

Applicants: various

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00000548/202510)

Background

Carbidopa/levodopa is a fixed-dose combination which belongs to the pharmacotherapeutic group of anti-Parkinson drugs, dopaminergic agents, dopa and dopa derivatives. It is indicated in patients with idiopathic Parkinson's disease, in particular to shorten the 'off' period in patients who have previously been treated with immediate-release levodopa/decarboxylase inhibitors or with just levodopa and who showed motor fluctuations.

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

Summary of recommendation(s) and conclusions

[20] Update of SmPC sections 4.4 and 4.5. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

- Based on the review of the data on safety and efficacy, the benefit-risk balance of carbidopa/levodopa-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning about seizures associated with decreased levels of vitamin B6 and to add vitamin B6 deficiency as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[21].
- In the next PSUR, the MAH(s) should continue monitoring cases in the standardized MedDRA query (SMQ) 'embolic and thrombotic events', as well as to monitor cases of the preferred term (PT) 'fibroma', providing detailed information only for cases in patients under 65 years of age, and review cases of "hostility/aggressive behaviour" from all available sources while considering whether product information updates 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.

6.3.5. Dinoprostone – EMA/PSUR/0000327945

Applicants: various

PRAC Rapporteur: Jenny-Maria Jönsson

Scope: Evaluation of a PSUSA procedure (PSUSA/00001104/202509)

Background

Dinoprostone is a prostaglandin of the E series (PGE2) which stimulates the myometrium of the gravid uterus to contract in a manner similar to that seen during labour. In addition to this oxytocic effect, dinoprostone has a local cervical effect in initiating softening, effacement, and dilatation. It is indicated in the induction of labour and therapeutic termination of pregnancy.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing dinoprostone 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 dinoprostone-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- The MAH Ferring should submit, within 3 months, a worksharing variation (Sweden acting as Rapporteur), with further assessment of medication errors. This review should include further information related to the cases' timing in relation to direct healthcare professional communication (DHPC) dissemination, DHPC distribution dates and Member

[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 CHMP for adoption of an opinion

States, and an assessment of whether additional risk minimisation measures 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.

6.3.6. Pipamperone – EMA/PSUR/0000327872

Applicants: various

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00002420/202510)

Background

Pipamperone is a weakly potent neuroleptic from the class of butyrophenones. It is indicated for several psychiatric indications, mainly psychosis, sleep disorders and agitation.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing pipamperone 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 pipamperone-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning about risks of long-term use in the paediatric population and to add weight increased and increased appetite as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[22].
- In the next PSUR, the MAH(s) should report patterns leading to medication errors.
- The MAH(s) should remove all safety concerns from the RMP at the next RMP update submission within six months.

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.

6.3.7. Ramipril / bisoprolol – EMA/PSUR/0000327914

Applicants: various

PRAC Rapporteur: Jana Pecherova

Scope: Evaluation of a PSUSA procedure (PSUSA/00011041/202510)

Background

[22] 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

Ramipril/bisoprolol is a fixed-dose combination of ramipril, an angiotensin converting enzyme (ACE) inhibitor, combined with bisoprolol, a beta-blocker. It is indicated as substitution therapy for treatment of hypertension, and/or hypertension with coexisting chronic coronary syndrome, chronic coronary syndrome (in patients with a history of myocardial infarction and/or revascularisation) and/or chronic heart failure with reduced systolic left ventricular function in adult patients, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing ramipril/bisoprolol 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 ramipril/bisoprolol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning and an interaction about the risk of severe hypoglycaemia associated with the concomitant use of ramipril/bisoprolol and sulfonylureas. Therefore, the current terms of the marketing authorisation(s) should be varied[23].

The frequency of PSUR submission should be revised from five-yearly to seven-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. Terbinafine – EMA/PSUR/0000327909

Applicants: various

PRAC Rapporteur: Jana Pecherova

Scope: Evaluation of a PSUSA procedure (PSUSA/00002896/202509)

Background

Terbinafine is an antimycotic agent for systemic and topical use. Systemic terbinafine is indicated for the treatment of fungal infections of the skin, hair and nails caused by dermatophytes such as Trichophyton (e.g. *T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum), Microsporum canis and Epidermophyton floccosum*; the treatment of ringworm (i.e*.,* tinea corporis, tinea cruris and tinea pedis) where oral therapy is considered appropriate due to the site, severity or extent of the infection; and the treatment of onychomycosis. Topical terbinafine is indicated for the treatment of fungal infections of the skin: infections caused by the dermatophytes (i.e., tinea pedis, tinea cruris and tinea corporis); candidiasis of the skin; and *Pityriasis versicolor.*

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

Summary of recommendation(s) and conclusions

[23] Update of SmPC sections 4.4. and 4.5. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

- Based on the review of the data on safety and efficacy, the benefit-risk balance of terbinafine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend a warning about haematological effects and to add thrombotic thrombocytopenic purpura as an undesirab*le* effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[24].
- In the next PSUR, the MAH(s) should continue routine pharmacovigilance monitoring of drug-induced bullous pemphigoid, lichenoid drug eruption and generalised pustular psoriasis, and provide a comprehensive description of relevant cases. Furthermore, the MAHs of systemic formulations should further monitor cases of renal impairment and suicidal behaviour/ideation. Finally, the MAHs Aurobindo and Medreich PLC should provide a more detailed evaluation of medication error cases, focusing on serious cases.

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 16.4.

6.5. Variation procedure(s) resulting from PSUSA evaluation

See Annex 16.5

6.6. Expedited summary safety reviews[25]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[26]

See also Annex 17.1

7.1.1. Donanemab – KISUNLA (CAP) – EMA/PASS/0000339404

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: PASS protocol [107n]: A registry-based observational study to characterise ARIA within a cohort of donanemab-treated patients in the EU (Protocol I5T-MC-B015)

[24] 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
[25] 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
[26] In accordance with Article 107n of Directive 2001/83/EC

Background

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

In order to fulfil the obligation to conduct a PASS imposed in accordance with Article 107n(3) of Directive 2001/83/EC, the MAH submitted on 23 March 2026 a PASS protocol version 1.0 to the EMA for Kisunla (donanemab).

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 1.0 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 objectives at this stage.
- PRAC therefore recommended to revise the study design and to propose a controlled observational study including one or more appropriate comparator populations and an extended follow-up duration. Depending on the specific study objectives, different comparator populations may be warranted. In addition, the MAH should justify the selection of each proposed comparator population, demonstrate its appropriateness for the corresponding study objectives, and provide evidence of the feasibility of the proposed comparative design within the selected data source(s). Where this cannot be adequately ensured, additional suitable data sources and/or registry initiatives should be explored.
- The MAH should submit a revised PASS protocol within 60 days to EMA. A 60 days-assessment timetable will be followed.

7.1.2. Donanemab – KISUNLA (CAP) – EMA/PASS/0000339391

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: PASS protocol [107n]: Secondary database study to characterise safety, drug utilisation and effectiveness of risk minimisation activities in donanemab treated patients in the EU (Protocol I5T-MC-B017)

Background

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

In order to fulfil the obligation to conduct a PASS imposed in accordance with Article 107n(3) of Directive 2001/83/EC, the MAH submitted on 23 March 2026 a PASS protocol version 1.0 to the EMA for Kisunla (donanemab).

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 1.0 in accordance with Article 107n of Directive 2001/83/EC, PRAC considered that the study is non-interventional but 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 objectives at this stage.

- PRAC therefore recommended to revise the study protocol, particularly with respect to the implementation of pooled analyses, clarification of interim reporting plans, the adequacy and completeness of the selected data sources for assessing compliance with risk minimisation measures, the predefinition of success criteria and thresholds for evaluating the effectiveness of these measures, and strengthening of analytical robustness—to ensure the study can reliably inform the real-world safety profile of donanemab and the effectiveness of its 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)[27]

See also Annex 17.2

7.2.1. Donanemab – KISUNLA (CAP) – EMA/PAM/0000338752

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Cat. 3 study: Healthcare provider survey to assess the effectiveness of the donanemab additional risk minimisation activities in the EU

Background

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

As part of the RMP for Kisunla (donanemab), the MAH for was required to conduct a study to evaluate the effectiveness of the additional risk minimisation measures (aRMMs) implemented for donanemab among healthcare professionals (HCPs). The MAH submitted protocol version 1.0 for the study which was assessed by the Rapporteur. PRAC was requested to provide advice to CHMP on the protocol submitted by the MAH.

Summary of advice

- The study protocol for Kisunla (donanemab) could be acceptable provided an updated protocol and satisfactory responses to a request for supplementary information (RSI) is submitted to EMA by 18 August 2026.
- Together with the revised protocol, the MAH should also submit the feasibility assessment results. In addition, the MAH should also revise the predefined effectiveness threshold, provide further clarification on the proposed country selection strategy and its impact on the representativeness and generalisability of the survey findings at EU level. Among others, the MAH should provide further information on data management, user testing methodology and quality control procedures, as well as further clarification on the proposed questionnaires.

[27] 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

- The review of the revised protocol will follow a 74-day timeline.

7.3. Results of PASS imposed in the marketing authorisation(s)[28]

See Annex 17.3

7.4. Results of PASS imposed and non-imposed in the marketing authorisation(s)[29]

See also Annex 17.4

7.4.1. Laronidase – ALDURAZYME (CAP) – EMA/VR/0000282056

Applicant: Sanofi B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Submission of the final report from PASS study ALID01803 listed as a category 3 study in the RMP. This is an observational, open-label study of the effects of Aldurazyme (laronidase) treatment on lactation in postpartum women with Mucopolysaccharidosis Type I and their breastfed infants. This study is to determine whether laronidase activity was present in the breast milk of mothers with MPS I disease and whether Aldurazyme affected the growth, development, and immunologic response of breastfed infants. The RMP version 2.0 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 Aldurazyme (laronidase), the MAH conducted a non-imposed non-interventional PASS to study the effects of Aldurazyme (laronidase) treatment on lactation in postpartum women with Mucopolysaccharidosis Type I and their breastfed infants. The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI).

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 considered that the product information should be updated to revise the wording of breastfeeding/lactation section (SmPC section 4.6 and package leaflet) to reflect that there is insufficient information regarding the excretion of laronidase in the human milk and that that no adverse effects have been reported in a very limited number of breastfed infants whose mothers were treated with Aldurazyme during breast-feeding. In addition, a decision whether to breastfeed during treatment with Aldurazyme should take into account the benefits of breast-feeding for mother and infant, the benefits of treatment for the mother, and the potential risk of adverse

[28] In accordance with Article 107p-q of Directive 2001/83/EC
[29] 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

reactions in the breastfed infant.

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

See Annex 17.5.

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

8.1. Annual reassessments of the marketing authorisation

See Annex 18.1

8.2. Conditional renewals of the marketing authorisation

See Annex 18.2

8.3. Renewals of the marketing authorisation

See Annex 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.

None

9.3. Others

None

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

10.1.1. Levofloxacin (intravenous and oral use) – DE/H/5119/001-003/II/118

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

PRAC Lead: Dennis Lex

Scope: PRAC consultation on a type II national variation to update the product information

regarding the risk of encephalopathy, at request of Germany.

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 the context of a type II national variation concerning the proposed inclusion of the risk of encephalopathy in the product information of levofloxacin-containing medicinal products for intravenous and oral use, 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 sufficient to support a causal relationship between levofloxacin and encephalopathy. In particular, PRAC noted data on encephalopathy from the literature and spontaneous reports, which included cases of close temporal relationship and positive dechallenge, as well as the existence of a plausible mechanism of action. As a consequence, PRAC considered it warranted to update the product information of levofloxacin-containing medicinal products (intravenous and oral use) to reflect the risk of encephalopathy (SmPC section 4.4, 4.7, 4.8 and 4.9 and package leaflet). Nonetheless, PRAC considered that further revisions to the proposed text for SmPC section 4.4 are warranted, taking into account existing warnings on encephalopathy included in the product information of other antibiotics. This text should be less stringent in the context of an immediate discontinuation of levofloxacin. Further on, PRAC confirmed that the updates to the product information to reflect the risk of encephalopathy applies to all levofloxacin-containing medicinal products for intravenous and oral use which were part of the PSUSA procedure (PSUSA/00010767/202310).

10.1.2. Mycobacterium bovis BCG, Danish strain 1331 – DK/H/3659/001/II/001

Applicant(s): AJ Vaccines A/S

PRAC Lead: Karin Erneholm

Scope: PRAC consultation on a type II national variation to update the product information, to implement additional risk minimisation measures and to disseminate a direct healthcare professional communication (DHPC) regarding the risk of reactivation of latent BCG infection, at request of Denmark.

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 the context of a type II national variation on the need for additional risk minimisation measures for Mycobacterium bovis, Danish strain 1331 (Vesiculture) regarding the risk of reactivation of latent BCG infection, Denmark requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC agreed that the currently implemented routine risk minimisation measures are sufficient to address this known

risk of reactivation of latent BCG infection, which is adequately reflected in the product information. PRAC considered that no new safety concerns have emerged that would warrant additional risk minimisation measures and therefore concluded that implementation of a patient card is not recommended. Similarly, a DHPC was not considered warranted. PRAC further agreed that a harmonised approach across all intravesical BCG immunotherapy products is desirable, as no product-specific increased risk has been identified. In this context, PRAC acknowledged that a patient card is currently implemented for certain products. For these products, the patient card may remain in place pending the planned reassessment by the MAH of its effectiveness. Following completion of this reassessment, expected in 2028, a final harmonised position should be considered across all intravesical BCG immunotherapy products regarding the implementation or discontinuation of a patient card. PRAC noted and acknowledged other PRAC members comments raised in relation to the SmPC and PL, but considered that these comments are outside the scope of the PRAC advice and/or outside the specific question(s) addressed to PRAC, which focuses solely on whether there is a need for a patient card, DHPC, and harmonization across all intravesical BCG immunotherapy products. PRAC suggested that these comments are addressed within the ongoing procedure (DK/H/3659/001/II/001) as part of the Concerned MS (CMS) comments.

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

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Extension of indication to include the treatment of severe alopecia areata (AA) in adult and adolescents 12 years and older for RINVOQ, based on interim results from 2 pivotal, Phase 3 studies (M23-716 Study 1 and Study 2); those are randomized, double blind, placebo-controlled, multi-center studies of Upadacitinib evaluating the efficacy and safety of Upadacitinib 15 mg QD and 30 mg QD versus placebo for the treatment of severe AA in subjects who are at least 12 years of age. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Annex II are updated in accordance. Version 18.0 of the RMP has also been submitted. As part of the application, the MAH is requesting a 1-year extension of the market protection.

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.

A type II variation proposing to update the product information of Rinvoq to include the treatment of severe alopecia areata (AA) is under evaluation at CHMP. The PRAC was requested to provide advice on this variation.

Summary of advice

- PRAC discussed the CHMP request for PRAC advice for Rinvoq (upadacitinib) on the applicability to the new alopecia areata (AA) indication of the class warning, implemented during the Article 20 procedure Janus kinase inhibitors (JAKi) (EMEA/H-A20/1517/C/004760/0017), stating that upadacitinib should only be used if no suitable

treatment alternatives are available in patients over 65 years of age, patients with cardiovascular risk factors or patients with malignancy risk factors.

- PRAC considered that the previously agreed class warning in section 4.4 of the SmPC implemented during the Article 20 procedure for JAKi (EMEA/H-A20/1517/C/004760/0017), including the boxed warning with recommendation to use upadacitinib in patients with risk factors only if no suitable treatment alternatives are available, is also applicable for upadacitinib in the newly proposed indication of AA.

  As per the conclusions of the Article 20 procedure, the serious adverse events of major adverse cardiovascular events (MACE), venous thromboembolism (VTE), malignancies and serious infections are considered class effects for the JAKis included in the procedure, applicable across all the approved indications. To minimise these risks, an approach focused on identifiable individual risk factors has been implemented. Although the incidence of patients with risk factors for these safety events might be lower in the AA population, the data submitted by the MAH in the ongoing extension of indication, including indirect comparisons with ritlecitinib, do not allow conclusion that such patients with risk factors are at lower risk of developing these adverse reactions when compared to patients with risk factors in any other approved indication of upadacitinib. The PRAC further noted that the AA indication was part of the Article 20 procedure, and that the class warning was also applied for this indication at that time. In conclusion, PRAC considered that the agreed wording of section 4.4 of the SmPC implemented during the Article 20 procedure, including the boxed warning, should be maintained for upadacitinib for the new indication of AA, as the concerned risks are primarily driven by patient-related risk factors and exposure to the JAK inhibitor rather than by the underlying disease.

- Based on the evaluation of the data submitted in the extension of indication procedure for Rinvoq in the treatment of AA, PRAC concluded that there is no new upadacitinib-specific evidence justifying an update of the warning for the new AA indication. Hence, PRAC concluded that it is not warranted to adapt the currently present warning in section 4.4 of the SmPC on risks of serious infection, malignancy, MACE, VTE and use in patients 65 years of age and older.

11. Scientific advice procedures

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

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The Chair welcomed Jenny-Maria Jönsson as the new alternate for Sweden replacing Karin Bolin who took over the role of member for Sweden.

12.1.2. Nominated proxy

None

12.1.3. Scientific Committee Meetings – alternating face-to-face and virtual meetings schedule for 2027

The EMA Secretariat presented the face-to-face and virtual meetings schedule for 2027. PRAC noted the information.

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. Healthcare Professionals Working Party (HCPWP) and Patients and Consumers Working Party (PCWP) – work plan 2025-2028

The EMA Secretariat informed PRAC about the 2025-2028 work plan for Patients' and Consumers' Working Party (PCWP) and the Healthcare Professionals' Working Party (HCPWP), including the shared work areas and objectives.

12.3.2. SAWP-PRAC consultation procedure – guidance update

The EMA Secretariat presented the updated guidance on PRAC consultation in scientific advice/protocol assistance procedure in order to include the process of PRAC involvement in qualification of novel methodology (QoNM) procedures. PRAC members were invited to send their comments by 25 June 2026.

Post-meeting note: The guidance document was endorsed by PRAC with no comments.

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

12.5.1. Opening procedures at EMA to non-EU authorities (OPEN) framework – PRAC involvement

The EMA Secretariat presented to PRAC the principles of OPEN framework and presented to PRAC the proposal to extend the scope to involve PRAC in the procedures part of this framework. Further information on the OPEN framework is available on the Agency's website under Scope and development of OPEN. The PRAC rules of procedure will be revised accordingly and will be presented for adoption at PRAC in July 2026. PRAC endorsed the proposal to broaden the scope of OPEN to include procedures where PRAC is involved.

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. 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 *June 2026*, reflecting the PRAC's comments impacting on the data lock point (DLP) and PSUR submission frequencies of the substances/combinations. PRAC endorsed the newly allocated Rapporteurs for upcoming PSUSAs in accordance with the principles previously endorsed by PRAC (see PRAC minutes April 2013).

Post-meeting note: following the PRAC meeting of June 2026, the updated EURD list was adopted by CHMP and CMDh at their June 2026 meetings and published on the EMA website, see: Home> Human Regulatory>Post-authorisation>Pharmacovigilance>Periodic

safety update reports>> List of Union reference dates and frequency of submission of periodic safety update reports (PSURs)

12.11. Signal management

12.11.1. Good Pharmacovigilance Practice (GVP) module IX on signal management – revision 2

PRAC lead: Dennis Lex

The EMA Secretariat presented to PRAC the scope of the revision 2 of the GVP Module IX on signal management, including an updated flowchart on EU signal management process and the timelines for drafting and publication. PRAC members were invited to provide their comments by 03 July 2026 .

Post-meeting note: Following comments received from PRAC members, the document has been revised and adopted by PRAC on 10 July 2026.

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. Benzyl alcohol and benzoic acid used as excipients in medicinal products - revised labelling requirements

The non-clinical working party Vice-chair, Karen van Malderen, presented to PRAC the proposed labelling requirements for medicinal products containing benzyl alcohol and benzoic acid, following the adoption of the revised report on benzyl alcohol and benzoic acid group used as excipients in support of the 'Questions and answers on benzyl alcohol used as an excipient in medicinal products for human use'. PRAC members were invited to provide their comments by 27 June 2026.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[30]

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[31].

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

14.1.1. Belzutifan – WELIREG (CAP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Dennis Lex

Scope: Signal of retinal oedema

EPITT 20278 – New signal

Lead Member State(s): DE

14.1.2. Cefpodoxime (NAP)

Applicant: various

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of drug interaction between cefpodoxime and proton pump inhibitor (PPIs) resulting in a potentially reduced efficacy of cefpodoxime

EPITT 20280

Lead Member State(s): IT

14.1.3. Lithium (NAP)

Applicants: various

PRAC Rapporteur: Dennis Lex

Scope: Signal of drug interaction between lithium and GLP-1 agonists leading to increased lithium levels

EPITT 20275 – New signal

Lead Member State: DE

[30] 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

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

14.1.4. Luspatercept - REBLOZYL (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Jo Robays

Scope: Signal of ventilation perfusion mismatch

EPITT 20281 – New signal

Lead Member State: BE

14.2. Signals follow-up and prioritisation

None

14.3. Variation procedure(s) resulting from signal evaluation

None

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

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

15.1.1. Omalizumab - (CAP MAA) - EMEA/H/C/006756

Scope (pre D-180 phase): Treatment of asthma, chronic rhinosinusitis with nasal polyps (CRSwNP) and chronic spontaneous urticaria (CSU)

15.1.2. Pegfilgrastim - (CAP MAA) - EMEA/H/C/006085

Scope (pre D-180 phase): Reduction of neutropoenia in adults

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. Bosentan – STAYVEER (CAP); TRACLEER (CAP) – EMA/VR/0000316336

Applicant: Janssen Cilag International

PRAC Rapporteur: Zoubida Amimour

Scope: Submission of an updated RMP version 12 for TRACLEER and STAYVEER to remove the Liver Safety Update Report (LSUR) as a routine pharmacovigilance activity for the

important identified risk of hepatotoxicity. The Annex II is updated accordingly. In addition, the MAH is updating the list of safety concerns in line with requests from PRAC in their assessment report for procedure PSUSA/00000425/202411.

15.2.2. Emtricitabine / Tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL ZENTIVA (CAP); NAP – EMA/VR/0000335678

Applicants: Zentiva k.s., various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: To update the RMP in line with the reference medicinal product:
To remove missing Information Safety in pregnancy and lactation. To add Annex 4: Specific Adverse Reaction Follow-up Questionnaire for Lack of efficacy in pre-exposure prophylaxis. And to remove Follow-up form for renal toxicity, Follow-up form for renal tubulopathy, Follow-up form for bone events, Pregnancy report form (to report pregnancy before outcome is known) and Pregnancy outcome report (to be used when pregnancy outcome is known).

15.2.3. Infliximab – REMICADE (CAP) – EMA/VR/0000338953

Applicant: Janssen Cilag International

PRAC Rapporteur: Karin Bolin

Scope: Submission of an updated RMP version 23.1 in order to reduce the planned duration of follow up in the DEVELOP registry from 20 years to 10 years for all patients currently active in the registry, which is listed as a category 3 study in the RMP, as well as to introduce additional changes to the RMP.

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

Applicant: Eisai GmbH

PRAC Rapporteur: Eva Jirsová

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

15.2.5. Tenofovir disoproxil - TENOFOVIR DISOPROXIL ZENTIVA (CAP), NAP – EMA/VR/0000342258

Applicants: Zentiva k.s., various

PRAC Rapporteur: Zoubida Amimour

Scope: Type IB, C.9.b – to provide an updated RMP update following adoption of the same changes for the reference product VIREAD RMP during procedure EMAVR0000280825.
Important Identified risks: Renal Toxicity; Bone events due to proximal renal tubulopathy / loss of bone mineral density and
Missing Information: Safety in pregnancy and lactation; Safety in patients with renal impairment were removed.
All Specific adverse reaction follow-up questionnaires were removed.

15.2.6. Teriflunomide - TERIFLUNOMIDE VIATRIS (CAP), NAP – EMA/VR/0000320266

Applicants: various

PRAC Rapporteur: Dennis Lex

Scope: C.I.11.z - to propose an updated RMP to align it with the one from reference product Aubagio® (teriflunomide) RMP version 9.1,
dated 28-Mar-2024 (MAH Sanofi), published by EMA on 12 June 2024.

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

15.3.1. Atogepant – AQUIPTA (CAP) – EMA/VR/0000334780

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Update of section 5.1 of the SmPC in order to update long term safety, tolerability and efficacy information based on final results from study 3101-312-002 listed as a category 3 study in the RMP; this is a phase 3, multicenter, open-label, 156-week extension study to evaluate the long-term safety and tolerability of oral atogepant for the prevention of migraine in participants with chronic or episodic migraine. The RMP version 2.3 has also been submitted.

15.3.2. Concizumab – ALHEMO (CAP) – EMA/VR/0000335954

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Extension of indication to include routine prophylaxis of bleeding in paediatric patients below 12 years of age with haemophilia A or B with or without inhibitors for ALHEMO, based on the results from the phase 3 study NN7415-4616; this is an open-label study investigating efficacy, safety and pharmacokinetics of concizumab prophylaxis in children below 12 years with haemophilia A or B with or without inhibitors. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor edits to the PI.

15.3.3. COVID-19 vaccine (recombinant, adjuvanted) – BIMERVAX (CAP) - EMA/VR/0000316063

Applicant: Hipra Human Health S.L.

PRAC Rapporteur: Zane Neikena

Scope: Update of section 4.5 of the SmPC in order to add coadministration information with seasonal influenza vaccines based on final results from study HIPRA-HH-11. HIPRA-HH-11 was a Phase II randomized, double-blind, multi-centre trial to evaluate the safety and immunogenicity of BIMERVAX when coadministered with seasonal surface antigen, inactivated adjuvanted influenza vaccine (SIIV) in adults older than 65 years of age fully vaccinated against COVID-19. The Package Leaflet is updated accordingly. The RMP version

3.0 is also submitted. In addition, the MAH took the opportunity to introduce minor changes to the PI.

15.3.4. Daratumumab – DARZALEX (CAP) – EMA/VR/0000334930

Applicant: Janssen Cilag International

PRAC Rapporteur: Carla Torre

Scope: Update of section 4.8 of the SmPC in order to add ''Hypotension and Weigt decreased'' to the list of adverse drug reactions (ADRs) with frequency ''Common'' and to update the description of the Summary of the safety profile to remove influenza of the serious adverse reactions based on final results from study AMY2009 listed as a category 3 study in the RMP; this is phase 2, a multicenter, prospective study of daratumumab-based therapy in newly diagnosed patients with Amyloid light-chain (AL) amyloidosis and with pre-existing Mayo Cardiac Stage II and IIIa cardiac involvement, to further characterize cardiac adverse effects in terms of incidence, severity, clinical presentation, management, and outcome, and to identify potential mitigation strategies. The package leaflet is updated accordingly. The RMP version 13.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.5. Dengue tetravalent vaccine (live, attenuated) – DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (CAP); QDENGA (CAP) – EMA/VR/0000323434

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Martirosyan

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update safety and efficacy information regarding the administration of a booster dose based on the final results of Part 5 from study DEN-301, listed as a category 3 study in the RMP; this is a Phase III, double-blind, randomized, placebo-controlled trial to investigate the efficacy, safety and immunogenicity of a Tetravalent Dengue Vaccine (TDV) administered subcutaneously in healthy children aged 4–16 years old, investigating a TDV booster dose in the booster phase (Parts 4 and 5) of the trial. The RMP version 3.3 has also been submitted. In addition, the MAH took the opportunity to introduce minor formatting changes to the PI and to update the list of local representatives in the Package Leaflet for Qdenga.

15.3.6. Dinutuximab beta – QARZIBA (CAP) – EMA/VR/0000316241

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: A grouped application, comprised of the following variations:

C.I.4: Update of sections 4.8 and 5.1 of the SmPC to introduce changes based on the final results from study APN311-304; this is a Phase II, interventional, single-arm, open-label study evaluating the anti-tumor activity and safety of dinutuximab beta (ch14.18/CHO) continuous infusion in pediatric patients with primary refractory or relapsed neuroblastoma. The Package Leaflet has been updated accordingly.

C.I.4: Update of sections 4.8 and 5.1 of the SmPC to introduce changes based on the final results from study APN311-202 V1/V2; this is a Phase I/II, interventional, multi-center, open-label study evaluating the tolerability, immunomodulatory efficacy, and anti-tumor activity of dinutuximab beta (ch14.18/CHO) administered as prolonged continuous infusion in combination with subcutaneous aldesleukin (IL-2) in pediatric patients with primary refractory or relapsed neuroblastoma. The Package Leaflet has been updated accordingly.

C.I.13: Submission of final results from study APN 311-201. This is a Phase II feasibility study using ch14.18/CHO antibody and subcutaneous interleukin 2 after haploidentical stem cell transplantation in children with relapsed neuroblastoma.

The RMP version 10.1 has also been submitted. In addition, the MAH took the opportunity to introduce changes to the PI for completion and to update excipient wording for polysorbates.

15.3.7. Enfortumab vedotin – PADCEV (CAP) – EMA/VR/0000336191

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include Padcev, in combination with pembrolizumab, as neoadjuvant treatment and then continued after radical cystectomy as adjuvant treatment, is indicated for the treatment of adults with muscle invasive bladder cancer (MIBC) who are eligible for cisplatin-containing chemotherapy, based on the results from Interim Analysis 1 of the pivotal Study KN-B15 (EV-304); this is a phase 3, randomized, open-label study to evaluate perioperative enfortumab vedotin plus pembrolizumab (MK-3475) versus neoadjuvant gemcitabine and cisplatin in cisplatin-eligible participants with Muscle-Invasive Bladder Cancer. As consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC have been updated; the Package Leaflet is updated accordingly. Version 6.1 of the RMP is submitted, to reflect the updated data. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.8. Ertugliflozin – STEGLATRO (CAP) – EMA/VR/0000335920

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of new paediatric population aged 10 years and older for STEGLATRO, based on final results from paediatric study study MK-8835-P059/B1521066 (P059). This is a randomised, double-blind, placebo-controlled trial to evaluate the safety and efficacy of two doses of ertugliflozin in paediatric patients from 10 years to less than 18 years of age with type 2 diabetes mellitus and inadequate glycaemic control on metformin therapy, ± insulin. 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 2.5 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to implement minor editorial/formatting corrections.

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

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Dennis Lex

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

15.3.10. Gemtuzumab ozogamicin – MYLOTARG (CAP) – EMA/VR/0000304835

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include, in combination with mitoxantrone and cytarabine (AraC), the treatment of paediatric patients aged 1 year to less than 18 years with newly diagnosed CD33-positive acute myeloid leukaemia (AML), except acute promyelocytic leukaemia (APL) for MYLOTARG, based on results from study MyeChild 01 (WI203680). This is a Phase 3, randomised, open-label, multicenter study incorporating an embedded dose finding study in children with newly diagnosed AML/high risk MDS /isolated myeloid sarcoma (de novo or secondary). 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 2.3 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 and to update the list of local representatives in the Package Leaflet.

15.3.11. Guanfacine – INTUNIV (CAP) – EMA/VR/0000334464

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 5.1 of the SmPC in order to update long term efficacy and safety information based on final results from study SPD503-401 listed as a specific obligation in Annex II; this is an interventional, a phase 4, long-term safety and efficacy study comprising a randomized, double-blind, parallel-group, placebo-controlled, active-comparator phase followed by an open-label phase conducted in children and adolescents aged 6 to 17 years with ADHD to assess long term safety of guanfacine; the Package Leaflet and Annex II of the PI are updated accordingly. The RMP version 5.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI.

15.3.12. Ivacaftor / Tezacaftor / Elexacaftor – KAFTRIO (CAP) – EMA/VR/0000320413

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Dennis Lex

Scope: Submission of Part A (week 96) clinical study report for study VX21-445-125 (study 125). This is a Phase 3, open-label study to evaluate the long-term safety, tolerability, efficacy, and pharmacodynamics of elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) in cystic fibrosis (CF) subjects ≥6 years of age who have qualifying non-F508del ELX/TEZ/IVA-responsive CFTR mutations. RMP version 10.3 has also been submitted.

15.3.13. Meningococcal Group A, C, W and Y conjugate vaccine – MENQUADFI (CAP) – EMA/VR/0000281377

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication for MENQUADFI to include the active immunisation of patients from 6 weeks of age based on final results from study MET58 and additional supportive clinical studies. Study MET58 is a Phase 3, immunogenicity and Safety Study of an Investigational Quadrivalent Meningococcal Conjugate Vaccine when Administered Concomitantly with Routine Pediatric Vaccines in Healthy Infants and Toddlers in Europe. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated Risk Management Plan (RMP) version 4.0 is also included.

15.3.14. Methylphenidate hydrochloride – TUZULBY (CAP) – EMA/X/0000327555

Applicant: Neuraxpharm Pharmaceuticals S.L.

PRAC Rapporteur: Dennis Lex

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (5 mg/ml powder for prolonged-release oral suspension).
The RMP version 1.1 is updated in accordance.

15.3.15. Mirabegron – BETMIGA (CAP) – EMA/VR/0000327362

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: A grouped application comprised of a Type IB and a Type II variation, as follows:

Type IB (C.7.a): To delete the Betmiga 8 mg/ml granules for prolonged-release oral suspension from the Betmiga marketing authorisation (EU/1/12/809/019, EU/1/12/809/020)

Type II (C.6.a): To modify the approved therapeutic indication for neurogenic detrusor overactivity (NDO) to patients less than 18 years of age, weighing 35 kg or more. The updated indication aligns the weight criteria for children with the remaining tablet posology. Consequently, sections 4.1, 4.2 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version 9.3 has been submitted. In addition, the MAH took the opportunity to introduce additional changes to the PI.

15.3.16. Nivolumab / Relatlimab – OPDUALAG (CAP) – EMA/VR/0000339077

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to revise the wording regarding Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis; and to add ''Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis'' to the list of adverse drug reactions (ADRs) with

frequency ''Uncommon'' based on postmarketing data and literature; the Package Leaflet is updated accordingly. The RMP version 6.0 has also been submitted.

15.3.17. Ocrelizumab – OCREVUS (CAP) – EMA/VR/0000309389

Applicant: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Extension of indication to include treatment of paediatric patients aged 10 years and older with relapsing remitting multiple sclerosis (RRMS) for OCREVUS, based on primary analysis results from the pivotal phase III study (WN42086/Operetta 2) and primary and updated results from a supportive phase II study (WA39085/Operetta 1). Operetta 1 is an open-label, parallel-group, dose-finding Phase II study to determine the dosing regimen of ocrelizumab to be further investigated in Operetta 2, and Operetta 2 is a Phase III, randomized, double-blind, double-dummy, parallel-group, multicenter, non-inferiority study to evaluate the efficacy and safety of intravenous ocrelizumab in comparison with fingolimod. As a consequence, sections 2, 4.1, 4.2, 4.4, 4.5, 4.6, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 15.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce updates to other sections of the SmPC and PL as per previous procedures linguistic review comments (sodium, pH and osmolality), updates to comply with the Excipient Guideline (polysorbates), changes to the list of local representatives in the Package Leaflet, as well as editorial and clarification changes to the PI.

15.3.18. Ocrelizumab – OCREVUS (CAP) – EMA/VR/0000313041

Applicant: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on 'Liver Injury' and to add it to the list of adverse drug reactions (ADRs) with frequency 'rare', based on a cumulative safety review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to submit a DHPC Letter and to introduce minor changes to the PI, including the Labelling section.

15.3.19. Olezarsen – TRYNGOLZA (CAP) – EMA/VR/0000336189

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of adult patients with severe hypertriglyceridemia for Tryngolza, based on final results from phase 3 studies ISIS 678354-CS5 (CORE), ISIS 678354-CS6 (CORE2) and ISIS 678354-CS9; and open-label extension study ISIS 678354-CS15. 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 1.1 of the RMP 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. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.20. Palbociclib – IBRANCE (CAP) – EMA/VR/0000316536

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Extension of indication to include, in combination with anti-HER2 and endocrine therapies, the maintenance treatment of adult patients with HR-positive, HER2-positive locally advanced or metastatic breast cancer (MBC) following induction treatment for IBRANCE, based on the interim results from the open-label Phase 3 study PATINA (AFT-38/WI215662). This is a randomized, open-label Phase 3 study evaluating the efficacy and safety of IBRANCE (palbociclib) in combination with anti-HER2 therapy and endocrine therapy compared to anti-HER2 therapy and endocrine therapy alone as a first-line maintenance therapy (following induction chemotherapy treatment) for patients with HR positive, HER2-positive MBC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. RMP version 1.10 has also been submitted.

15.3.21. Pembrolizumab – KEYTRUDA (CAP) – EMA/VR/0000336194

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include KEYTRUDA, in combination with enfortumab vedotin, as neoadjuvant treatment and then continued after radical cystectomy as adjuvant treatment, is indicated for the treatment of adults with muscle invasive bladder cancer (MIBC) who are eligible for cisplatin containing chemotherapy, based on the results from Interim Analysis 1 of the pivotal Study KN-B15 (EV-304); this is a phase 3, randomized, open-label study to evaluate perioperative enfortumab vedotin plus pembrolizumab (MK-3475) versus neoadjuvant gemcitabine and cisplatin in cisplatin-eligible participants with Muscle-Invasive Bladder Cancer. As consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC have been updated; the Package Leaflet is updated accordingly. Version 54.1 of the RMP is submitted, to reflect the updated data.

15.3.22. Pirtobrutinib – JAYPIRCA (CAP) – EMA/VR/0000316267

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adult patients with chronic lymphocytic leukaemia (CLL) for JAYPIRCA, based on interim results from studies LOXO-BTK-20023 (BRUIN-CLL-313) and LOXO-BTK-20030 (BRUIN-CLL-314). Study 20023 is a phase 3 open-label, randomized study of pirtobrutinib (LOXO-305) versus bendamustine plus rituximab in untreated patients with CLL/SLL. Study 20030 is a phase 3 open-label, randomized study of pirtobrutinib (LOXO-305) versus ibrutinib in patients with CLL/SLL. As a consequence, sections 4.1, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted.

15.3.23. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – mRESVIA (CAP) – EMA/VR/0000320244

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update clinical efficacy and safety information on the use of mRESVIA in immunocompromised individuals 18 years of age and older, based on interim results from study mRNA-1345-P303 Part B; this is a Phase 3 study to evaluate the immunogenicity and safety of mRNA-1345, an mRNA vaccine targeting respiratory syncytial virus, in high-risk adults. The updated RMP version 6.0 has also been submitted.

15.3.24. Rimegepant – VYDURA (CAP) – EMA/VR/0000339929

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to introduce an every day (QD) posology regimen for prophylaxis of migraine and to amend an existing warning on medication overuse headache (MOH), as well as to update clinical safety and efficacy information based on results from studies C4951010 and C4951011. Study C4951010 is a phase 4 randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of rimegepant in episodic migraine prevention with multiple dosing regimens, while study C4951011 is a phase 4, open-label study to evaluate the safety and tolerability of daily dosing of rimegepant in episodic migraine prevention. The Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted.

15.3.25. Ruxolitinib – OPZELURA (CAP) – EMA/VR/0000313318

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of moderate atopic dermatitis in adult patients who are inadequately controlled with, have a contraindication to, or are intolerant to topical corticosteroids and topical calcineurin inhibitors for OPZELURA, based on the results of the pivotal Phase III study INCB 18424-326 and the two supportive Phase III studies INCB 18424-303 and INCB 18424-304. INCB 18424-326 is a Phase 3b, double-blind, multicenter, randomized, vehicle-controlled, efficacy, and safety study of ruxolitinib cream in adults with moderate atopic dermatitis. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.0 of the RMP has also been submitted.

15.3.26. Sotorasib – LUMYKRAS (CAP) – EMA/VR/0000339051

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: To update Annex II and the RMP to request an 18-month extension of the due dates for the Specific Obligation (SOB) SOB2 related to the Phase 3 Study 20190341.

15.3.27. Teclistamab – TECVAYLI (CAP) – EMA/VR/0000336274

Applicant: Janssen Cilag International

PRAC Rapporteur: Veronika Macurova

Scope: Extension of indication to include treatment of adult patients with relapsed or refractory multiple myeloma who have received at least one prior therapy, for TECVAYLI as monotherapy, based on interim analysis data from the pivotal study 64007957MMY3006 (MajesTEC-9). This is a Phase 3 randomized study comparing teclistamab monotherapy versus pomalidomide, bortezomib, dexamethasone (PVd) or carfilzomib, dexamethasone (Kd) in participants with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy, including an anti-CD38 monoclonal antibody and lenalidomide. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Labelling and Package Leaflet are updated accordingly. The RMP version 6.2 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI and to update the list of local representatives in the Package Leaflet.

15.3.28. Tezepelumab – TEZSPIRE (CAP) – EMA/VR/0000321455

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

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

C.I.13: Submission of the report from study D5180C00024 (SUNRISE) listed as a category 3 study in the RMP. This is a randomised, double-blind, parallel-group, placebo-controlled 28-week phase 3 efficacy and safety study of tezepelumab in reducing oral corticosteroid use in adults with oral corticosteroid dependent asthma. The RMP version 7 has also been updated accordingly.

C.I.11: Submission of an updated RMP version 7 in order to add study D5241C00006 (EMBARK) and study D5241C00007 (JOURNEY) as additional pharmacovigilance activities to further characterize the important potential risks: “Serious infections” and “Malignancies”.

15.3.29. Tucatinib – TUKYSA (CAP) – EMA/VR/0000337235

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include in combination with trastuzumab and pertuzumab for the maintenance treatment of adult patients with unresectable locally advanced or metastatic HER2-positive breast cancer based on final results from Study H2C05. This is a Phase 3, global,randomized, double-blind, placebo-controlled study of tucatinib vs placebo in combination with trastuzumab and pertuzumab as maintenance therapy in participants with advanced HER2+ breast cancer who had last received trastuzumab, pertuzumab, and a taxane with no evidence of progression. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection.

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. Acoramidis – BEYONTTRA (CAP) – EMA/PSUR/0000327953

Applicant: Bayer AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00011106/202511)

16.1.2. Andexanet alfa – ONDEXXYA (CAP) – EMA/PSUR/0000327908

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010764/202510)

16.1.3. Axicabtagene ciloleucel – YESCARTA (CAP) – EMA/PSUR/0000327951

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00010703/202510)

16.1.4. Aztreonam / Avibactam – EMBLAVEO (CAP) – EMA/PSUR/0000327924

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure (PSUSA/00011055/202510)

16.1.5. Belantamab mafodotin – BLENREP (CAP) – EMA/PSUR/0000327952

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Jenny-Maria Jönsson

Scope: Evaluation of a PSUSA procedure (PSUSA/00010869/202510)

16.1.6. Beremagene geperpavec – VYJUVEK (CAP) – EMA/PSUR/0000327959

Applicant: Krystal Biotech Netherlands B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011131/202511)

16.1.7. Bevacizumab gamma – LYTENAVA (CAP) – EMA/PSUR/0000327928

Applicant: Outlook Therapeutics NL B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00011065/202511)

16.1.8. Bezlotoxumab – ZINPLAVA (CAP) – EMA/PSUR/0000327891

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010576/202510)

16.1.9. Bupivacaine – EXPAREL LIPOSOMAL (CAP) – EMA/PSUR/0000327916

Applicant: Pacira Ireland Limited

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00010889/202510)

16.1.10. Capivasertib – TRUQAP (CAP) – EMA/PSUR/0000327927

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011061/202511)

16.1.11. Ceritinib – ZYKADIA (CAP) – EMA/PSUR/0000327894

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jenny-Maria Jönsson

Scope: Evaluation of a PSUSA procedure (PSUSA/00010372/202510)

16.1.12. Conestat alfa – RUCONEST (CAP) – EMA/PSUR/0000327863

Applicant: Pharming Group N.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000873/202510)

16.1.13. COVID-19 mRNA vaccine – KOSTAIVE (CAP) – EMA/PSUR/0000327932

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011115/202511)

16.1.14. Delamanid – DELTYBA (CAP) – EMA/PSUR/0000327880

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00010213/202510)

16.1.15. Dinutuximab beta – QARZIBA (CAP) – EMA/PSUR/0000327902

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010597/202511)

16.1.16. Dopamine hydrochloride – NEOATRICON (CAP) – EMA/PSUR/0000327930

Applicant: BrePco Biopharma Limited

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00011066/202511)

16.1.17. Eculizumab – BEKEMV (CAP); EPYSQLI (CAP); SOLIRIS (CAP) – EMA/PSUR/0000327869

Applicant: Alexion Europe

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Evaluation of a PSUSA procedure (PSUSA/00001198/202510)

16.1.18. Etranacogene dezaparvovec – HEMGENIX (CAP) – EMA/PSUR/0000327921

Applicant: CSL Behring GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011037/202511)

16.1.19. Exagamglogene autotemcel – CASGEVY (CAP) – EMA/PSUR/0000327950

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000244/202511)

16.1.20. Hydrocortisone – EFMODY (CAP); PLENADREN (CAP) – EMA/PSUR/0000327910

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00009176/202511)

16.1.21. Insulin degludec / Liraglutide – XULTOPHY (CAP) – EMA/PSUR/0000327890

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010272/202509)

16.1.22. Irinotecan hydrochloride trihydrate – ONIVYDE PEGYLATED LIPOSOMAL (CAP) – EMA/PSUR/0000327915

Applicant: Les Laboratoires Servier

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010534/202510)

16.1.23. Ivacaftor / Tezacaftor / Elexacaftor – KAFTRIO (CAP) – EMA/PSUR/0000327903

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00010868/202510)

16.1.24. Larotrectinib – VITRAKVI (CAP) – EMA/PSUR/0000327912

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00010799/202511)

16.1.25. Latanoprost – CATIOLANZE (CAP) – EMA/PSUR/0000327866

Applicant: Santen Oy

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00000202/202511)

16.1.26. Lazertinib – LAZCLUZE (CAP) – EMA/PSUR/0000327949

Applicant: Janssen Cilag International

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00011110/202511)

16.1.27. Linvoseltamab – LYNOZYFIC (CAP) – EMA/PSUR/0000327948

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00011130/202510)

16.1.28. Lonafarnib – ZOKINVY (CAP) – EMA/PSUR/0000327913

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011005/202511)

16.1.29. Loncastuximab tesirine – ZYNLONTA (CAP) – EMA/PSUR/0000327917

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00011027/202510)

16.1.30. Mirvetuximab soravtansine – ELAHERE (CAP) – EMA/PSUR/0000327931

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00011097/202511)

16.1.31. Nintedanib – OFEV (CAP) – EMA/PSUR/0000327881

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00010319/202510)

16.1.32. Nintedanib – VARGATEF (CAP) – EMA/PSUR/0000327882

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Georgia Gkegka

Scope: Evaluation of a PSUSA procedure (PSUSA/00010318/202510)

16.1.33. Niraparib / Abiraterone acetate – AKEEGA (CAP) – EMA/PSUR/0000327922

Applicant: Janssen Cilag International

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00011051/202510)

16.1.34. Nirogacestat – OGSIVEO (CAP) – EMA/PSUR/0000327941

Applicant: Merck Europe B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011163/202511)

16.1.35. Obecabtagene autoleucel – AUCATZYL (CAP) – EMA/PSUR/0000327934

Applicant: Autolus GmbH

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00011160/202511)

16.1.36. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) – PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) – EMA/PSUR/0000327887

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010501/202511)

16.1.37. Panitumumab – VECTIBIX (CAP) – EMA/PSUR/0000327879

Applicant: Amgen Europe B.V.

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure (PSUSA/00002283/202509)

16.1.38. Parathyroid hormone – NATPAR (CAP) – EMA/PSUR/0000327892

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00010591/202510)

16.1.39. Piperaquine tetraphosphate / Artenimol – EURARTESIM (CAP) – EMA/PSUR/0000327942

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00001069/202510)

16.1.40. Prucalopride – RESOLOR (CAP) – EMA/PSUR/0000327877

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00002568/202510)

16.1.41. rADAMTS13 – ADZYNMA (CAP) – EMA/PSUR/0000327926

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00011077/202511)

16.1.42. Raltegravir – ISENTRESS (CAP) – EMA/PSUR/0000327884

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00010373/202509)

16.1.43. RdESAT-6 / rCFP-10 – SIILTIBCY (CAP) – EMA/PSUR/0000327947

Applicant: Serum Life Science Europe GmbH

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011104/202511)

16.1.44. Repotrectinib – AUGTYRO (CAP) – EMA/PSUR/0000327933

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00011102/202511)

16.1.45. Selpercatinib – RETSEVMO (CAP) – EMA/PSUR/0000327889

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010917/202511)

16.1.46. Setmelanotide – IMCIVREE (CAP) – EMA/PSUR/0000327886

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Miroslava Gocova

Scope: Evaluation of a PSUSA procedure (PSUSA/00010941/202511)

16.1.47. Sirolimus – HYFTOR (CAP) – EMA/PSUR/0000327938

Applicant: Plusultra Pharma GmbH

PRAC Rapporteur: Jenny-Maria Jönsson

Scope: Evaluation of a PSUSA procedure (PSUSA/00000025/202511)

16.1.48. Sotorasib – LUMYKRAS (CAP) – EMA/PSUR/0000327925

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010970/202511)

16.1.49. Tofersen – QALSODY (CAP) – EMA/PSUR/0000327929

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00011064/202510)

16.1.50. Vamorolone – AGAMREE (CAP) – EMA/PSUR/0000327937

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00000223/202510)

16.1.51. Vandetanib – CAPRELSA (CAP) – EMA/PSUR/0000327919

Applicant: Esteve Pharmaceuticals S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00009327/202510)

16.1.52. Volanesorsen – WAYLIVRA (CAP) – EMA/PSUR/0000327897

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00010762/202511)

16.1.53. Zanidatamab – ZIIHERA (CAP) – EMA/PSUR/0000327940

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Jenny-Maria Jönsson

Scope: Evaluation of a PSUSA procedure (PSUSA/00011147/202511)

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

16.2.1. Deferasirox - DEFERASIROX ACCORD (CAP); DEFERASIROX MYLAN (CAP); EXJADE (CAP), NAP – EMA/PSUR/0000327939

Applicants: Accord Healthcare S.L.U. (Deferasirox Accord), Mylan Pharmaceuticals Limited (Deferasirox Mylan), Novartis Europharm Limited (Exjade), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00000939/202510)

16.2.2. Stiripentol - DIACOMIT (CAP), NAP – EMA/PSUR/0000327885

Applicants: Biocodex (Diacomit), various

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00002789/202511)

16.2.3. Tadalafil - ADCIRCA (CAP); CIALIS (CAP); TADALAFIL LILLY (CAP), NAP – EMA/PSUR/0000327895

Applicants: Eli Lilly Nederland B.V. (Adcirca, Cialis, Tadalafil Lilly), various

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00002841/202510)

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

16.3.1. A-tocopherol / ergocalciferol / phytomenadion / retinol palmitate – EMA/PSUR/0000327883

Applicants: various

PRAC Rapporteur: Miroslava Gocova

Scope: Evaluation of a PSUSA procedure (PSUSA/00002633/202511)

16.3.2. Acetylsalicylic acid / chlorphenamine / phenylephrine – EMA/PSUR/0000327862

Applicants: various

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00000694/202511)

16.3.3. Aluminium chloride hexahydrate – EMA/PSUR/0000327918

Applicants: various

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00009050/202511)

16.3.4. Aminosalicylic acid – EMA/PSUR/0000327860

Applicants: various

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00000165/202510)

16.3.5. Amlodipine / atorvastatin / perindopril, amlodipine / atorvastatin / rampiril – EMA/PSUR/0000327896

Applicants: various

PRAC Rapporteur: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00010431/202510)

16.3.6. Artemether / lumefantrin (apart from the dispersible tablet) – EMA/PSUR/0000327946

Applicants: various

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00000236/202510)

16.3.7. Ascorbic acid / caffeine / paracetamol / phenylephrine hydrochloride / terpine – EMA/PSUR/0000327878

Applicants: various

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00002305/202511)

16.3.8. Bromhexine – EMA/PSUR/0000327935

Applicants: various

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000437/202509)

16.3.9. Cinnarizine / dimenhydrinate – EMA/PSUR/0000327867

Applicants: various

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000767/202511)

16.3.10. Clenbuterol – EMA/PSUR/0000327861

Applicants: various

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000794/202509)

16.3.11. Cyanocobalamin / folic acid, cyanocobalamin / folic acid / potassium iodide – EMA/PSUR/0000327944

Applicants: various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00000892/202511)

16.3.12. Desogestrel / ethinylestradiol – EMA/PSUR/0000327943

Applicants: various

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00000967/202509)

16.3.13. Felbamate – EMA/PSUR/0000327920

Applicants: various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00010155/202509)

16.3.14. Human coagulation factor VII – EMA/PSUR/0000327871

Applicants: various

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00001619/202510)

16.3.15. Isoflurane – EMA/PSUR/0000327868

Applicants: various

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00001786/202510)

16.3.16. Minoxidil (non topical formulations) – EMA/PSUR/0000327876

Applicants: various

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00002066/202510)

16.3.17. Perindopril – EMA/PSUR/0000327874

Applicants: various

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00002354/202510)

16.3.18. Prothipendyl – EMA/PSUR/0000327875

Applicants: various

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00002564/202510)

16.3.19. Salmeterol – EMA/PSUR/0000327888

Applicants: various

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00002681/202510)

16.3.20. Sulbutiamine – EMA/PSUR/0000327905

Applicants: various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00002801/202511)

16.3.21. Valsartan, Rosuvastatin – EMA/PSUR/0000327899

Applicants: various

PRAC Rapporteur: Polona Golmajer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010735/202510)

16.4. Follow-up to PSUR/PSUSA procedures

16.4.1. Semaglutide – RYBELSUS (CAP) – EMA/PAM/0000337900

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Karin Bolin

Scope: Safety review. To assess the potential association between semaglutide exposure and cardioembolic stroke as part of a post-authorisation measure (LEG). - EMEA/H/C/PSUSA/00010671/202505. (LEG/01968/1)

16.4.2. Semaglutide – WEGOVY (CAP); WEGOVY FLEXTOUCH (CAP) – EMA/PAM/0000337800

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Karin Bolin

Scope: To assess the potential association between semaglutide exposure and cardioembolic stroke as part of a post-authorisation measure (LEG). -EMEA/H/C/PSUSA/00010671/202505

16.4.3. Semaglutide – OZEMPIC (CAP) – EMA/PAM/0000338018

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Karin Bolin

Scope: Safety review. To assess the potential association between semaglutide exposure and cardioembolic stroke as part of a post-authorisation measure (LEG). -EMEA/H/C/PSUSA/00010671/202505. (LEG/01969/1)

16.4.4. Voretigene neparvovec – LUXTURNA (CAP) – EMA/PAM/0000339319

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Dirk Mentzer

Scope: SPKRPE-PASS final clinical study report requested during PSUSA/00010742/202507 by PRAC

16.5. Variation procedure(s) resulting from PSUSA evaluation

16.5.1. Tacrolimus ADVAGRAF (CAP); MODIGRAF (CAP), NAP – EMA/VR/0000319175

Applicants: Astellas Pharma Europe B.V., various

PRAC Rapporteur: Eamon O Murchu

Scope: Update of section 4.8 of the SmPC in order to include the missing frequency estimations to the list of adverse drug reactions (ADRs) following PSUSA/00002839/202403 procedure. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to implement editorial changes to the PI.

16.6. Expedited summary safety reviews[32]

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.

[32] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

17.1. Protocols of PASS imposed in the marketing authorisation(s)[33]

17.1.1. Mirdametinib – EZMEKLY (CAP) – EMA/PASS/0000340654

Applicant: Merck Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: PASS protocol [107n]: Non-interventional PASS to confirm the long-term safety of mirdametnib, in the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric and adult patients with neurofibromatosis type 1 (NF1) aged 2 years and above.

17.1.2. Topiramate (NAP) – EMA/PASS/0000340662

Applicants: various

PRAC Rapporteur: Karin Bolin

Scope: PASS amendment [107o]: Post-Authorization Safety Study to assess the effectiveness of the newly implemented Risk Minimization Measures for Topiramate: HCP and patient knowledge and behavior survey.

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[34]

17.2.1. Ciltacabtagene autoleucel – CARVYKTI (CAP) – EMA/PAM/0000338559

Applicant: Janssen Cilag International

PRAC Rapporteur: Jo Robays

Scope: Amendment of the protocol for PASS study PCSONCA0014: Post-authorization Safety Study Survey to Evaluate the Effectiveness of the Ciltacabtagene Autoleucel HCP Educational Program and the Product Handling Training.

17.2.2. COVID-19 mRNA vaccine – MNEXSPIKE (CAP) – EMA/PAM/0000339594

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of the post-authorisation safety study (PASS) protocol v2.0 for mRNA-1283-P901; this is a PASS in the United States aimed to estimate the incidence and to compare the risks of myocarditis and pericarditis among in people who receive mNEXSPIKE and in those who have not received the prior seasonal formulation of COVID-19 vaccine or the same seasonal formulation previously.

17.2.3. Efgartigimod alfa – VYVGART (CAP) – EMA/PAM/0000343589

Applicant: Argenx

[33] In accordance with Article 107n of Directive 2001/83/EC
[34] 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: Rhea Fitzgerald

Scope: Amendment of the protocol (PAS Registration Number EUPAS1000000005) for the pregnancy registry - A worldwide pregnancy safety study to assess maternal, foetal, and infant outcomes following exposure to efgartigimod alfa during pregnancy and/or breastfeeding.

17.2.4. Resmetirom – REZDIFFRA (CAP) – EMA/PAM/0000339780

Applicant: Madrigal Pharmaceuticals EU Limited

PRAC Rapporteur: Lina Seibokiene

Scope: Submission of study protocol for a real-world longitudinal data study to address liver and CV related outcomes in resmetirom treated patients, as compared with a real-world control arm

17.2.5. Teprotumumab – TEPEZZA (CAP) – EMA/PAM/0000310214

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Draft protocol for PASS (non-imposed) 20250081: Drug utilization study to evaluate the effectiveness of teprotumumab aRMMs.

17.2.6. Tofacitinib – XELJANZ (CAP) – EMA/PAM/0000316639

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of amended protocols for the non-imposed (category 3) Post Authorisation Safety Study (PASS) - version 6.0 (A3921312), and version 6.0 (A3921316) for Tofacitinib (Xeljanz).

- A3921312: UK, British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA)
- A3921316: Spain (ES), Registry of Adverse Events of Biological Therapies and Biosimilars in Rheumatoid Diseases (BIOBADASER)

17.2.7. Upadacitinib – RINVOQ (CAP) – EMA/PAM/0000339078

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Protocol amendment for study P21-825: a drug utilisation study evaluating the additional risk minimisation measures for upadacitinib in the treatment of atopic dermatitis in Europe

17.2.8. Vonicog alfa – VEYVONDI (CAP) – EMA/PAM/0000337712

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Karin Bolin

Scope: Protocol for Study TAK-577-4009/EUHASS registry - post-authorisation safety study: safety surveillance of Veyvondi using secondary data from the EUHASS registry.

17.3. Results of PASS imposed in the marketing authorisation(s)[35]

17.3.1. Belimumab – BENLYSTA (CAP) – EMA/PASS/0000306411

Applicant: Glaxosmithkline (Ireland) Limited

PRAC Rapporteur: Karin Bolin

Scope: PASS results [107q]: A 5-Year prospective observational registry to assess adverse events of interest and effectiveness in adults with active, autoantibody-positive systemic Lupus erythematosus treated with or without BENLYSTA (belimumab)

17.4. Results of PASS imposed and non-imposed in the marketing authorisation(s)[36]

17.4.1. COVID-19 mRNA vaccine – COMIRNATY (CAP); COMIRNATY JN.1 (CAP); COMIRNATY KP.2 (CAP); COMIRNATY LP.8.1 (CAP); COMIRNATY OMICRON XBB.1.5 (CAP); COMIRNATY ORIGINAL/OMICRON BA.4-5 (CAP) – EMA/VR/0000334558

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the final clinical study report for the non-interventional study C4591022, listed as a category 3 study in the RMP. This is a non-interventional post-approval safety study of pregnancy and infant outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry.

17.4.2. Ivacaftor / Tezacaftor / Elexacaftor – KAFTRIO (CAP) – EMA/VR/0000319887

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Dennis Lex

Scope: Submission of the final report from the 5-year Post Authorisation Safety Study (PASS) VX20-445-120, listed as a category 3 study in the RMP. This is a longitudinal, registry based study evaluating the real-world effects and utilisation patterns of elexacaftor, tezacaftor, and ivacaftor combination therapy (ELX/TEZ/IVA) in patients with cystic fibrosis (CF). The RMP version 10.2 has also been submitted.

17.4.3. Semaglutide – OZEMPIC (CAP); RYBELSUS (CAP) – EMA/VR/0000334523

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Karin Bolin

[35] In accordance with Article 107p-q of Directive 2001/83/EC
[36] 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

Scope: Submission of the final report from the non-interventional post-authorisation safety study NN9535-4447, listed as a category 3 study in the RMP for Ozempic and Rybelsus. This is an epidemiological assessment of the risk for pancreatic cancer associated with the use of semaglutide in patients with type 2 diabetes: a cohort study based on Nordic registry data.

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

17.5.1. Avacopan – TAVNEOS (CAP) – EMA/PAM/0000336195

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the first interim report for the required additional pharmacovigilance activity (Category 3), AVACOSTAR (CS-AVA-2022-0016), which is a post-authorisation safety study (PASS) to evaluate incidence of safety events of interest in patients treated with avacopan for ANCA-associated vasculitis (AAV). In the frame of procedure MEA 002 EMEA/H/C/005523, it was agreed in the RMP version 2.1 that interim reports for AVACOSTAR PASS are submitted every 24 months (after first patient first visit).

17.5.2. Cabotegravir – VOCABRIA (CAP) – EMA/PAM/0000339050

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Dennis Lex

Scope: Interim study results. 4th interim report. PASS: A real-world five-year Drug Utilisation Study (DUS). This observational cohort study will aim to better understand the patient population receiving cabotegravir long acting injection and/or rilpivirine long acting injection containing regimens in routine clinical practice. The study will assess usage patterns, adherence, and post marketing clinical effectiveness of these regimens and monitor for resistance among virologic failures for whom data on resistance testing are available. (ANX/01282/2)

17.5.3. Cabotegravir – VOCABRIA (CAP) – EMA/PAM/0000339531

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Dennis Lex

Scope: Interim study results. PASS No. 215162 (EuroSIDA): A prospective observational cohort study to monitor for hepatotoxicity and regimen discontinuation due to liver related adverse events among patients initiating CAB containing antiretroviral regimen. Summary objectives: Monitor for hepatotoxicity; Estimate the number of patients discontinuing CAB based ARV regimen due to adverse events, and adverse events related to hepatic events. (MEA/01256/2)

17.5.4. COVID-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP); NUVAXOVID JN.1 (CAP); NUVAXOVID XBB.1.5 (CAP) – EMA/PAM/0000317251

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Dirk Mentzer

Scope: Revised Third Interim Report for PASS 2019nCoV-402: UK A Study Using the Clinical Practice Research Datalink (CPRD): A surveillance study to characterise the safety profile of Nuvaxovid in adults aged 18 years and older in the real-world setting using the UK CPRD.

17.5.5. Damoctocog alfa pegol – JIVI (CAP) – EMA/PAM/0000303584

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Fourth interim report of study number 20904 (HA-SAFE), 'Observational study evaluating long-term safety of real-world treatment with damoctocog alfa pegol in previously treated patients with hemophilia A'. The HA-SAFE study is a post-authorisation measure defined in Annex II.D of the Jivi EU PI.

17.5.6. Efgartigimod alfa – VYVGART (CAP) – EMA/PAM/0000339564

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Third interim report ARGX-113-PAC-2206: A worldwide pregnancy safety study to assess maternal, fetal, and infant outcomes following exposure to Vyvgart (efgartigimod) during pregnancy and/or breastfeeding.

17.5.7. Fenfluramine – FINTEPLA (CAP) – EMA/PAM/0000339786

Applicant: UCB Pharma

PRAC Rapporteur: Dennis Lex

Scope: Final study result. P46 RWE1624 is a descriptive, retrospective, non-interventional longitudinal cohort analysis of patients with Cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) in the United States, utilizing data from the Komodo claims database. (P46/01995/1)

17.5.8. Lecanemab – LEQEMBI (CAP) – EMA/PAM/0000339581

Applicant: Eisai GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Cat 3 PASS BAN2401-G000-301 OLE

Evaluate the long-term safety and tolerability of LEC10-BW in subjects with early Alzheimer's disease in the Extension Phase. (MEA/01037/1)

17.5.9. Maribavir – LIVTENCITY (CAP) – EMA/PAM/0000334575

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of interim results from study TAK-620-4007, an RMP category 3 retrospective chart review of safety outcomes associated with use of maribavir in patients with post-transplant refractory cytomegalovirus (CMV) infection and comorbid end-stage renal disease (ESRD) or comorbid severe chronic renal disease requiring peritoneal dialysis or haemodialysis.

17.5.10. Mercaptamine – CYSTADROPS (CAP) – EMA/PAM/0000339522

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: The fourth interim report for category 3 PASS CYT-DS-001; an open-label, longitudinal, post authorization safety study to assess the safety of Cystadrops in paediatric and adult cystinosis patients in long term Use.

17.5.11. Ofatumumab – KESIMPTA (CAP) – EMA/PAM/0000308145

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: First Annual Interim Study Report for long-term PASS, study COMB157G2406 entitled Kesimpta long-term retrospective safety study utilizing real-world data from existing multiple sclerosis registries and databases from multiple countries

17.5.12. Ofatumumab – KESIMPTA (CAP) – EMA/PAM/0000337728

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: 5th Interim Report of PASS COMB157G2399 (ALITHIOS): An open-label, single arm, multi-center extension study evaluating long-term safety, tolerability and effectiveness of ofatumumab in subjects with relapsing multiple sclerosis.

17.5.13. Rilpivirine – REKAMBYS (CAP) – EMA/PAM/0000338758

Applicant: Janssen Cilag International

PRAC Rapporteur: Liana Martirosyan

Scope: Interim study results. 4th interim report. PASS: A real-world five-year Drug Utilisation Study (DUS). This observational cohort study will aim to better understand the patient population receiving cabotegravir long acting injection and/or rilpivirine long acting injection containing regimens in routine clinical practice. The study will assess usage patterns, adherence, and post marketing clinical effectiveness of these regimens and monitor for resistance among virologic failures for whom data on resistance testing are available. (ANX/01281/2)

17.5.14. Sarilumab – KEVZARA (CAP) – EMA/PAM/0000339607

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: SARILC08312 Interim Report#5: Post-authorization Safety study Surveillance Program for Sarilumab using Rheumatoid Arthritis Registries in Germany, Spain, Sweden, and in the United Kingdom (EUPASS35468).

17.5.15. Tofacitinib – XELJANZ (CAP) – EMA/PAM/0000334570

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Next interim study report for Study A3921352 is an active surveillance, post-authorization study to characterize the safety of tofacitinib in patients with moderately to severely active ulcerative colitis in the real-world setting using data from the United Registries for Clinical Assessment and Research (UR-CARE) in the European Union (EU), as requested in MEA/01034/1 (EMA/PAM/0000247897).

17.5.16. Velaglucerase alfa – VPRIV (CAP) – EMA/PAM/0000339048

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Dennis Lex

Scope: Submission of Feasibility Assessment Report for study TAK-669-4018, a Survey among Patients, Caregivers and Home Infusion Nurses based in the European Union to Assess their Awareness and Understanding of the Risk Minimization Measures in the Educational Materials Supporting VPRIV Infusion at Home

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. Amifampridine – FIRDAPSE (CAP) – EMA/S/0000337252

Applicant: Serb

PRAC Rapporteur: Karin Bolin

Scope: Annual reassessment of the marketing authorisation

18.1.2. Clofarabine – EVOLTRA (CAP) – EMA/S/0000335797

Applicant: Sanofi B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual reassessment of the marketing authorisation

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

Applicant: Serb

PRAC Rapporteur: Dennis Lex

Scope: Annual reassessment of the marketing authorisation

18.1.4. Maralixibat – LIVMARLI (CAP) – EMA/S/0000317715

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.1.5. Velmanase alfa – LAMZEDE (CAP) – EMA/S/0000336192

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

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

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Conditional renewal of the marketing authorisation

18.2.2. Pirtobrutinib – JAYPIRCA (CAP) – EMA/R/0000339971

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Abrocitinib – CIBINQO (CAP) – EMA/R/0000336009

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Petar Mas

Scope: 5-year renewal of the marketing authorisation

18.3.2. Anifrolumab – SAPHNELO (CAP) – EMA/R/0000335943

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

18.3.3. Artesunate – ARTESUNATE AMIVAS (CAP) – EMA/R/0000333258

Applicant: Amivas Ireland Limited

PRAC Rapporteur: Dennis Lex

Scope: 5-year renewal of the marketing authorisation

18.3.4. Eptinezumab – VYEPTI (CAP) – EMA/R/0000336059

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

18.3.5. Semaglutide – WEGOVY (CAP); WEGOVY FLEXTOUCH (CAP) – EMA/R/0000336288

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Karin Bolin

Scope: 5-year renewal of the marketing authorisation

18.3.6. Sitagliptin fumarate – SITAGLIPTIN SUN (CAP) – EMA/R/0000335931

Applicant: Sun Pharmaceutical Industries (Europe) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

19. Annex II – List of participants

Including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 08-11 June 2026 PRAC meeting, which was held remotely.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Ulla Wändel Liminga	Chair	Sweden	No interests declared	
Jan Neuhauser	Member	Austria	No interests declared	
Sonja Radowan	Alternate	Austria	No interests declared	
Jean-Michel Dogné	Member	Belgium	No restrictions applicable to this meeting	
Jo Robays	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva	Member	Bulgaria	No interests declared	
Stanislav Stoilov	Alternate	Bulgaria	No interests declared	
Petar Mas	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi	Alternate	Croatia	No interests declared	
Panagiotis Psaras	Member	Cyprus	No interests declared	
Elena Kaisis	Alternate	Cyprus	No interests declared	
Eva Jirsová	Member	Czechia	No interests declared	
Veronika Macurova	Alternate	Czechia	No interests declared	
Marie Louise Schougaard Christiansen	Member	Denmark	No interests declared	
Karin Erneholm	Alternate	Denmark	No interests declared	
Maia Uusküla	Member	Estonia	No interests declared	
Terhi Lehtinen	Member	Finland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Kimmo Jaakkola	Alternate	Finland	No interests declared	
Tiphaine Vaillant	Member	France	No interests declared	
Zoubida Amimour	Alternate	France	No participation in discussion, final deliberations and voting on:	4.1.2. Atezolizumab – TECENTRIQ (CAP); avelumab – BAVENCIO (CAP); cemiplimab - LIBTAYO (CAP);, dostarlimab – JEMPERLI (CAP); durvalumab – IMFINZI (CAP); ipilimumab – YERVOY (CAP); nivolumab – OPDIVO (CAP); nivolumab / relatlimab – OPDUALAG (CAP); pembrolizumab – KEYTRUDA (CAP); retifanlimab – ZYNYZ (CAP); serplulimab - HETRONIFLY (CAP); sugemalimab – CEJEMLY (CAP); tislelizumab – TEVIMBRA (CAP); toripalimab – LOQTORZI (CAP); tremelimumab – IMJUDO (CAP) 14.1.4. Luspatercept -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				REBLOZYL (CAP) 15.3.16. EMA/VR/00003 39077 16.1.44. EMA/PSUR/00 00327933
Dennis Lex	Member	Germany	No interests declared	
Dirk Mentzer	Alternate	Germany	No interests declared	
Georgia Gkegka	Member	Greece	No interests declared	
Maria Poulianiti	Alternate	Greece	No participation in discussion, final deliberations and voting on:	4.2.2. Gemcitabine (NAP) 4.2.3. Valproate (NAP) and related substances 16.2.1. EMA/PSUR/00 00327939
Julia Pallos	Member	Hungary	No participation in discussion, final deliberations and voting on:	4.1.2. Atezolizumab – TECENTRIQ (CAP); avelumab – BAVENCIO (CAP); cemiplimab - LIBTAYO (CAP);, dostarlimab – JEMPERLI (CAP); durvalumab – IMFINZI (CAP); ipilimumab – YERVOY (CAP); nivolumab – OPDIVO (CAP); nivolumab / relatlimab – OPDUALAG

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				(CAP); pembrolizumab – KEYTRUDA (CAP); retifanlimab – ZYNYZ (CAP); serplulimab - HETRONIFLY (CAP); sugemalimab – CEJEMLY (CAP); tislelizumab – TEVIMBRA (CAP); toripalimab – LOQTORZI (CAP); tremelimumab – IMJUDO (CAP) 14.1.4. Luspatercept - REBLOZYL (CAP) 15.3.16. EMA/VR/00003 39077 16.1.44. EMA/PSUR/00 00327933
Melinda Palfi	Alternate	Hungary	No interests declared	
Guðrún Stefánsdóttir	Member	Iceland	No participation in discussion, final deliberations and voting on:	15.3.26. EMA/VR/00003 39051 16.1.17. EMA/PSUR/00 00327869 16.1.37. EMA/PSUR/00 00327879 16.1.48. EMA/PSUR/00 00327925

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				17.2.5. EMA/PAM/0000 310214
Rhea Fitzgerald	Member	Ireland	No interests declared	
Eamon O Murchu	Alternate	Ireland	No interests declared	
Amelia Cupelli	Member	Italy	No interests declared	
Zane Neikena	Member	Latvia	No interests declared	
Diana Litenboka	Alternate	Latvia	No interests declared	
Rugile Pilviniene	Member	Lithuania	No restrictions applicable to this meeting	
Lina Seibokiene	Alternate	Lithuania	No interests declared	
Anne-Cecile Vuillemin	Member	Luxembourg	No interests declared	
Liana Martirosyan	Member (Vice-Chair)	Netherlands	No interests declared	
Bianca Mulder	Alternate	Netherlands	No restrictions applicable to this meeting	
David Olsen	Member	Norway	No participation in discussion, final deliberations and voting on:	4.2.1. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004 790/SDA/005 4.2.5. X-ray contrast agents: Iobitridol (NAP); Iodixanol (NAP); Iohexol (NAP); Iomeprol (NAP); Iopamidol (NAP); Iopromide (NAP); Ioversol

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				(NAP); loxitalamic acid (NAP) 16.1.1. EMA/PSUR/00 00327953 16.1.24. EMA/PSUR/00 00327912 16.3.2. EMA/PSUR/00 00327862 17.5.5. EMA/PAM/0000 303584
Pernille Harg	Alternate	Norway	No interests declared	
Adam Przybylkowski	Member	Poland	No restrictions applicable to this meeting	
Katarzyna Ziolkowska	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins	Member	Portugal	No interests declared	
Carla Torre	Alternate	Portugal	No restrictions applicable to this meeting	
Roxana Dondera	Member	Romania	No interests declared	
Roxana Stefania Udrescu	Alternate	Romania	No interests declared	
Miroslava Gocova	Member	Slovakia	No interests declared	
Jana Pecherova	Alternate	Slovakia	No interests declared	
Marjetka Plementas	Alternate	Slovenia	No interests declared	
Maria del Pilar Rayon	Member	Spain	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Maria Martinez Gonzalez	Alternate	Spain	No interests declared	
Karin Bolin	Member	Sweden	No restrictions applicable to this meeting	
Jenny-Maria Jönsson	Alternate	Sweden	No restrictions applicable to this meeting	
Annalisa Capuano	Member	Independent scientific expert	No restrictions applicable to this meeting	
Milou-Daniel Drici	Member	Independent scientific expert	No restrictions applicable to this meeting	
Maria Teresa Herdeiro	Member	Independent scientific expert	No restrictions applicable to this meeting	
Patricia McGettigan	Member	Independent scientific expert	No restrictions applicable to this meeting	
Hedvig Marie Egeland Nordeng	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark	Member	Independent scientific expert	No restrictions applicable to this meeting	
Roberto Frontini	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Martin Votava	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Yiannoula Koulla	Member	Patients' Organisation Representative	No interests declared	
Michal Rataj	Alternate	Patients' Organisation Representative	No interests declared	
Ingrid Bourges	Expert	Belgium	No restrictions applicable to this meeting	
Violette Dirix	Expert	Belgium	No restrictions applicable to this meeting	
Sophie Goethals	Expert	Belgium	No restrictions applicable to this meeting	
Marta Romano	Expert	Belgium	No restrictions applicable to this meeting	
Karen van Malderen	Expert	Belgium	No interests declared	
Chloé Wyndham-Thomas	Expert	Belgium	No restrictions applicable to this meeting	
Behija Hudina	Expert	Croatia	No restrictions applicable to this meeting	
Lucie Skalova	Expert	Czech Republic	No interests declared	
Kirsten Egebjerg Juul	Expert	Denmark	No interests declared	
Cecilie Louise Pedersen	Expert	Denmark	No participation in discussion, final deliberations and voting on:	4.2.4. EMEA/H/C/002717/SDA/011 15.3.2. EMA/VR/0000335954

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				16.1.21. EMA/PSUR/00 00327890 16.4.1. EMA/PAM/0000 337900 16.4.2. EMA/PAM/0000 337800 16.4.3. EMA/PAM/0000 338018 17.4.3. EMA/VR/00003 34523 18.3.4. EMA/R/000033 6059 18.3.5. EMA/R/000033 6288
Casper Holmkvist Moos	Expert	Denmark	No interests declared	
Lærke Nilausen	Expert	Denmark	No restrictions applicable to this meeting	
Moritz Sander	Expert	Denmark	No restrictions applicable to this meeting	
Aynur Sert	Expert	Denmark	No interests declared	
Eeva Sofia Leinonen	Expert	Finland	No interests declared	
Pauline Dayani	Expert	France	No interests declared	
Guillaume de Preneuf	Expert	France	No interests declared	
Rosemary Dray-Spira	Expert	France	No restrictions	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			applicable to this meeting	
Emilie Vittaz	Expert	France	No interests declared	
Dario Ortiz	Expert	Germany	No interests declared	
Karin Seifert	Expert	Germany	No interests declared	
Janus Seiler	Expert	Germany	No interests declared	
Laura Zein	Expert	Germany	No interests declared	
Marianne Klanker	Expert	Netherlands	No interests declared	
Margje Monster-Simons	Expert	Netherlands	No restrictions applicable to this meeting	
Paul ten Berg	Expert	Netherlands	No interests declared	
Gunnar Rimul	Expert	Norway	No interests declared	
Helena Back	Expert	Sweden	No interests declared	
Charlotte Backman	Expert	Sweden	No interests declared	
Rolf Gedeborg	Expert	Sweden	No restrictions applicable to this meeting	
Sonny Larsson	Expert	Sweden	No interests declared	
Elin Magnusdottir	Expert	Sweden	No interests declared	
Oskar Skog	Expert	Sweden	No restrictions applicable to this meeting	
Miriam Taekema	Expert	Sweden	No interests declared	
Mari Thorn	Expert	Sweden	No restrictions	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			applicable to this meeting	
A representative from the European Commission attended the meeting.				
Observers from Health Canada (Canada) attended the meeting.				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

None

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

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

(Items 2 and 3 of the PRAC minutes)

A referral is a procedure used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral, EMA is requested to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the European Union (EU). For further detailed information on safety related referrals please see: Referral procedures: human medicines | European Medicines Agency (europa.eu)

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

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

may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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

Article 58 (EU-M4all) procedure allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU).

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

22. Unidentified

None