06 March 2026
EMA/PRAC/46601/2026
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 12-15 January 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
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

1. Introduction

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

The Chairperson opened the 12-15 January 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) and thanked the departing members/alternates for their contributions to the Committee.

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

The Chair announced the start of the Cypriot presidency of the Council of the European Union (EU).

1.2. Agenda of the meeting on 12-15 January 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 24-27 November 2025

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

Post-meeting note: the PRAC minutes of the meeting held on 24-27 November 2025 were published on the EMA website on 12 February 2026 (EMA/PRAC/21905/2026).

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

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

Applicants: various

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

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

Background

A referral procedure under Article 31 of Directive 2001/83/EC is ongoing for levamisole-containing medicines. For further background, see PRAC minutes December 2025[1].

Summary of recommendation(s)/conclusions

- PRAC discussed the list of experts for the meeting of the Scientific Advisory Group (SAG) on vaccines and therapies for infectious diseases and adopted a revised timetable for the procedure. For further details, see Levamisole-containing medicinal products - referral | European Medicines Agency (EMA).

Post meeting note: PRAC endorsed the list of experts for the meeting of the Scientific Advisory Group (SAG) on vaccines and therapies for infectious diseases via written procedure on 27 January 2026.

[1] Held 24-27 November 2025

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

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

Applicants: various

PRAC Lead: Pernille Harg

Scope: Signal of fixed drug eruption

EPITT 20229 – New signal

Lead Member State(s): NO, IE, FR

Background

Iodinated X-ray contrast agents are water-soluble agents indicated for angiography, phlebography, angiocardiography, head and body computed tomography (CT), urography, endoscopic retrograde cholangio-pancreatography (ERCP), cholangiography, cavernosography, fistulography, myelography, discography, arthrography, dacrocystography, sialography, hysterosalpingography and galactography.

During national surveillance monitoring, a signal of fixed drug eruption was identified by France, based on 2 cases of special interest and 16 cases retrieved from EudraVigilance following administration of iomeprol. Other cases were identified in EudraVigilance as well as in the literature following administration of other iodinated X ray contrast agents (iohexol, iopamidol, iopromide, ioversol, iodixanol, iobitridol). Norway, as the Lead Member State (LMS) for iomeprol, iohexol, iopromide, iodixanol, and Ireland, as the Lead Member State

[2] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[3] 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

(LMS) for ioversol, iopamidol, iobitridol, confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from the case reports in EudraVigilance and literature, PRAC agreed that further evaluation on the signal of fixed drug eruption is warranted.

PRAC appointed Pernille Harg as PRAC Lead for the signal.

Summary of recommendation(s)

- The MAHs of iomeprol and iopamidol (Bracco Imaging), iohexol and iodixanol (GE Healthcare), iopromide (Bayer), ioversol, iobitridol, ioxitalamic acid (Guerbet), should submit to EMA, a cumulative review of all cases of fixed eruption, generalised bullous fixed drug eruption and related terms associated with iomeprol, iopamidol, iohexol, iodixanol, iopromide, ioversol, iobitridol and ioxitalamic acid as suspect drugs, including a review of the published literature, data from spontaneous reports and reports from studies as well as a discussion on possible biological plausibility and mechanism of this association including potential immunological pathways or other potential triggers or risk factors. The MAHs should also discuss the need for any potential amendment to the product information (PI) and/ or the risk management plan (RMP).
- A 60-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.2. Signals follow-up and prioritisation

4.2.1. Cefazolin (NAP); cefazolin/lidocaine hydrochloride (NAP)

Applicant(s): various

PRAC Lead: Sonja Radowan

Scope: Signal of Kounis syndrome

EPITT 20204 – Follow-up to September 2025

Background

For background information, see PRAC minutes September 2025.

The MAH for the innovator product (ASTRO-PHARMA GMBH) replied to the request for information on the signal of Kounis syndrome and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance and the literature, including the responses submitted by the MAH for the innovator product, PRAC agreed that there is sufficient evidence to support a causal association between cefazolin and Kounis syndrome. Therefore, the product information should be updated to include a warning on Kounis syndrome and to add Kounis syndrome as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAHs for cefazolin-containing products should submit to the national competent authorities, within 60 days, a variation to update the product information[4].

4.2.2. Erdafitinib - BALVERSA (CAP) - EMEA/H/C/006050/SDA/003

Applicant: Janssen Cilag International

PRAC Rapporteur: Bianca Mulder

Scope: Signal of growth accelerated

EPITT 20194 – Follow-up to September 2025

Background

For background information, see PRAC minutes September 2025.

The MAH replied to the request for information on the signal of growth accelerated 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 concluded that there is sufficient evidence to establish a causal relationship between erdafitinib and the development of growth acceleration and/or epiphysiolysis of the femoral head in paediatric population (off label use). Therefore, the product information should be updated to include information about cases of growth acceleration and epiphysiolysis of the femoral head in paediatric patients (<18 years of age) receiving erdafitinib in clinical trials outside of the authorised indication and as off label in the post-marketing setting.

Summary of recommendation(s)

- The MAH for Balversa (erdafitinib) should submit to EMA, within 60 days, a variation to update the product information[5].
- Having considered recent meta-analysis by *Huang J., et al. (2025)* where musculoskeletal adverse events were reported by adult patients with urothelial cancer or other solid tumours, PRAC agreed that the MAH should submit within the PSUR, with data lock point 11 April 2026, a cumulative review of musculoskeletal disorders with erdafitinib in adult patients, including data from literature, clinical cases, and post-marketing sources, and discuss the need for any potential amendment to the product information (PI) and/ or the risk management plan (RMP). PRAC will assess the data within the PSUR procedure PSUSA/00011072/202604.

4.2.3. Pegylated liposomal doxorubicin – CAELYX PEGYLATED LIPOSOMAL (CAP) - EMEA/H/C/000089/SDA/022; CELDOXOME PEGYLATED LIPOSOMAL (CAP); ZOLSKETIL PEGYLATED LIPOSOMAL (CAP) - EMEA/H/C/005320/SDA/002; NAP

Applicants: Accord Healthcare S.L.U. (Zolsketil pegylated liposomal), Baxter Holding B.V. (Caelyx pegylated liposomal, Celdoxome pegylated liposomal), various

PRAC Rapporteur: Eva Jirsová

[4] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly
[5] Update of SmPC sections 4.2, 4.8 and 5.1. The package leaflet is updated accordingly

Scope: Signal of renal-limited thrombotic microangiopathy

EPITT 20193 – Follow-up to September 2025

Background

For background information, see PRAC minutes September 2025.

The MAHs Baxter Holding B.V. and Accord Healthcare S.L.U. replied to the request for information on the signal of renal-limited thrombotic microangiopathy and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence from case reports in EudraVigilance and the literature, including the cumulative review submitted by the MAHs, PRAC agreed that there is sufficient evidence to support a causal association between pegylated liposomal doxorubicin and renal-limited thrombotic microangiopathy. Therefore, the product information should be updated to add renal-limited thrombotic microangiopathy as undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAHs of pegylated liposomal doxorubicin should submit to EMA, within 60 days, a variation to update the product information[6].

4.2.4. Pemetrexed – ALIMTA (CAP) - EMEA/H/C/000564/SDA/028; ARMISARTE (CAP); PEMETREXED ACCORD (CAP); PEMETREXED FRESENUIS KABI (CAP); PEMETREXED MEDAC (CAP); PEMETREXED PFIZER (CAP); NAP

Applicants: Accord Healthcare S.L.U. (Pemetrexed accord), Actavis Group Ptc ehf. (Armisarte), Eli Lilly Nederland B.V. (Alimta), Fresenius Kabi Deutschland GmbH (Pemetrexed fresenuis kabi), Medac Gesellschaft für klinische Spezialpräparate mbH (Pemetrexed medac), Pfizer Europe MA EEIG (Pemetrexed pfizer), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Signal of lupus erythematosus

EPITT 20185 – Follow-up to September 2025

Background

For background information, see PRAC minutes September 2025.

The MAH of Alimta (Eli Lilly Nederland B.V.) replied to the request for information on the signal of lupus erythematosus and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance and literature and the responses submitted by the above-mentioned MAH, PRAC concluded that the current evidence is insufficient to establish a causal relationship between pemetrexed and lupus erythematosus to further warrant an update to the product information and/or risk management plan at present.

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

Summary of recommendation(s)

- The MAHs of pemetrexed-containing products should monitor the risk of drug-induced lupus erythematosus in the next PSUR with data lock point 4 February 2029 and present an interval review of new data from all available sources, including a detailed analysis and causality assessment.

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. Apitegromab (CAP MAA) - EMEA/H/C/005909, PRIME, Orphan

Applicant: Scholar Rock Netherlands B.V.

Scope (pre D-180 phase): Treatment of 5q spinal muscular atrophy (SMA)

5.1.2. Lurbinectedin (CAP MAA) - EMEA/H/C/006673, Orphan

Applicant: Pharma Mar S.A.

Scope (pre D-180 phase): Maintenance treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC)

5.1.3. Iloperidone (CAP MAA) - EMEA/H/C/006561

Scope (pre-opinion phase): Treatment of schizophrenia, acute treatment of manic or mixed episodes associated with bipolar I disorder

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

See Annex I 15.2.

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

See also Annex I 15.3.

5.3.1. Sipavibart – KAVIGALE (CAP) – EMA/VR/0000287106

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.4 of the SmPC in order to add a new warning on cardiovascular and/or thrombo-embolic events, based on the currently available safety information including the updated post-authorisation data. The Package Leaflet is updated accordingly. The RMP version 2 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

Background

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

CHMP is evaluating a type II variation for Kavigale, a centrally authorised product containing sipavibart, to update the product information in order to add a new warning on cardiovascular and/or thrombo-embolic events, based on the currently available safety information including the updated post-authorisation data. 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 2.3 for Kavigale (sipavibart) in the context of the variation under evaluation by CHMP is considered acceptable.
- PRAC considered that 'cardiovascular and thromboembolic events (CVTEs)' should not be included as important potential risk in the safety specification of the RMP. Consequently, the targeted safety questionnaires for these events should also not be included. However, CVTEs should be included as non-important potential risk in the RMP. In addition, PRAC agreed with the removal of the category 3 PASS to assess the safety of sipavibart during pregnancy from the RMP and considered that, at this stage, routine pharmacovigilance is sufficient to monitor the use of Kavigale (sipavibart) during pregnancy, with relevant data to be summarised in the PSURs. PRAC also considered that the targeted follow-up questionnaires for pregnancy proposed by the MAH should be removed from the RMP, as they are regarded as part of routine pharmacovigilance activity to achieve sufficient information for medical assessment.

6. Periodic safety update reports (PSURs)

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

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

See also Annex I 16.1.

6.1.1. Atezolizumab – TECENTRIQ (CAP) – EMA/PSUR/0000296544

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010644/202505)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tecentriq, a centrally authorised medicine containing atezolizumab 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 Tecentriq (atezolizumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning regarding other immune-mediated adverse reactions, and to add neutropenia and autoimmune haemolytic anaemia as undesirable effects with frequency 'common' and 'rare', respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[7].
- In the next PSUR, the MAH should continue to closely monitor cardiac arrythmia events.

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

6.1.2. Dabrafenib – FINLEE (CAP); TAFINLAR (CAP) – EMA/PSUR/0000296502

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010084/202505)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Finlee and Tafinlar, centrally authorised medicines containing dabrafenib 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 Finlee and Tafinlar (dabrafenib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information of Tafinlar (dabrafenib) should be updated to add radiation toxicity as a warning and an undesirable effect with a frequency 'common', and to add an interaction regarding potentiation of radiation toxicity. Therefore, the current terms of the marketing authorisation(s) should be varied[8]. The product information of

[7] 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.
[8] Update of SmPC sections 4.4 and 4.5 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.

Finlee (dabrafenib) should be updated to add radiation toxicity as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[9].

- In the next PSUR, the MAH should submit a cumulative review and analysis of all cases of diabetes reported with dabrafenib as monotherapy or in combination with trametinib from all sources, focusing on immune-mediated diabetes. In addition, the MAH should discuss the need for an update of the product information, as warranted. Finally, the MAH should include cases of Vogt-Koyanagi-Harada (VKH)-like syndrome as part of the discussion related to the important identified risk of uveitis.

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

6.1.3. Fenfluramine – FINTEPLA (CAP) – EMA/PSUR/0000296555

Applicant: UCB Pharma

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010907/202506)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Fintepla, a centrally authorised medicine containing fenfluramine 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 Fintepla (fenfluramine) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing warning on aortic or mitral valvular heart disease (VHD) and pulmonary arterial hypertension (PAH) to reflect the new evidence regarding VHD/PAH and the need for echocardiographic monitoring. Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAH should include as safety concerns the following: important identified risks of PAH, VHD and serotonin syndrome; important potential risks of growth retardation, and suicidal ideation and behaviour; missing information of long-term safety and off-label use (in wider paediatric epilepsies and obesity). Regarding growth retardation, the MAH should submit all relevant data and discuss the need to adjust the risk minimisation measures, as warranted. Finally, the MAH should continue to closely monitor the risk of medication errors (particularly those related to the PTs 'accidental overdose', 'extra dose administered' and 'incorrect dose administered').

[9] 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.
[10] Update of SmPC sections 4.4 and 4.8. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.

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

6.1.4. Gadopiclenol – ELUCIREM (CAP); VUEWAY (CAP) – EMA/PSUR/0000296586

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

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000232/202504)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Elucirem and Vueway, centrally authorised medicines containing gadopiclenol 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 Elucirem and Vueway (gadopiclenol) 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 provide a cumulative review of acute pancreatitis and acute kidney injury including an assessment of a potential class effect, of accumulation and retention of gadolinium in the brain and in other organs or tissues, including an assessment on the impact of gadolinium deposition on the interpretation of subsequent MRIs following administration of macrocyclic GdCA and a discussion on the need for an update of the product information and/or additional pharmacovigilance activities, as warranted. The MAHs should also continue to monitor 'Kounis syndrome and hypersensitivity reactions with cardiovascular involvement', and add safety in children <2years of age as missing information in the PSUR safety specification.

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. Hydroxycarbamide – SIKLOS (CAP); XROMI (CAP) – EMA/PSUR/0000296554

Applicants: Lipomed GmbH, Theravia

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00001692/202506)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Siklos and Xromi, centrally authorised medicines containing hydroxycarbamide 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 Siklos and Xromi (hydroxycarbamide) in the approved indication(s) remains unchanged.

- Nevertheless, the product information should be updated to add limbal stem cell deficiency as a warning and an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[11].

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

6.1.6. Lumacaftor / Ivacaftor – ORKAMBI (CAP) – EMA/PSUR/0000296584

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00010455/202505)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Orkambi, a centrally authorised medicine containing lumacaftor/ivacaftor 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 Orkambi (lumacaftor/ivacaftor) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning regarding elevated transaminases and hepatic injury, as well as the warning regarding depression. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAH should provide a cumulative review of behavioural adverse event cases. The MAH should also keep severe cutaneous reactions and intercranial hypertension under close monitoring.

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

6.1.7. Mirabegron – BETMIGA (CAP) – EMA/PSUR/0000296505

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00010031/202506)

Background

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

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Betmiga, a centrally authorised medicine containing mirabegron 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 Betmiga (mirabegron) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide cumulative reviews of cases of lupus erythematous, pemphigus, and hepatobiliary disorders other than transaminases increase, especially drug-induced liver injury (DILI), liver injury and hepatitis. The MAH should also continue conducting a literature review for dementia and amnesia/memory loss and provide a detailed discussion. Finally, the MAH should continue to closely monitor epilepsy/seizures, hallucinations and ANCA vasculitis cases, and of concomitant treatment with CYP2D6 substrates with narrow therapeutic indices or individually dose-titrated, as well as to provide detailed analyses of medication errors (ME) where mirabegron is contraindicated and ADRs associated with this type of MEs, of new cases of the important potential risk QT prolongation (especially the cases with ventricular tachycardia) and of atrial flutter, autoimmune hepatitis, severe cutaneous adverse reactions (SCARs) and erythema multiforme.

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

6.1.8. Polatuzumab vedotin – POLIVY (CAP) – EMA/PSUR/0000296524

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010817/202506)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Polivy, a centrally authorised medicine containing polatuzumab vedotin 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 Polivy (polatuzumab vedotin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add infusion site extravasation injury as a warning and undesirable effect with frequency 'uncommon'. In addition, the existing undesirable effect of transaminases increased should be moved under the SOC Hepatobiliary disorders. Therefore, the current terms of the marketing authorisation(s) should be varied[13].

[13] 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.

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.

6.1.9. Respiratory syncytial virus vaccine (bivalent, recombinant) – ABRYSVO (CAP) – EMA/PSUR/0000296493

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000102/202505)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Abrysvo, a centrally authorised medicine containing respiratory syncytial virus vaccine (bivalent, recombinant) 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 Abrysvo (respiratory syncytial virus vaccine (bivalent, recombinant)) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to reword the indication to 'active immunisation of pregnant individuals to protect infants from birth through 6 months of age against lower respiratory tract disease caused by respiratory syncytial virus (RSV)'. Therefore, the current terms of the marketing authorisation(s) should be varied[14].
- In the next PSUR, the MAH should provide EU data on 'maternal exposure during pregnancy', in addition to the UK and US data. The MAH should also discuss the article of *Gabet, A et al, 2026*[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.

6.1.10. Semaglutide – OZEMPIC (CAP); RYBELSUS (CAP); WEGOVY (CAP) – EMA/PSUR/0000296561

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010671/202505)

Background

[14] Update of SmPC section 4.1. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[15] Gabet A, Bertrand M, Jabagi MJ, et al. Maternal and Neonatal Outcomes After Respiratory Syncytial Virus Prefusion F Protein Vaccination During Pregnancy: Analysis From the 2024-2025 Immunization Campaign in France. Obstet Gynecol. 2026 Jan 1;147(1):118-126. doi: 10.1097/AOG.0000000000006121. Epub 2025 Nov 13

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Ozempic, Rybelsus and Wegovy, centrally authorised medicines containing semaglutide, 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 Ozempic, Rybelsus and Wegovy (emaglutide) 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 continue to closely monitor medication errors and to discuss information from literature related among others to semaglutide-induced Wernicke encephalopathy, liver damage, chronic cough, and ophthalmic issues.
- The MAH is requested to submit, within 2 months, to EMA a pooled analysis of all CVOTs studies as part of a post-authorisation measure (LEG), including a discussion on the need for any potential amendments to the product information and/or the RMP, as warranted.

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

6.1.11. Toripalimab – LOQTORZI (CAP) – EMA/PSUR/0000296630

Applicant: Topalliance Biosciences Europe Limited

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00011094/202506)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Loqtorzi, a centrally authorised medicine containing toripalimab 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 Loqtorzi (toripalimab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding immune-mediated adverse reactions in patients with pre-existing autoimmune disease. Therefore, the current terms of the marketing authorisation(s) should be varied[16].
- In the next PSUR, the MAH should provide an updated review on the topic of lichen disease and discuss the need to update the product information, as warranted. The MAH should also address the publication by *Jiang P et al., 2025*,[17], present any new and

[16] Update of SmPC section 4.4. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[17] Jiang P, Wei S, Li C, et al. Safety and efficacy of toripalimab plus concurrent chemoradiotherapy for locally advanced cervical cancer: a single-arm, phase Ib trial. BMC Cancer. 2025 Oct 14;25(1):1566. doi: 10.1186/s12885-025-15059-y.

significant safety findings for hemophagocytic lymphohistiocytosis, and discuss the need to update the product information, as warranted.

The frequency of PSUR submission should be revised from 6-monthly 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.

6.1.12. Trametinib – MEKINIST (CAP); SPEXOTRAS (CAP) – EMA/PSUR/0000296499

Applicant: Novartis Europharm Limited

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010262/202505)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Mekinist and Spexotras, centrally authorised medicines containing trametinib 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 Mekinist and Spexotras (trametinib) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide a cumulative review of all cases of diabetes reported with dabrafenib and trametinib from all sources focusing on immune-mediated diabetes, and a discussion on the need to the product information and/or risk minimisation measures, as warranted.

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

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

See also Annex I 16.2.

6.2.1. Bromfenac – YELLOX (CAP); NAP – EMA/PSUR/0000296580

Applicants: Bausch + Lomb Ireland Limited, various

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00000436/202505)

Background

Bromfenac is a non-steroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative ocular inflammation following cataract extraction in adults.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Yellox, (a) centrally authorised medicine(s) containing bromfenac, and nationally authorised medicines containing bromfenac 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 bromfenac-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning regarding the risks with use in pregnancy due to uncertainties for the systemic exposure and the known risk for other NSAIDs. Therefore, the current terms of the marketing authorisations should be varied[18].
- In the next PSUR, the MAHs should maintain or include as a minimum the following safety concerns: 'corneal epithelial events' and 'respiratory events related to asthma, urticaria or rhinitis' as important identified risks; 'severe cutaneous adverse reactions' as an important potential risk; 'use of bromfenac beyond 2 weeks' and 'use in patients with impaired liver function', as missing information topics.

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.

6.2.2. Human normal immunoglobulin – DEQSIGA (CAP); FLEBOGAMMA DIF (CAP); HIZENTRA (CAP); HYQVIA (CAP); KIOVIG (CAP); PRIVIGEN (CAP); NAP – EMA/PSUR/0000296525

Applicants: Takeda Manufacturing Austria AG, BAXALTA INNOVATIONS GmbH, CSL Behring GmbH, Instituto Grifols S.A., various

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00001633/202505)

Background

Human normal immunoglobulin (IgG) is a category of immunotherapy drugs, specifically classified as immune sera and immunoglobulins. Derived from pooled human plasma, it acts as a passive immunization agent to treat primary/secondary immune deficiencies, infections, and autoimmune disorders, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Deqsiga, Flebogamma DIF, Hizentra, Hyqvia, Kiovig and Privigen, centrally authorised medicines containing human normal immunoglobulin, and nationally authorised medicines containing human normal immunoglobulin (IgG) and issued a recommendation on their marketing authorisation(s).

Summary of recommendation(s) and conclusions

[18] Update of SmPC section 4.6. 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 human normal immunoglobulin (IgG)-containing product(s) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisations for all human normal immunoglobulin (IgG), except Clayrig, Iqymune and Tegeline, should be maintained.
- Nevertheless, the product information of Clayrig, Iqymune and Tegeline should be updated to add exfoliative dermatitis as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisations should be varied[19].
- In the next PSUR, the MAH of Privigen should present an assessment of cases related to exfoliative dermatitis, exfoliative dermatitis generalised, and erythroderma, and discuss the need to update the product information, as warranted. The MAH of Hizentra should closely monitor renal events to further evaluate whether renal failure should be included in the safety concerns as a potential risk. The MAHs of Yimmugo and Intratect should present the off-label use data, while both these MAHs and the MAH of Pentaglobin to continue to closely monitor any cases concerning the interaction of iv IgG and mAb products. The MAH of Xembify should provide an evaluation of serious infusion site reactions, and separately the cases associated with ulcerations and necrosis, and discuss the need to update the product information, as warranted. Finally, the MAH of Cuvitru should provide detailed information on the two deaths following the use of Cuvitru in pregnant and breastfeeding women and the seven events with a fatal outcome in neonates or infants <2 years old.
- The MAH Grifols of Xembify is requested to upgrade the important potential risk 'hypersensitivity reactions including anaphylactic reaction' to an important identified risk, at the next regulatory opportunity or at the latest within 12 months, and submit the RMP to the relevant national competent authorities.

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.

6.2.3. Mycophenolate mofetil – CELLCEPT (CAP); MYCLAUSEN (CAP); MYCOPHENOLATE MOFETIL TEVA (CAP); MYFENAX (CAP); NAP; mycophenolic acid (NAP) – EMA/PSUR/0000296546

Applicants: Teva B.V., Roche Registration GmbH, Passauer Pharma GmbH, various

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00010550/202505)

Background

Mycophenolate mofetil is a prodrug of mycophenolic acid, a cytostatic and immunosuppressive agent acting as a potent inhibitor of *de novo* synthesis of purines essential for T- and B-cell proliferation. Mycophenolate mofetil or mycophenolic acid in combination with corticosteroids and either ciclosporin A or tacrolimus is indicated for the prophylaxis of acute organ rejection and for the treatment of first or refractory organ

[19] 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.

rejection in patients receiving allogeneic renal transplant, for the prophylaxis of acute organ rejection in patients receiving allogeneic cardiac transplants as well as for the prophylaxis of acute organ rejection in patients receiving allogeneic hepatic transplants.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Cellcept, Myclausen, Mycophenolate Mofetil Teva and Myfenax, centrally authorised medicines containing mycophenolate mofetil, and nationally authorised medicines containing mycophenolate mofetil or mycophenolic acid, 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 mycophenolate mofetil- and mycophenolic acid-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add anaphylactic reactions as undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisations should be varied[20].
- In the next PSUR, the MAHs Novartis and Roche should present an updated review of new cases of alveolar proteinosis, and discuss any relevant literature being published in the reporting interval.
- The MAH Roche should update their RMP at the next regulatory opportunity or at the latest by six months, in order to remove the missing information 'long term safety (growth retardation, pubertal maturation and fertility, bone health, metabolic problems and neurocognitive development)' from the RMP. In addition, the two questionnaires listed in the pharmacovigilance plan (module III.1) in the RMP regarding effectiveness of risk minimisation measures should be deleted. The questionnaires are included in annex 4 of the RMP and the documents are titled "Guided Questionnaire for Patients reporting CellCept Exposure during Pregnancy" and "Guided Questionnaire for Health Care Providers reporting CellCept Exposure during Pregnancy".
- All MAHs with medicinal products containing mycophenolate mofetil and mycophenolate acid approved under article 10(1) and 10.a of Directive 2001/83/EC, as amended, should update their RMP's to ensure that the obligation to submit PSUR's no longer is mentioned in the RMP's, which would impact Part III and Part VI in the RMP's. This should be done in the next RMP update to be submitted within an upcoming regulatory procedure affecting the RMP or at the latest within six months after finalisation of this PSUSA procedure to the relevant national competent authority or the EMA.

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

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

6.3.1. Caffeine / codeine / paracetamol / propyphenazone (NAP), acetylsalicylic acid / caffeine / codeine / paracetamol (NAP) – EMA/PSUR/0000296512

Applicants: various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00002312/202506)

Background

Caffeine/codeine/paracetamol/propyphenazone and acetylsalicylic acid/caffeine/codeine/paracetamol are fixed dose combinations, generally indicated for the short-term symptomatic treatment of mild to strong pain (varies between products), particularly when such pain is not adequately relieved by analgesics such as paracetamol or ibuprofen alone. Additionally, acetylsalicylic acid/caffeine/codeine/paracetamol is indicated for the symptomatic treatment of fever and inflammatory processes of the upper respiratory tract, accompanied by cough and fever.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing acetylsalicylic acid/caffeine/codeine/paracetamol or caffeine/codeine/paracetamol/propyphenazone 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 acetylsalicylic acid/caffeine/codeine/paracetamol-containing medicinal products and of caffeine/codeine/paracetamol/propyphenazone-containing medicinal products in the approved indication(s) remain unchanged.
- Nevertheless, the product information should be updated to add a warning about central sleep apnoea (CSA), hyperalgesia, hepatobiliary disorders, Kounis syndrome, and information related to tolerance and opioid use disorder (abuse and dependence), as needed. In addition, the product information should be updated to add the drug-drug interaction with gabapentinoids, and to add pancreatitis, sphincter of Oddi dysfunction and Kounis syndrome as undesirable effects with a frequency 'not known'. The package leaflet should also be updated to highlight the need to store the product in a safe and secure place. Therefore, the current terms of the marketing authorisation(s) should be varied[21].
- In the next PSUR, the MAH(s) should update the list of PSUR safety concerns and keep it as follows: opioid toxicity (respiratory depression and sedation) and opioid use disorder (abuse, misuse, dependence, addiction, tolerance, withdrawal) as important identified risks; effect on fertility as missing information.

The frequency of PSUR submission should be revised from seven-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.

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

6.3.2. Cefixime (NAP) – EMA/PSUR/0000296579

Applicants: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00000594/202506)

Background

Cefixime is a β-lactam antibiotic indicated for the treatment of acute and chronic infections of various severity caused by cefixime susceptible bacteria that can be treated orally, such as infections of the upper respiratory tract, infections of the lower respiratory tract, infections of the kidney and efferent urinary tract, infections of the bile passages and scarlet fever.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing cefixime 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 cefixime-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add encephalopathy as a warning and an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[22].
- In the next PSUR, all MAH(s) should provide a cumulative review of Kounis syndrome, and of acute generalised exanthematous pustulosis (AGEP) including a discussion on the need to update the product information as warranted. In addition, all MAH(s) should provide new cases of encephalopathy and discuss the need to update the product information, as warranted. All MAH(s) should closely monitor cases of IgA bullous dermatosis/Linear IgA bullous disease. The MAHs Menarini Industrie Farmaceutiche Riunite S.r.l. and Merck Healthcare KGaA should include at least the following minimum to the list of safety concerns for purposes of PSURs: severe cutaneous adverse reactions (SCARs) and pseudomembranous colitis as important identified risks; antibiotic resistance as important potential risk; pregnancy and lactation as missing information. Finally, the MAH ADVANZ PHARMA should discuss all closed signals in detail and provide a discussion on the need to update the product information, as warranted.

The frequency of PSUR submission should be revised from eight-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.

6.3.3. Etodolac (NAP) – EMA/PSUR/0000296549

Applicants: various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00001324/202505)

[22] Update of SmPC sections 4.4, 4.8 and 4.9. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.

Background

Etodolac is a nonsteroidal anti-inflammatory drug (NSAID), indicated for the treatment of inflammatory conditions such as osteoarthritis (spondylarthrosis and other degenerative joint diseases), rheumatoid arthritis, ankylosing spondylitis and pain from other inflammatory situations, in the postoperative period and in acute injuries (trauma).

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing etodolac 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 etodolac-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include acute generalised exanthematous pustulosis (AGEP) to the existing warning regarding skin reactions, and to add AGEP, fixed drug eruption and anaphylactic reaction as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[23].
- In the next PSUR, all MAHs are requested to include, as a minimum, the following safety concerns: liver injury, gastrointestinal haemorrhage, ulceration and perforation, serious cutaneous adverse reactions (SCARs), hypersensitivity, and cardiovascular and cerebrovascular events.

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.

6.3.4. Gadobenic acid (NAP) – EMA/PSUR/0000296542

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00001500/202504)

Background

Gadobenic acid is a contrast enhancer agent to improve image quality with magnetic resonance imaging (MRI) scans.

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

Summary of recommendation(s) and conclusions

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of gadobenic acid-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH(s) should provide a cumulative review of cases of acute pancreatitis, of acute kidney injury, associated with gadolinium-based contrast agents (GBCAs), including an assessment of a potential class effect of GBCAs. In addition, the MAH(s) should provide a cumulative review of cases of accumulation and retention of gadolinium in the brain, and in other organs or tissues than the brain. Finally, the MAH(s) should provide an evaluation of effectiveness of the follow-up questionnaires adopted by PRAC regarding potential long-term symptoms associated with GBCAs to be used for follow-up.

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. Gadobutrol (NAP) – EMA/PSUR/0000296537

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00001502/202504)

Background

Gadobutrol is a contrast enhancer indicated for generally facilitating visualisation of abnormal structures or lesions and helping in the differentiation between healthy and pathological tissue in various organs.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing gadobutrol 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 gadobutrol-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH(s) should provide a cumulative review of cases of acute pancreatitis, of acute kidney injury, and of acute generalized exanthematous pustulosis (AGEP) associated with gadolinium-based contrast agents (GBCAs), including an assessment of a potential class effect of GBCAs. In addition, the MAH(s) should provide a cumulative review of cases of accumulation and retention of gadolinium and the impact of gadolinium deposition on the interpretation of subsequent magnetic resonance imaging (MRI) following administration of macrocyclic GBCA, as well as discuss the need for an update of the product information and/or additional pharmacovigilance activities, as warranted. The MAH(s) should also provide an evaluation of effectiveness of the follow-up questionnaires adopted by PRAC regarding potential long-term symptoms

associated with GBCAs to be used for follow-up. Finally, the MAH Bayer should also continue to routinely monitor fatal cases, and remove from PSUR summary of safety concerns the following important identified risks: anaphylactoid reactions, acute respiratory distress syndrome (ARDS)/pulmonary oedema.

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. Gadodiamide (NAP) – EMA/PSUR/0000296538

Applicants: various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00001503/202504)

Background

Gadodiamide is a contrast enhancer agent, indicated for cranial and spinal magnetic resonance imaging (MRI) and for general MRI of the body as well as cardiac MRI.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing gadodiamide 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 gadodiamide-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained (remaining suspended).
- In the next PSUR, the MAH(s) should provide a cumulative review of cases of accumulation and retention of gadolinium in the brain, and in other organs or tissues than the brain. Finally, the MAH(s) should provide an evaluation of effectiveness of the follow-up questionnaires adopted by PRAC regarding potential long-term symptoms associated with GBCAs to be used for follow-up.

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

6.3.7. Gadopentetic acid (NAP) – EMA/PSUR/0000296588

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00001504/202504)

Background

Gadopentetic acid is a contrast agent for magnetic resonance imaging (MRI).

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing gadopentetic acid 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 gadopentetic acid-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH(s) should provide a cumulative review of cases of accumulation and retention of gadolinium in the brain, and in other organs or tissues than the brain. In addition, the MAH(s) should provide a cumulative review of cases of acute pancreatitis associated with gadolinium-based contrast agents (GBCAs), including an assessment of a potential class effect of GBCAs. The MAH(s) should remove from the summary of safety concerns of PSUSA the following important identified risks: anaphylactoid reactions, seizures/convulsions. The MAH(s) should also stop reporting of Magnevist enteral since it is neither registered nor marketed in any country for more than a decade, unless upon any change in the marketing authorisation status of Magnevist enteral. Finally, the MAH(s) should provide an evaluation of effectiveness of the follow-up questionnaires adopted by PRAC regarding potential long-term symptoms associated with GBCAs to be used for follow-up.

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.

6.3.8. Gadoteric acid (IV and intravascular formulations) (NAP) – EMA/PSUR/0000296563

Applicants: various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001506/202504)

Background

Gadoteric acid (IV and intravascular formulations) is a contrast agent indicated for use for intensification of the contrast in magnetic resonance imaging (MRI).

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing gadoteric acid (IV and intravascular formulations) 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 gadoteric acid (IV and intravascular formulations)-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH(s) should provide a cumulative review of cases of accumulation and retention of gadolinium and the impact of gadolinium deposition on

the interpretation of subsequent MRIs following administration of macrocyclic gadolinium-based contrast agents (GBCAs), as well as discuss the need for an update of the product information and/or additional pharmacovigilance activities, as warranted. The MAH(s) should also provide an evaluation of effectiveness of the follow-up questionnaires adopted by PRAC regarding potential long-term symptoms associated with GBCAs to be used for follow-up. Finally, the MAH of Dotarem should remove from the PSUR summary of safety concerns the important potential risk of anaphylaxis.

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.

6.3.9. Gadoteridol (NAP) – EMA/PSUR/0000296571

Applicants: various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00001507/202504)

Background

Gadoteridol is a contrast agent indicated for or use in magnetic resonance imaging (MRI) to produce contrast enhancement in the central nervous system (CNS) (brain and spine) and surrounding tissues. Gadoteridol is also indicated for whole body MRI, including the head, neck, liver, breast, musculoskeletal system, and soft tissue pathologies.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing gadoteridol 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 gadoteridol-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH(s) should provide a cumulative review of cases of accumulation and retention of gadolinium and the impact of gadolinium deposition on the interpretation of subsequent MRIs following administration of macrocyclic gadolinium-based contrast agents (GBCAs), as well as discuss the need for an update of the product information and/or additional pharmacovigilance activities, as warranted. In addition, in line with the important potential risk of 'adverse clinical effects of accumulation and retention of gadolinium in the brain, and in other organs or tissues than the brain', the MAH(s) should present a cumulative review on this topic taking into account all data sources available. The MAH(s) should also provide an evaluation of effectiveness of the follow-up questionnaires adopted by PRAC regarding potential long-term symptoms associated with GBCAs to be used for follow-up.

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.

6.3.10. Gadoxetic acid disodium (NAP) – EMA/PSUR/0000296534

Applicants: various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00001509/202504)

Background

Gadoxetic acid disodium is a contrast agent indicated for the detection of focal liver lesions and provides information on the character of lesions in T1-weighted magnetic resonance imaging (MRI).

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing gadoxetic acid disodium 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 gadoxetic acid disodium-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH(s) should provide a cumulative review of cases of accumulation and retention of gadolinium and the impact of gadolinium deposition on the interpretation of subsequent MRIs following administration of macrocyclic gadolinium-based contrast agents (GBCAs), as well as discuss the need for an update of the product information and/or additional pharmacovigilance activities, as warranted. The MAH(s) should also provide an evaluation of effectiveness of the follow-up questionnaires adopted by PRAC regarding potential long-term symptoms associated with GBCAs to be used for follow-up. Finally, the MAH(s) should also provide a cumulative review of cases of non-anaphylactic non-cardiogenic pulmonary oedema, as well as to discuss the need to update the product information and/or the RMP, as 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.

6.3.11. Ioversol (NAP) – EMA/PSUR/0000296526

Applicants: various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00001775/202506)

Background

Ioversol is an X-ray contrast medium for diagnostic use only, indicated for arteriography, angiocardiography, venography, aortography, computed tomography (CT), intravenous urography, and in some countries for myelography.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing ioversol 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 ioversol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add Kounis syndrome as a warning and an undesirable 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 provide a cumulative review of all data sources for evidence of exacerbation of myasthenia gravis.

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.

6.3.12. Levomethadone (NAP) – EMA/PSUR/0000296494

Applicants: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00001855/202505)

Background

Levomethadone is an opioid analgesic in adults for oral substitution treatment of opioid dependence within a framework of medical, social and psychological treatment, and in adults for severe pain, and opioid type dependence, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing levomethadone 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 levomethadone-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding hepatobiliary disorders and hyperalgesia, to add Sphincter of Oddi dysfunction and acute pancreatitis as undesirable effects with a frequency 'not known', and to reflect available information related to congenital malformations and neurodevelopmental impairment in children born to opioid-dependent mothers treated with methadone during pregnancy. Therefore, the current terms of the marketing authorisation(s) should be varied[25].

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

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

6.3.13. Methadone (NAP) – EMA/PSUR/0000296520

Applicants: various

PRAC Lead: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00002004/202505)

Background

Methadone is a synthetic opioid analgesic, indicated for the treatment of moderate to severe pain and opioid addiction, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing methadone 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 methadone-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding hepatobiliary disorders and hyperalgesia, and to add sphincter of Oddi dysfunction and acute pancreatitis as undesirable effects with a frequency 'not known'. The product information should also be updated to reflect available information from some observational studies related to congenital malformations and neurodevelopmental impairment in children born to opioid-dependent mothers treated with methadone during pregnancy, as well as their limitations including confounding by maternal familial and socioenvironmental factors associated with opioid use disorders which preclude drawing conclusions regarding the contribution of methadone. Therefore, the current terms of the marketing authorisation(s) should be varied[26].

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

6.3.14. Nicardipine (NAP) – EMA/PSUR/0000296516

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00002149/202505)

Background

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

Nicardipine is a vasodilator indicated for the treatment of prophylaxis of patients with chronic stable angina, treatment of hypertension considered to be mild to moderate in severity, prevention and treatment of ischaemia due to cerebral infarction and its sequelae, prevention of neurological deterioration caused by cerebral vasospasm secondary to subarachnoid haemorrhage for oral formulations and treatment of acute life-threatening hypertension, particularly in the event of malignant arterial hypertension/hypertensive encephalopathy, aortic dissection, when short acting beta-blocker therapy is not suitable, or in combination with a beta-blocker when beta-blockade alone is not effective, severe pre-eclampsia, when other intravenous antihypertensive agents are not recommended or are contraindicated, treatment of post-operative hypertension for IV formulations, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing nicardipine 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 nicardipine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding careful monitoring of oxygenation in patients with pre-existing pulmonary disorders or other conditions that may compromise respiratory function, and to add hypoxia as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[27].
- In the next PSUR, the MAH(s) should closely monitor cases of hypoxia occurred in nicardipine oral formulation and should provide a cumulative review of all cases of cutaneous vasculitis.

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.

6.3.15. Pneumococcal polysaccharide vaccine (NAP) – EMA/PSUR/0000296552

Applicants: various

PRAC Lead: Pernille Harg

Scope: Evaluation of a PSUSA procedure (PSUSA/00002453/202505)

Background

Pneumococcal polysaccharide vaccine is indicated for vaccination against pneumococcal disease caused by those pneumococcal types included in the vaccine.

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

[27] Update of SmPC sections 4.4 (for all nicardipine formulations) and 4.8 (for i.v. formulations only). The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Pneumococcal polysaccharide vaccine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add injection site necrosis as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[28].
- In the next PSUR, the MAH(s) should provide a cumulative review of cases of erythema multiforme, including but not limited to the MedDRA PT erythema multiforme, of cases of injection site streaking and lymphangitis including but not limited to the MedDRA preferred terms (PTs) 'Injection site streaking' and 'Lymphangitis', and of cases of diarrhoea. In addition, the MAH(s) should discuss the need for any potential amendment to the product information, as warranted by the above cumulative reviews.

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

6.3.16. Tamoxifen (NAP) – EMA/PSUR/0000296514

Applicants: various

PRAC Lead: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00002846/202504)

Background

Tamoxifen is an antineoplastic (anti-tumour) hormonal agent, indicated for the treatment of breast cancer, prevention of breast cancer in women at high risk, the treatment of anovulatory infertility, and the treatment of endometrial cancer, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing tamoxifen 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 tamoxifen-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add decreased bone mineral density in premenopausal women as a warning and an undesirable effect with a frequency 'not known', and to add a precaution regarding measures to maintain bone health for premenopausal women. In addition, the product information should be updated to add prolongation of the QT interval on the electrocardiogram (ECG) as a warning and an undesirable effect with a frequency 'not known', and a recommendation for monitoring of patients with underlying risks for QT prolongation including patients

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

concomitantly treated with other medicinal products known to prolong the QT interval. Therefore, the current terms of the marketing authorisation(s) should be varied[29].

- In the next PSUR, all MAHs should closely monitor diabetes mellitus and cognitive disorders, and should review cumulatively events of libido decreased/loss of libido and related terms (e.g. vulvovaginal dryness, dyspareunia) reported with tamoxifen including a discussion on the need to update the product information, as warranted. In addition, the MAH Sandoz should provide any safety information that is relevant to the benefit-risk profile of tamoxifen from study 2017-004554-42.

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

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

See also Annex I 16.5.

6.5.1. Tafamidis – VYNDAQEL (CAP) – EMA/VR/0000297114

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Zoubida Amimour

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to add a new warning on co-administration tafamidis meglumine/tafamidis and BCRP substrates, update drug-drug interaction information with BCRP substrates following the PRAC PSUR assessment report for procedure no.: EMEA/H/C/PSUSA/00002842/202405. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the European Medicines Agency website address in line with the latest EU CP QRD template version 10.4.

Background

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

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit a variation to update the product information. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation. For background information, see PRAC Minutes December 2024[30].

Summary of recommendation(s)

[29] Update of SmPC sections 4.4, 4.5. 4.8 and 4.9. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position
[30] Held 25 - 28 November 2024

- Based on the available data and the Rapporteur's assessment, PRAC agreed that the product information should be updated to include a warning on co-administration of tafamidis and BCRP substrates, as well as update the information related to the drug-drug interaction with BCRP sustrates (sections 4.4 and 4.5 and package leaflet).
- The MAH should submit, to EMA, within 30 days, responses to the request for supplementary information (RSI).

6.6. Expedited summary safety reviews[31]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[32]

None

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

See Annex I 17.2.

7.3. Results of PASS imposed in the marketing authorisation(s)[34]

7.3.1. 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)

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 submit the results of an imposed non-interventional PASS: '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)' in accordance with Article 107p of Directive 2001/83/EC, the MAH submitted to EMA the final study report on 04 November 2025. PRAC discussed the final study results.

[31] 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
[32] In accordance with Article 107n of Directive 2001/83/EC
[33] 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
[34] In accordance with Article 107p-q of Directive 2001/83/EC

Summary of recommendation(s) and conclusions

- Based on the review of the final report of the non-interventional PASS, PRAC considered that a request for supplementary information (RSI) is necessary before a recommendation can be made. PRAC requested the MAH to discuss whether safety concerns, for which no additional pharmacovigilance activities or risk minimisation measures remain, should be removed from the RMP. In addition, the MAH was requested to discuss whether an update of the product information is warranted based on the data regarding abscess and cellulitis events upon completion of the study.
- Nevertheless, PRAC considered that the terms of the marketing authorisation(s) for Benlysta (belimumab) should be varied to remove the PASS from Annex II-D 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'. Consequently, PRAC agreed to remove the product from the additional monitoring list, and to update the RMP accordingly.
- The MAH should submit responses to the RSI within 60 days to EMA. A 60 days-assessment timetable will be followed.

7.4. Results of PASS non-imposed in the marketing authorisation(s)[35]

See also Annex I 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 ALID01803 to assess the effects of Aldurazyme (laronidase) treatment on lactation in women with MPS I and their breastfed infant. 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

[35] 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

review, PRAC considered that the ongoing variation assessing the final study report could be considered acceptable provided that the MAH submits satisfactory responses to an RSI.

- PRAC supported the removal of 'use of laronidase in pregnant and lactating women' from the list of safety concerns in the RMP. However, this topic should be maintained as a safety concern within the PSUR in order to enable close monitoring of pregnancy and breastfeeding cases in the upcoming reporting periods. The safety concern should be renamed 'use of laronidase in pregnant and breastfeeding women'. Moreover, the MAH should discuss the need to revise the product information regarding pregnancy and breastfeeding, as warranted. Finally, the MAH should submit the final report of the Pregnancy Sub registry PASS study (ALID04911) as part of the RSI of this procedure.

7.4.2. Tocilizumab – ROACTEMRA (CAP) – EMA/VR/0000261482

Applicant: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of the final report for study ML28664 (RABBIT), listed as a category 3 study in the RMP. This was a non-interventional post-authorisation safety study aimed at collecting and analysing safety data related to the use of tocilizumab in rheumatoid arthritis patients in Germany. The RMP version 30.0 has also been submitted. In addition, the MAH removed the education materials from the RMP and PI as agreed by PRAC during procedure PSUSA/00002980/202204. Furthermore, the MAH took the opportunity to introduce editorial and formatting changes to the PI and to align the wording used for the pre-filled syringe and the pre-filled pen, as well as to update the list of local representatives in the Package Leaflet.

Background

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

As stated in the RMP of RoActemra (tocilizumab), the MAH conducted a non-imposed non-interventional PASS ML28664 (RABBIT) to collect and analyse safety data related to the use of tocilizumab in rheumatoid arthritis patients in Germany. 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 supported the removal of the educational materials (Healthcare Provider Brochure, Dosing Guide, and Patient Brochure); however, PRAC did not support the removal of the patient card. PRAC considered that the patient card should remain as an additional risk minimisation measure in the RMP, and that the product information should be updated accordingly, as the card informs patients about the risks associated with tocilizumab and the necessary actions to be taken, particularly in situations requiring emergency care.

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

See Annex I 17.5.

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

8.1. Annual reassessments of the marketing authorisation

See also Annex I 18.1.

8.1.1. Lomitapide – LOJUXTA (CAP) – EMA/S/0000290089

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Annual reassessment of the marketing authorisation

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.

Lojuxta, a centrally authorised product containing lomitapide, was authorised in 2013 under exceptional circumstances. The benefit-risk of Lojuxta is reviewed on a yearly basis by CHMP based on the submission and assessment of additional post-authorisation data (i.e. specific obligations). PRAC is responsible for providing advice to CHMP on this annual re-assessment with regard to safety and risk management aspects.

Summary of advice

- Based on the review of the available information on the status of the fulfilment of specific obligations and safety data submitted, PRAC considered that the annual re-assessment procedure for Lojuxta (lomitapide) could only be finalised if satisfactory clarification is given on some pending issues.
- PRAC supported the termination of the Lomitapide Observational Worldwide Evaluation Registry (LOWER) and requested the MAH to provide updated Annexes IID, IIE, as well as an updated RMP, to remove all references to the registry. In addition, in order to ensure adequate monitoring of safety and efficacy after termination of LOWER study, the MAH should continue to provide yearly updates on any new information concerning the safety and efficacy of Lojuxta as specific obligation for the marketing authorisation under exceptional circumstances. These annual reports will be submitted each year in parallel with the PSURs.

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2.

8.3. Renewals of the marketing authorisation

See Annex I 18.3.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

Disclosure of information on results of pharmacovigilance inspections could undermine the protection of the purpose of these inspections, investigations and audits. Therefore, such information is not reported in the minutes.

9.3. Others

None

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

10.1.1. Lithium sulphate (NAP) - SE/H/xxxx/WS/943

Applicant: Karo Pharma AB (Lithionit)

PRAC Lead: Karin Bolin

Scope: PRAC consultation on a worksharing variation procedure (SE/H/xxxx/WS/943) to update the product information regarding the development of Darier disease following administration of lithium containing products, at request of Sweden.

Background

Lithium belongs to the pharmacotherapeutic group of neuroleptics. Lithionit (lithium sulphate) is indicated in the treatment of bipolar disorder, where it has a prophylactic effect against manic as well as depressive phases, and a therapeutic effect in acute manic states.

In the context of the evaluation of a worksharing variation procedure on the need to update the product information of lithium-containing products regarding the development of Darier disease, Sweden requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC supported the addition of 'exacerbation of Darier's disease' as undesirable effect for lithium sulphate products and considered this update relevant to be implemented for all lithium-containing products.

11. Scientific advice procedures

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

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The Chair thanked Irina Sandu for her contribution as a member representing Romania, and welcomed Roxana Stefania Udrescu as the new alternate.The Chair also welcomed Michal Rataj as the new alternate for the Patients' Organisation Representative and Jana Pecherova as the new alternate for Slovakia, as Miroslava Gocova has now taken the role of the member.

12.1.2. Nominated proxy

Rugile Pilviniene (Lithuania) gave a proxy to Zane Neikena (Latvia) for part of the meeting.

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2026

PRAC lead: Ulla Wändel Liminga, Liana Martirosyan

The EMA Secretariat presented to PRAC the final PRAC work plan for 2026. PRAC members

were invited to send their final comments or suggestions on the draft final work plan before its adoption.

Post meeting note: the PRAC work plan was adopted on 22 January 2026 and published on 23 January 2026 (EMA/PRAC/352294/2025).

12.8. Planning and reporting

None

12.8.1. Marketing authorisation applications (MAA) forecast for 2025 – planning update dated Q4 2025

The EMA Secretariat presented for information to PRAC a quarterly updated report on marketing authorisation applications (MAA) planned for submission (the business 'pipeline') in Q4 2025, along with the new more interactive format. PRAC noted the information.

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

None

12.10.3. PSURs repository

None

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

In line with the criteria for plenary presentation of updates to the EURD List adopted by PRAC in December 2021, PRAC endorsed the draft revised EURD list, version January 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 January 2026, the updated EURD list was adopted by CHMP and CMDh at their January 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

None

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. PRAC Risk Minimisation Alliance (PRISMA) - Mandate for operational phase

PRAC leads: Ulla Wändel Liminga, Liana Martirosyan

The EMA Secretariat presented to PRAC a summary of the PRISMA activities of the past two years along with the draft mandate for the new phase of this group from pilot to operational, including the PRISMA composition and the immediate plans for 2026. PRAC members were invited to provide comments in writing to the EMA lead by 31 January 2026.

Post meeting note: The mandate of the PRISMA was adopted via written procedure on 10 February 2026.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[36]

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[37].

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Atropine (eyedrops indicated for slowing the progression of myopia in paediatric patients) – RYJUNEA (CAP); NAP

Applicant: Santen Oy, various

PRAC Rapporteur: Martin Huber

Scope: Signal of strabismus

EPITT 20244 – New signal

Lead Member State(s): DE

14.1.2. Darolutamide – NUBEQA (CAP)

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Signal of angioedema

EPITT 20237 – New signal

Lead Member State(s): BE

14.1.3. Oxacillin (NAP)

Applicant(s): various

PRAC Lead: Eva Jirsová

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

[36] 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

[37] 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

EPITT 20223 – New signal

Lead Member State(s): CZ

14.1.4. Vortioxetine - BRINTELLIX (CAP)

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Jo Robays

Scope: Signal of acute pancreatitis

EPITT 20234 – New signal

Lead Member State(s): BE

14.1.5. Zolbetuximab – VYLOY (CAP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Signal of protein-losing gastroenteropathy

EPITT 20236 – New signal

Lead Member State(s): NL

14.1.6. Zuranolone – ZURZUVAE (CAP)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Guðrún Stefánsdóttir

Scope: Signal of suicidal ideation

EPITT 20232 – New signal

Lead Member State(s): IS

14.2. New signals detected from other sources

None

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

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

15.1.1. Liraglutide (CAP MAA) - EMEA/H/C/006620

Scope (pre D-180 phase): Treatment of diabetes and weight management

15.1.2. Liraglutide (CAP MAA) - EMEA/H/C/006615

Scope (pre D-180 phase): Treatment of adults, adolescents and children aged 10 years and above with insufficiently controlled type 2 diabetes as an adjunct to diet and exercise

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. Acalabrutinib – CALQUENCE (CAP) – EMA/VR/0000304591

Applicant: AstraZeneca AB

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Submission of an updated RMP version 9 in order to revise the list of safety concerns, based on the currently available post-marketing and clinical data.

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

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

15.2.3. Avatrombopag – DOPTELET (CAP) – EMA/VR/0000296242

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: A grouped application consisting of:

C.I.11 for RMP: Submission of an updated RMP version 4.0 to propose the removal of missing information Use in splenectomy patients with chronic liver disease, Use in patients receiving interferon products and Safety in patients undergoing invasive procedures.

C.I.11 for RMP: Submission of an updated RMP version 4.0 to propose to remove Targeted Medical Event Questionnaires.

C.I.11 for RMP: Submission of an updated RMP version 4.0 to update information on immune thrombocytopenia (ITP) PASS and chronic liver disease (CLD) PASS studies

15.2.4. Ciclosporin – IKERVIS (CAP); VERKAZIA (CAP) – EMA/VR/0000296156

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: C.I.11.z - the MAH submitted a worksharing (WS) application to revise the ciclosporin Risk Management plan (PAES study completion). In addition the follow up form in the current RMP is revised to be in compliance with latest version of Guideline on specific adverse reaction follow-up questionnaires (Specific AR FUQ).

15.2.5. Denosumab – PROLIA (CAP) – EMA/VR/0000288149

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of an updated RMP version 33.0 in order to remove and reclassify important identified risks, potential risks, and to remove completed category 3 Study 20090522. Update in RMP of the information about Patient reminder cards for osteonecrosis of the jaw have been reflected in Annex II of the PI.

15.2.6. Elvitegravir / Cobicistat / Emtricitabine / Tenofovir alafenamide – GENVOYA (CAP) – EMA/VR/0000308403

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Amelia Cupelli

Scope: A grouped application consisting of three Type II variations, as follows:

C.I.11 for RMP: Submission of an updated RMP version 6.1 in order to propose the removal of the Important Identified Risk of 'Suicidal ideation/suicide attempt in patients with a preexisting history of depression or psychiatric illness'.

C.I.11 for RMP: Submission of an updated RMP version 6.1 in order to propose the removal of the Important Identified Risk of 'Concurrent use of drugs whose coadministration with Genvoya is contraindicated'.

C.I.11 for RMP: Submission of an updated RMP version 6.1 in order to propose the removal of the following Missing Information: 'Safety in patients with cardiac conduction disorders'.

15.2.7. 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.

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

Applicant: Santen Oy

PRAC Rapporteur: Maria del Pilar Rayon

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

15.2.9. Reslizumab – CINQAERO (CAP) – EMA/VR/0000309197

Applicant: Teva B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of an updated RMP version 6.0 in order to remove follow-up questionnaires and routine antidrug antibody testing, remove an uninitiated PASS study for malignancy and update the list of safety concerns to remove the important identified risk of severe hypersensitivity reactions, as well as the important potential risks of malignancy and medication errors.

15.2.10. Zanubrutinib – BRUKINSA (CAP) – EMA/VR/0000301572

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an updated RMP version 6.1 in order to reclassify the risks of hepatotoxicity (including hepatic failure) and drug-drug interaction with CYP3A inducers.

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

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

15.3.1. Abemaciclib – VERZENIOS (CAP) – EMA/VR/0000307389

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carla Torre

Scope: Update of section 5.1 of the SmPC in order to update efficacy information based on final OS data from study monarchE (I3Y-MC-JPCF) listed as a PAES in the Annex II; this is a randomized, open-label, phase 3 study of abemaciclib combined with standard adjuvant endocrine therapy versus standard adjuvant endocrine therapy alone in patients with high risk, node positive, early stage, hormone receptor positive, human epidermal receptor 2 negative, breast cancer. The Annex II and Package Leaflet are updated accordingly. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes and to update the list of local representatives in the Package Leaflet.

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

Applicants: Mylan Pharmaceuticals Limited, various

PRAC Rapporteur: Maria del Pilar Rayon

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

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

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

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

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

15.3.3. Adalimumab – HUMIRA (CAP) – EMA/VR/0000303439

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Karin Bolin

Scope: Submission of the final report from study M10-870 listed as a category 3 study in the RMP. This is a Phase 3, Multi-Center, Open-Label Study of the Human Anti-TNF Monoclonal Antibody Adalimumab to Evaluate Long-Term Safety and Tolerability of Repeated Administration of Adalimumab in Pediatric Subjects with Ulcerative Colitis Who Completed the Study M11-290. The RMP version 17.0 has also been submitted.

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

Applicant: Glaxosmithkline (Ireland) Limited

PRAC Rapporteur: Karin Bolin

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

15.3.5. Budesonide / Formoterol - BIRESP SPIROMAX (CAP) - EMEA/H/C/WS2806/G; Budesonide / Formoterol - DUORESP SPIROMAX (CAP) - EMEA/H/C/WS2806/G

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: A grouped application consisting of:

C.I.6: Extension of the asthma indication to include the anti-inflammatory reliever (AIR) use

for DuoResp Spiromax and BiResp Spiromax, based on the latest GINA report, the European Respiratory Society guidelines, and literature data. In addition, the Applicant referred to changes made for Symbicort (UK). As a consequence, sections 4.1, 4.2, 4.4, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI introduced editorial changes, and is brought in line with the latest QRD template version. The RMP version 4.0 has also been submitted.

C.I.2.a: To update sections 4.5 and 5.1 of the SmPC following assessment of the same change for the reference product Symbicort Turbohaler (SE/H/0229/001- 002) and also Symbicort (UK).

15.3.6. Bempedoic acid – NILEMDO (CAP); Bempedoic acid / Ezetimibe – NUSTENDI (CAP) – EMA/VR/0000284929

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.6 of the SmPC in order to update information on breast-feeding and lactation, based on final results from study 1002FDC-075. This is an open-label, phase 4, postmarketing milk-only lactation study to evaluate the concentration of bempedoic acid and bempedoic acid/ ezetimibe in the breast milk of healthy lactating women administered therapeutic doses of bempedoic acid or bempedoic acid/ezetimibe fixed combination drug product (FCDP). The Package Leaflet is updated accordingly. The updated RMP version 8.1 has also been submitted.

15.3.7. Decitabine / Cedazuridine – INAQOVI (CAP) – EMA/VR/0000304730

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Extension of indication to include treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are ineligible for standard induction chemotherapy for INAQOVI in combination with venetoclax, based on interim results from study ASTX727-07; this is a single-arm, open-label pharmacokinetic, safety, and efficacy study of ASTX727 in combination with venetoclax in adult patients with acute myeloid leukemia. 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 1.3 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and bring editorial changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.8. Deucravacitinib – SOTYKTU (CAP) – EMA/VR/0000282554

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Extension of indication to include, for SOTYKTU, alone or in combination with conventional synthetic disease modifying antirheumatic drugs (DMARDs), the treatment of active psoriatic arthritis (PsA) in adults who have had an inadequate response or who have

been intolerant to a prior DMARD therapy, based on results from the following phase 3 studies: Study IM011-054 (POETYK PsA-1); this is a phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of deucravacitinib in participants with active psoriatic arthritis who are naïve to biologic disease-modifying anti-rheumatic drugs, and Study IM011-055 (POETYK PsA-2); this is a multi-center, randomized, double-blind, placebo-controlled phase 3 study to evaluate the efficacy and safety of BMS-986165 in participants with active psoriatic arthritis (PsA) who are naïve to biologic disease modifying anti-rheumatic drugs or had previously received TNFα inhibitor treatment. 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 3.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet, as well as introduce administrative changes to the PI.

15.3.9. Deucravacitinib – SOTYKTU (CAP) – EMA/VR/0000309456

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Update of sections 4.6, 5.2 and 5.3 of the SmPC based on final results from study IM011-1123. This is a Phase 4, open-label, single-group, single-dose study evaluating deucravacitinib concentrations in the breast milk and plasma of healthy lactating female subjects. The updated RMP (version 4.0) has also been submitted.

15.3.10. Dupilumab – DUPIXENT (CAP) – EMA/VR/0000282164

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of moderate to severe chronic spontaneous urticaria (CSU) in children aged 2 to 11 years whose disease is inadequately controlled by H1 antihistamines and who are naive to anti-IgE therapy for CSU for DUPIXENT, based on the results from study PKM16982; this is a multi-center, single-arm study to investigate the pharmacokinetics and safety of dupilumab in male and female participants ≥2 years to <12 years of age with uncontrolled chronic spontaneous urticaria (CSU). Consequently, 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 14.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template.

15.3.11. Durvalumab – IMFINZI (CAP) – EMA/VR/0000282058

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication for IMFINZI to include in combination with FLOT chemotherapy as neoadjuvant and adjuvant treatment, followed by adjuvant IMFINZI monotherapy, for the treatment of adults with resectable gastric or gastro-oesophageal junction adenocarcinoma , based on interim results from study MATTERHORN, (D910GC00001); this is a randomized, double-blind, placebo-controlled, phase 3 study of

neoadjuvant-adjuvant durvalumab and FLOT chemotherapy followed by adjuvant durvalumab in patients with resectable gastric and gastroesophageal junction cancer (GC/GEJC). 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. Version 14.0 of the RMP has also been submitted.

15.3.12. Eltrombopag – REVOLADE (CAP) – EMA/VR/0000288153

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study CETB115E2201, listed as a category 3 study in the RMP. This is a paediatric phase II, open-label, uncontrolled, intra-patient dose escalation study to characterise the pharmacokinetics after oral administration of eltrombopag in paediatric patients with refractory, relapsed severe aplastic anaemia or recurrent aplastic anemia. The RMP version 57.0 has also been submitted.

15.3.13. Encorafenib – BRAFTOVI (CAP) – EMA/VR/0000304994

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to include, in combination with cetuximab and FOLFOX, the first line treatment of adult patients with metastatic colorectal cancer with a BRAF V600E mutation for BRAFTOVI, based on the interim results from the pivotal Study C4221015 (BREAKWATER). This is an open-label, multicenter, 3-arm, randomized Phase 3 study of encorafenib plus cetuximab (EC) alone or in combination with mFOLFOX6 versus standard of care chemotherapy in first-line participants with BRAF V600E-mutant mCRC. 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. The version 3.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI.

15.3.14. Epinephrine – EURNEFFY (CAP) – EMA/X/0000248440

Applicant: Alk-Abello A/S

PRAC Rapporteur: Terhi Lehtinen

Scope: Extension application to introduce a new strength (1 mg nasal spray, solution). The new strength is indicated for children with a body weight of 15 kg to less than 30 kg.

15.3.15. Faricimab – VABYSMO (CAP) – EMA/VR/0000308736

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Update of sections 4.4 and 5.1 of the SmPC in order to update safety information, based on final results from study GR42691 (AVONELLE-X) listed as category 3 study in the RMP. This was a multicenter, open-label extension study to evaluate the long-term safety

and tolerability of faricimab in patients with neovascular Age-related Macular Degeneration (nAMD). The Package Leaflet is updated accordingly. The RMP version 8.0 has also been submitted. In addition, the MAH took the opportunity to introduce administrative and editorial changes to the PI, including to the Annex II, Labelling and to the list of local representatives in the Package Leaflet.

15.3.16. Finerenone – KERENDIA (CAP) – EMA/X/0000248026

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new strength 40 mg for film-coated tablets, grouped with a type II variations C.I.6: Extension of indication to include the treatment of symptomatic chronic heart failure with left ventricular ejection fraction (LVEF) ≥ 40% in adults for KERENDIA, based on final results from the phase 3 study FINEARTS-HF (20103); this is a randomized, double-blind, placebo-controlled phase 3 study evaluating the efficacy and safety of finerenone on morbidity and mortality in participants with symptomatic heart failure with left ventricular ejection fraction (LVEF) ≥40%.; Type II variation C.I.13: Submission of the final report from non-clinical study T105281-7, R-14405 - Juvenile toxicology study in rats; Type IB variation C.I.z: Minor correction of numbers in the currently approved SmPC due to a previously communicated GCP violation affecting the FIDELIO-DKD and FIGARO-DKD trials.

As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3, 6.1, 6.6 and 8 of the SmPC are updated. The Labelling and Package Leaflet are updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial and administrative changes to the PI and to bring it in line with the latest QRD template version 10.4.

15.3.17. Ganaxolone – ZTALMY (CAP) – EMA/VR/0000263646

Applicant: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application consisting of:

C.I.4: Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from a transgenic mouse carcinogenicity study listed as a category 3 study in the RMP; this is a 26-week Oral Gavage Carcinogenicity Study of Ganaxolone in Hemizygous CByB6F1-Tg(HRAS)2Jic Mice. The RMP version 3.2 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.

C.I.4: Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from non-clinical study for juvenile toxicity in M2 (metabolite) listed as a category 3 study in the RMP; this is an Oral (Gavage) administration juvenile toxicity study of M2 (Ganaxolone Metabolite) in CD (Sprague Dawley) IGS Rats.

15.3.18. Ganaxolone - ZTALMY (CAP) - EMEA/H/C/005825/II/0004/G, Orphan

Applicant: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application comprised of 8 Type II variations as follows:
1 Type II (C.I.4): Update of section 5.2 of the SmPC in order to update ganaxolone metabolite pattern at steady state based on re-analysis of 1042-TQT-1001 listed as a category 3 study in the RMP to evaluate the ganaxolone steady-state metabolite.
7 Type II (C.I.13): Submission of the final non-clinical study reports for the in vitro DDI potential and in vivo PK of the metabolite M17 listed as category 3 studies in the RMP.
The RMP version 1.2 has also been submitted. In addition, the MAH took the opportunity to introduce updates to the PI that reflect clarifications and typographical corrections, including to sections 4.2 and 4.4 of the SmPC.

15.3.19. Ganaxolone - ZTALMY (CAP) - EMEA/H/C/005825/II/0015/G, Orphan

Applicant: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application consisting of five Type II variations, as follows:

C.I.13: Submission of the final report from non-clinical study 1022-9241 listed as a category 3 study in the RMP. This is a 26-Week Toxicity Study of Ganaxolone Metabolite, M2, by Oral Gavage in the Sprague-Dawley rat with a 2-Week Recovery Period. The RMP version 3 has also been submitted.

C.I.13: Submission of the final report from non-clinical study 20447815 listed as a category 3 study in the RMP. This is a An Oral (Gavage) Study of the Effects of M2 (Ganaxolone Metabolite) Administration on Embryo/Fetal Development in CD (Sprague Dawley) IGS Rat. The RMP version 3 has also been submitted.

C.I.13: Submission of the final report from Weight of Evidence (WoE) assessment to evaluate the need for a 2-year carcinogenicity study in rats with GNX, listed as a category 3 study in the RMP.

C.I.13: Submission of the final report from WoE assessment to evaluate the need for a 2-year carcinogenicity study in rats with M2, listed as a category 3 study in the RMP.

C.I.13: Submission of the final report from WoE assessment to evaluate the need for a juvenile toxicity study with M2, listed as a category 3 study in the RMP.

15.3.20. 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.

15.3.21. Human normal immunoglobulin – PRIVIGEN (CAP) – EMA/VR/0000304719

Applicant: CSL Behring GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: A grouped application consisting of:

C.I.6: Extension of indication to include treatment of patients with measles pre/post-exposure prophylaxis in whom active immunisation is contraindicated or not advised, for PRIVIGEN, in alignment with the IVIg core SmPC (EMA/CHMP/BPWP/94038/2007 Rev). As a consequence, sections 2, 4.1, 4.2 and 5.2 of the SmPC. The Package Leaflet is updated accordingly. The RMP version 9 has also been submitted.

15.3.22. Hydrocortisone – EFMODY (CAP) – EMA/VR/0000282500

Applicant: Neurocrine Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of adrenal insufficiency (AI) in adolescents aged 12 years and over and adults for Efmody, based on final results from study DIUR-016-AI; this is a double-blind, double-dummy, two-way cross-over, randomised, phase II study of efficacy, safety and tolerability of modified-release hydrocortisones: Chronocort (Efmody) versus Plenadren, in AI. Consequently, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, e-mail of MAH was updated. Version 2.0 of the RMP has also been submitted.

15.3.23. Isatuximab – SARCLISA (CAP) – EMA/X/0000281242

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (1400 mg) and a new route of administration (subcutaneous use). The RMP (version 3.0) is updated in accordance.

15.3.24. Marstacimab – HYMPAVZI (CAP) – EMA/VR/0000304590

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Extension of indication to include treatment of routine prophylaxis of bleeding episodes in patients 12 years of age and older with haemophilia A with factor VIII inhibitors or haemophilia B with factor IX inhibitors for HYMPAVZI, based on final results from study B7841005 and interim results from supportive study B7841007. Study B7841005 is an open-label study in adolescent and adult severe (coagulation factor activity ≤2%) with or without

inhibitors comparing standard treatment to PF-06741086 Prophylaxis. Study B7841007 is an open-label extension study to evaluate the long-term safety, tolerability, and efficacy of marstacimab prophylaxis in severe (coagulation factor activity <1%) hemophilia A participants with or without inhibitors or moderately severe to severe hemophilia B participants (coagulation factor activity ≤2%) with or without inhibitors. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted.

15.3.25. Methoxy polyethylene glycol-epoetin beta – MIRCERA (CAP) – EMA/VR/0000309070

Applicant: Roche Registration GmbH

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Update of section 4.4 of the SmPC in order to discontinue provision of free anti-erythropoietin antibody (AEAB) testing (or re-testing). The RMP version 13.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.26. Mexiletine – NAMUSCLA (CAP) – EMA/X/0000258210

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Extension application to add new strengths of 62 mg and 83 mg grouped with an Extension of indication to include the symptomatic treatment of myotonia in children and adolescents (from 6 to 18 years of age) with non-dystrophic myotonic disorders for NAMUSCLA, based on final results from study MEX-NM-301 as well as population pharmacokinetic analysis of mexiletine in healthy volunteers and myotonic patients; MEX-NM-301 is an open-label, multi-centre, single arm, interventional study to describe the steady-state PK, safety, and efficacy of mexiletine in pediatric patients (6 to <18 years of age) with myotonic disorders. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI and update the list of local representatives in the Package Leaflet.

15.3.27. Niraparib / Abiraterone acetate – AKEEGA (CAP) – EMA/VR/0000282377

Applicant: Janssen Cilag International

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include AKEEGA with prednisone or prednisolone for the treatment of adult patients with metastatic hormone-sensitive prostate cancer (mHSPC) and HRR-mutations (germline and/or somatic, based on interim results from study 67652000PCR3002 (AMPLITUDE); this is a phase 3 randomized, placebo-controlled, double-blind study of niraparib in combination with abiraterone acetate and prednisone versus abiraterone acetate and prednisone for the treatment of participants with deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-sensitive prostate cancer (mCSPC). 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 3.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. In addition, the MAH is requesting an additional year of market protection for a new indication.

15.3.28. Nivolumab – OPDIVO (CAP) – EMA/VR/0000282199

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Extension of indication for OPDIVO to include treatment of paediatric and adult patients with relapsed/refractory classical Hodgkin Lymphoma, based on results from study CA209744; a phase 2, open-label study of nivolumab + brentuximab vedotin for children, adolescents, and young adults with R/R CD30+ classical Hodgkin lymphoma after failure of first-line therapy, followed by brentuximab vedotin + bendamustine for participants with a suboptimal response. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 44.0 of the RMP has also been submitted

15.3.29. Nivolumab – OPDIVO (CAP) – EMA/VR/0000304938

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Extension of indication to include OPDIVO for the treatment of adults and adolescents 12 years of age and older with previously untreated Stage III or IV classical Hodgkin Lymphoma (cHL), based on results from the pivotal study CA2098UT (SWOG 1826), a Phase 3, randomized, open-label study of nivolumab (Opdivo) + AVD (N-AVD) versus brentuximab vedotin (Adcetris) + AVD (Bv-AVD) in patients (age ≥12 years) with newly diagnosed, advanced stage cHL. 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 51.0 of the RMP has also been submitted.

15.3.30. Nivolumab / Relatlimab – OPDUALAG (CAP) – EMA/VR/0000303785

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Extension of indication to include patients with tumour cell PD-L1 expression ≥ 1% in the first-line treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents 12 years of age and older for OPDUALAG, based on updated descriptive 4-year data from pivotal Study CA224047; this is a randomized, double-blind phase 2/3 study of relatlimab combined with nivolumab versus nivolumab in participants with previously untreated metastatic or unresectable melanoma. 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 3.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to remove Annex IV from the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.31. Ozanimod – ZEPOSIA (CAP) – EMA/VR/0000291324

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 5.1 of the SmPC in order to update efficacy and safety information based on the final results from study RPC01-3102, listed as a category 3 study in RMP. This is a Phase 3, multicenter, open-label extension trial of oral RPC1063 as therapy for moderate to severe ulcerative colitis. The RMP version 11.0 has also been submitted.

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

Applicant: Biomarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

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

C.I.6: Extension of indication to include treatment of adolescent patients aged 12 to <16 years with phenylketonuria (PKU) for PALYNZIQ, based on interim results from study 165-306; this is a Phase 3 open label, randomized, controlled, 2-arm, multicenter study designed to evaluate the safety and efficacy of pegvaliase in adolescent participants 12 to <18 years old with PKU. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI to include editorial changes and remove references to the route of administration of adrenaline (injection) to allow physicians to prescribe any approved adrenaline device.

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

The RMP version 5.0 has also been submitted.

15.3.33. Pertuzumab – PERJETA (CAP) – EMA/VR/0000307073

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy data, based on final results from post-authorisation efficacy study BO25126 (APHINITY) listed as a specific obligation in the Annex II; this is a phase III, randomized multicenter, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer; the Package Leaflet and Annex II are updated accordingly. The RMP version 15.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorials changes to the PI.

15.3.34. Regorafenib – STIVARGA (CAP) – EMA/VR/0000312922

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to update paediatric information based on results from paediatric Study 7. The RMP version 7.3 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4.

15.3.35. Risankizumab – SKYRIZI (CAP) – EMA/X/0000296763

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: Extension application to introduce a new strength of 55 mg solution for injection grouped with a type II variation C.I.6.a to include treatment of paediatric plaque psoriasis (6 to < 18 years) for Skyrizi, based on final results from study M19-977 and interim results from study M19-973. M19-977 is a randomized, active-controlled, efficacy assessor-blinded study to evaluate pharmacokinetics, safety, and efficacy of risankizumab in patients from 6 to less than 18 years of age with moderate to severe plaque psoriasis; M19-973 is a phase 3 multicenter, single-arm, open-label extension study to assess the safety, tolerability, and efficacy of risankizumab in subjects with moderate to severe plaque psoriasis who have completed participation in study M19-977. As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 6.1, 6.4, 6.5, 6.6, and 8 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 7.0 of the RMP has also been submitted.

15.3.36. Selpercatinib – RETSEVMO (CAP) – EMA/VR/0000282012

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include paediatric patients 2 years and older with: (1) Advanced RET fusion-positive thyroid cancer who are radioactive iodine-refractory, (2) Advanced RET-mutant medullary thyroid cancer, (3) Advanced RET fusion-positive solid tumours, when treatment options not targeting RET provide limited clinical benefit, or have been exhausted, for RETSEVMO, based on final results from study J2G-OX-JZJJ (LOXO RET 18036, LIBRETTO-121); this is a multicentre, open-label Phase 1/2 study in paediatric patients with advanced solid or primary central nervous system (CNS) tumours harbouring an activating RET alteration. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 6.6 of the SmPC are updated. The Package Leaflet and labelling are updated in accordance. Version 15.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the information related to Quality part of the dossier.

15.3.37. Semaglutide – WEGOVY (CAP) – EMA/X/0000296344

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Extension application to introduce a new pharmaceutical form (tablet), associated with four new strengths (1.5 mg, 4 mg, 9mg and 25 mg) and a new route of administration (oral use).

15.3.38. Tirzepatide – MOUNJARO (CAP) – EMA/VR/0000271898

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Update of section 4.6 of the SmPC in order to include information on breast-feeding based on results from study I8F-MC-GPIN (GPIN); this was a Phase I, single-site, open-label, single-treatment arm, single-dose, lactation study, assessing pharmacokinetics of tirzepatide in breastmilk and plasma in healthy lactating women. The Package Leaflet is also updated accordingly. The RMP version 6.1 has also been submitted.

15.3.39. Tolvaptan – JINARC (CAP) – EMA/VR/0000246866

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to update information based on final results from study 156-12-299 listed as a category 1 study in the RMP. This is a 7.5-year, Multicentre, Non-interventional, Post-authorisation Safety Study for Patients Prescribed JINARC for Autosomal Dominant Polycystic Kidney Disease. This study was intended to explore the safety profile and usage of Jinarc when used in the real-world setting in Europe, particularly with relation to the risk of liver injury. The Package Leaflet is updated accordingly. The RMP version 15.1 has also been submitted. In addition, the MAH took the opportunity to update Annex II section D, to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.4.

15.3.40. Vedolizumab – ENTYVIO (CAP) – EMA/VR/0000255408

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study MLN0002SC-3030 listed as a category 3 study in the RMP; this is a phase 3b open-label study to determine the long-term safety and efficacy of vedolizumab subcutaneous in subjects with ulcerative colitis and Crohn's disease; the Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to bring the PI in line with the latest QRD template, and to introduce changes to the PI that are pre-agreed in the previous procedures.

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/0000296585

Applicant: Bayer AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00011106/202505)

16.1.2. Adagrasib – KRAZATI (CAP) – EMA/PSUR/0000296576

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00000214/202506)

16.1.3. Alpelisib – PIQRAY (CAP) – EMA/PSUR/0000296587

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010871/202505)

16.1.4. Amivantamab – RYBREVANT (CAP) – EMA/PSUR/0000296559

Applicant: Janssen Cilag International

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010977/202505)

16.1.5. Anakinra – KINERET (CAP) – EMA/PSUR/0000296578

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00000209/202505)

16.1.6. Arpraziquantel – ARPRAZIQUANTEL (Art 58) – EMA/PSUR/0000294554

Applicant: Merck Europe B.V.

PRAC Rapporteur: Adam Przybyłkowski

Scope: Evaluation of a PSUSA procedure (PSUV)

16.1.7. Artesunate – ARTESUNATE AMIVAS (CAP) – EMA/PSUR/0000296558

Applicant: Amivas Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010958/202506)

16.1.8. Bevacizumab gamma – LYTENAVA (CAP) – EMA/PSUR/0000296623

Applicant: Outlook Therapeutics Limited

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00011065/202505)

16.1.9. Sipavibart – KAVIGALE (CAP) – EMA/PSUR/0000296621

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00011113/202506)

16.1.10. Binimetinib – MEKTOVI (CAP) – EMA/PSUR/0000296615

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010717/202506)

16.1.11. Cholera vaccine – VAXCHORA (CAP) – EMA/PSUR/0000296628

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010862/202506)

16.1.12. COVID-19 mRNA vaccine – KOSTAIVE (CAP) – EMA/PSUR/0000296565

Applicants: Seqirus Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011115/202505)

16.1.13. Dantrolene sodium, hemiheptahydrate – AGILUS (CAP) – EMA/PSUR/0000296582

Applicant: Norgine B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011063/202505)

16.1.14. Datopotamab deruxtecan – DATROWAY (CAP) – EMA/PSUR/0000296568

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00011129/202506)

16.1.15. Dolutegravir / Rilpivirine – JULUCA (CAP) – EMA/PSUR/0000296626

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00010689/202505)

16.1.16. Dopamine hydrochloride – NEOATRICON (CAP) – EMA/PSUR/0000296599

Applicant: BrePco Biopharma Limited

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00011066/202505)

16.1.17. Drospirenone / Estetrol – DROVELIS (CAP); LYDISILKA (CAP) – EMA/PSUR/0000296619

Applicants: Estetra, Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010938/202505)

16.1.18. Efmoroctocog alfa – ELOCTA (CAP) – EMA/PSUR/0000296496

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010451/202506)

16.1.19. Elacestrant – ORSERDU (CAP) – EMA/PSUR/0000296492

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000120/202506)

16.1.20. Eladocagene exuparvovec – UPSTAZA (CAP) – EMA/PSUR/0000296569

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011004/202506)

16.1.21. Elafibranor – IQIRVO (CAP) – EMA/PSUR/0000296570

Applicant: Ipsen Pharma

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00011092/202506)

16.1.22. Encorafenib – BRAFTOVI (CAP) – EMA/PSUR/0000296574

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00010719/202506)

16.1.23. Entrectinib – ROZLYTREK (CAP) – EMA/PSUR/0000296595

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010874/202506)

16.1.24. Etranacogene dezaparvovec – HEMGENIX (CAP) – EMA/PSUR/0000296612

Applicant: CSL Behring GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011037/202505)

16.1.25. Flortaucipir (^{18}F) – TAUVID (CAP) – EMA/PSUR/0000296625

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011073/202505)

16.1.26. Formoterol / Glycopyrronium bromide / Budesonide – RILTRAVA AEROSPHERE (CAP); TRIXEO AEROSPHERE (CAP) – EMA/PSUR/0000296609

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010908/202506)

16.1.27. Givinostat – DUVYZAT (CAP) – EMA/PSUR/0000296566

Applicant: Italfarmaco S.p.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011141/202506)

16.1.28. Givosiran – GIVLAARI (CAP) – EMA/PSUR/0000296590

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010839/202505)

16.1.29. Glibenclamide – AMGLIDIA (CAP) – EMA/PSUR/0000296601

Applicant: AMMTek

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00010690/202505)

16.1.30. Human papillomavirus 9-valent Vaccine (Recombinant, adsorbed) – GARDASIL 9 (CAP) – EMA/PSUR/0000296500

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010389/202506)

16.1.31. Human papillomavirus vaccine [types 6, 11, 16, 18] (recombinant, adsorbed) – GARDASIL (CAP) – EMA/PSUR/0000296551

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00001634/202505)

16.1.32. Imetelstat – RYTELO (CAP) – EMA/PSUR/0000296613

Applicant: Geron Netherlands B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011117/202506)

16.1.33. Indacaterol / Glycopyrronium bromide / Mometasone – ENERZAIR BREEZHALER (CAP); ZIMBUS BREEZHALER (CAP) – EMA/PSUR/0000296547

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010861/202507)

16.1.34. Indacaterol / Mometasone – ATECTURA BREEZHALER (CAP); BEMRIST BREEZHALER (CAP) – EMA/PSUR/0000296553

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010850/202505)

16.1.35. Inebilizumab – UPLIZNA (CAP) – EMA/PSUR/0000296564

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010996/202506)

16.1.36. Insulin icodec – AWIQLI (CAP) – EMA/PSUR/0000296618

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011053/202505)

16.1.37. Iptacopan – FABHALTA (CAP) – EMA/PSUR/0000296594

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure (PSUSA/00011054/202506)

16.1.38. Larotrectinib – VITRAKVI (CAP) – EMA/PSUR/0000296535

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00010799/202505)

16.1.39. Latanoprost / Netarsudil – ROCLANDA (CAP) – EMA/PSUR/0000296556

Applicant: Santen Oy

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010905/202506)

16.1.40. Lazertinib – LAZCLUZE (CAP) – EMA/PSUR/0000296610

Applicant: Janssen Cilag International

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00011110/202505)

16.1.41. Levofloxacin – QUINSAIR (CAP) – EMA/PSUR/0000296515

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00010429/202505)

16.1.42. Lidocaine / Prilocaine – FORTACIN (CAP) – EMA/PSUR/0000296529

Applicant: Recordati Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00010110/202505)

16.1.43. Lonafarnib – ZOKINVY (CAP) – EMA/PSUR/0000296604

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011005/202505)

16.1.44. Luspatercept – REBLOZYL (CAP) – EMA/PSUR/0000296531

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00010860/202506)

16.1.45. Maribavir – LIVTENCITY (CAP) – EMA/PSUR/0000296562

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011024/202505)

16.1.46. Eplontersen – WAINZUA (CAP) – EMA/PSUR/0000296602

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00011120/202506)

16.1.47. Mosunetuzumab – LUNSUMIO (CAP) – EMA/PSUR/0000296629

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010999/202506)

16.1.48. Onasemnogene abeparvovec – ZOLGENSMA (CAP) – EMA/PSUR/0000296536

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010848/202505)

16.1.49. Ozanimod – ZEPOSIA (CAP) – EMA/PSUR/0000296528

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00010852/202505)

16.1.50. Palopegteriparatide – YORVIPATH (CAP) – EMA/PSUR/0000296591

Applicant: Ascendis Pharma Bone Diseases A/S

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure (PSUSA/00000173/202505)

16.1.51. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) – PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) – EMA/PSUR/0000296545

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010501/202505)

16.1.52. Pegvaliase – PALYNZIQ (CAP) – EMA/PSUR/0000296541

Applicant: Biomarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00010761/202505)

16.1.53. Pertuzumab / Trastuzumab – PHESGO (CAP) – EMA/PSUR/0000296614

Applicant: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010906/202506)

16.1.54. Piflufolastat (^{18}F) – PYLCLARI (CAP) – EMA/PSUR/0000296490

Applicant: Curium Pet France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00000097/202505)

16.1.55. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) – PREVENAR 20 (CAP) – EMA/PSUR/0000296603

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010981/202506)

16.1.56. Pneumococcal polysaccharide conjugate vaccine (21-valent) – CAPVAXIVE (CAP) – EMA/PSUR/0000296567

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00011121/202506)

16.1.57. Quizartinib – VANFLYTA (CAP) – EMA/PSUR/0000296557

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00000176/202506)

16.1.58. Relugolix / Estradiol / Norethisterone acetate – RYEQO (CAP) – EMA/PSUR/0000296598

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010942/202505)

16.1.59. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – MRESVIA (CAP) – EMA/PSUR/0000296622

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00011075/202505)

16.1.60. Rozanolixizumab – RYSTIGGO (CAP) – EMA/PSUR/0000296581

Applicant: UCB Pharma

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00000216/202506)

16.1.61. Satralizumab – ENSPRYNG (CAP) – EMA/PSUR/0000296560

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010944/202505)

16.1.62. Sotorasib – LUMYKRAS (CAP) – EMA/PSUR/0000296611

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010970/202505)

16.1.63. Sugemalimab – CEJEMLY (CAP) – EMA/PSUR/0000296627

Applicant: Cstone Pharmaceuticals Ireland Limited

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00011080/202506)

16.1.64. Trastuzumab deruxtecan – ENHERTU (CAP) – EMA/PSUR/0000296589

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010894/202506)

16.1.65. Vadadustat – VAFSEO (CAP) – EMA/PSUR/0000296607

Applicant: Medice Arzneimittel Puetter GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00011050/202506)

16.1.66. Vutrisiran – AMVUTTRA (CAP) – EMA/PSUR/0000296597

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011021/202506)

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

16.2.1. Topotecan – HYCAMTIN (CAP); TOPOTECAN HOSPIRA (CAP); NAP – EMA/PSUR/0000296506

Applicants: Sandoz Pharmaceuticals d.d., Pfizer Europe MA EEIG, various

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00002997/202505)

16.2.2. Treprostinil sodium – TREPULMIX (CAP); NAP – EMA/PSUR/0000296507

Applicants: SciPharm S.a.r.l., various

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure (PSUSA/00003013/202505)

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

16.3.1. Amiloride (NAP); amiloride / furosemide (NAP); amiloride / hydrochlorothiazide (NAP); amiloride / hydrochlorthiazide / timolol (NAP); amiloride / bumetanide (NAP); amiloride / chlortalidone (NAP) – EMA/PSUR/0000296593

Applicants: various

PRAC Lead: Guðrún Stefánsdóttir

Scope: Evaluation of a PSUSA procedure (PSUSA/00000148/202506)

16.3.2. Azelaic acid (NAP) – EMA/PSUR/0000296491

Applicants: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000276/202506)

16.3.3. Benzoyl peroxide / clindamycin phosphate (NAP) – EMA/PSUR/0000296608

Applicants: various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00000796/202505)

16.3.4. Bifonazole (NAP) – EMA/PSUR/0000296617

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000411/202505)

16.3.5. Calcipotriol (NAP) – EMA/PSUR/0000296620

Applicants: various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00000492/202506)

16.3.6. Carmellose (eye preparation) (NAP) – EMA/PSUR/0000296572

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00000562/202506)

16.3.7. Ceftriaxone sodium / lidocaine hydrochloride (NAP) – EMA/PSUR/0000296550

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000614/202505)

16.3.8. Ciprofloxacin / dexamethasone (ear drops, suspension) (NAP) – EMA/PSUR/0000296519

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010012/202504)

16.3.9. Clotiazepam (NAP) – EMA/PSUR/0000296600

Applicants: various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00000827/202505)

16.3.10. Diphtheria / tetanus vaccines (adsorbed) (NAP); diphtheria vaccines (adsorbed) (NAP) – EMA/PSUR/0000296575

Applicants: various

PRAC Lead: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00001128/202505)

16.3.11. Etamsylate (NAP) – EMA/PSUR/0000296606

Applicants: various

PRAC Lead: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00001294/202506)

16.3.12. Fenticonazole (NAP) – EMA/PSUR/0000296592

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00001371/202506)

16.3.13. Ferucarbotran (NAP) – EMA/PSUR/0000296616

Applicants: various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00001382/202506)

16.3.14. Flunisolide (NAP) – EMA/PSUR/0000296543

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00001417/202505)

16.3.15. Formoterol (NAP) – EMA/PSUR/0000296605

Applicants: various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00001469/202505)

16.3.16. Fotemustine (NAP) – EMA/PSUR/0000296596

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00001477/202506)

16.3.17. Fusidic acid (systemic use) (NAP) – EMA/PSUR/0000296498

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00010226/202505)

16.3.18. Gadoteric acid (intra articular formulation) (NAP) – EMA/PSUR/0000296573

Applicants: various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001505/202504)

16.3.19. Gemfibrozil (NAP) – EMA/PSUR/0000296533

Applicants: various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00001521/202505)

16.3.20. Hyoscine butylbromide / paracetamol (NAP) – EMA/PSUR/0000296523

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002303/202505)

16.3.21. Indobufen (NAP) – EMA/PSUR/0000296521

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00001736/202505)

16.3.22. Isradipine (NAP) – EMA/PSUR/0000296532

Applicants: various

PRAC Lead: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00001797/202506)

16.3.23. Levofloxacin/dexamethasone (ocular use) (NAP) – EMA/PSUR/0000296624

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010881/202506)

16.3.24. Levonorgestrel (for emergency contraception only) (NAP) – EMA/PSUR/0000296539

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010827/202505)

16.3.25. Levosulpiride (NAP); sulpiride (NAP) – EMA/PSUR/0000296527

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00001859/202506)

16.3.26. Lodoxamide (NAP) – EMA/PSUR/0000296522

Applicants: various

PRAC Lead: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00001898/202506)

16.3.27. Magnesium pidolate (NAP) – EMA/PSUR/0000296501

Applicants: various

PRAC Lead: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00010041/202506)

16.3.28. Mebendazole (NAP) – EMA/PSUR/0000296583

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00001939/202505)

16.3.29. Methoxyflurane (NAP) – EMA/PSUR/0000296548

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010484/202505)

16.3.30. Metolazone (NAP) – EMA/PSUR/0000296530

Applicants: various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00002037/202506)

16.3.31. Misoprostol (gynaecological indication - labour induction) (NAP) – EMA/PSUR/0000296504

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010353/202505)

16.3.32. Nicergoline (NAP) – EMA/PSUR/0000296517

Applicants: various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure (PSUSA/00002150/202505)

16.3.33. Ozenoxacin (NAP) – EMA/PSUR/0000296540

Applicants: various

PRAC Lead: Maria Martinez Gonzalez

Scope: Evaluation of a PSUSA procedure (PSUSA/00010651/202505)

16.3.34. Rifaximin (NAP) – EMA/PSUR/0000296518

Applicants: various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00002642/202505)

16.3.35. Sertaconazole (NAP) – EMA/PSUR/0000296509

Applicants: various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00002694/202506)

16.3.36. Solifenacin (NAP) – EMA/PSUR/0000296513

Applicants: various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00002769/202506)

16.3.37. Somatostatin (NAP) – EMA/PSUR/0000296510

Applicants: various

PRAC Lead: Maria Martinez Gonzalez

Scope: Evaluation of a PSUSA procedure (PSUSA/00002771/202506)

16.3.38. Ticlopidine (NAP) – EMA/PSUR/0000296508

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00002952/202505)

16.3.39. Torasemide (NAP) – EMA/PSUR/0000296503

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002998/202506)

16.3.40. Valsartan (NAP); hydrochlorothiazide / valsartan (NAP) – EMA/PSUR/0000296497

Applicants: various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010396/202504)

16.3.41. Zotepine (NAP) – EMA/PSUR/0000296511

Applicants: various

PRAC Lead: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00003154/202505)

16.4. Follow-up to PSUR/PSUSA procedures

None

16.5. Variation procedure(s) resulting from PSUSA evaluation

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

Applicant: Biomarin International Limited

PRAC Rapporteur: Eamon O Murchu

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

16.6. Expedited summary safety reviews[38]

None

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

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

17.1. Protocols of PASS imposed in the marketing authorisation(s)[39]

None

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

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

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Karin Erneholm

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

[38] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC
[39] In accordance with Article 107n of Directive 2001/83/EC
[40] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

17.2.2. Alemtuzumab – LEMTRADA (CAP) – EMA/PAM/0000303207

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the initial protocol and Statistical Analysis Plan for a substudy of LEMPASS (OBS13434/EUPAS7346): an external comparison cohort study to support the contextualization of the long-term safety profile of LEMTRADA® (alemtuzumab) in patients with relapsing forms of multiple sclerosis

17.2.3. Chikungunya vaccine (live) – IXCHIQ (CAP) – EMA/PAM/0000284934

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of the protocols for the post-authorisation safety studies VLA1553-403 (version 4.0) and VLA1553-406 (version 4.0) which are category 3 studies in the RMP. VLA1553-403 is an observational study to evaluate the safety of VLA1553 in pregnant women exposed to the vaccine in Brazil. VLA1553-406 is a prospective safety cohort study.

17.2.4. Chikungunya vaccine (recombinant, adsorbed) – VIMKUNYA (CAP) – EMA/PAM/0000276447

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the protocol for the post-authorisation safety study BN-CV-317-011 (version 1.0) which is a category 3 study in the RMP. BN-CV-317-011 is an observational prospective study to evaluate the safety of Vimkunya in pregnant women and their offspring.

17.2.5. COVID-19 mRNA vaccine – KOSTAIVE (CAP) – EMA/PAM/0000310312

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Protocol for PASS Category 3 study V206_06, a retrospective post-authorisation safety study to assess the risk of cardiac inflammatory and thromboembolic events following vaccination with sa-mRNA COVID-19 vaccine in adult individuals, reflected as a milestone in the Risk Management Plan.

17.2.6. COVID-19 vaccine (recombinant, adjuvanted) – BIMERVAX (CAP) – EMA/PAM/0000310979

Applicant: Hipra Human Health S.L.

PRAC Rapporteur: Zane Neikena

Scope: Submission of protocol version 3.0 for the non-imposed, non-interventional, category 3 post authorisation observational study to assess the safety of Bimervax using electronic health record (HER) databases in Europe (PASS VAC4EU).

17.2.7. Crovalimab – PIASKY (CAP) – EMA/PAM/0000281171

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Responses to the List of Questions raised in the assessment report of EMEA/H/C/006061/MEA/002 and submission of the revised draft non-interventional-PASS protocol MO45473. This is a post-authorization safety study (PASS) to characterize safety events and special conditions such as pregnancy and infant outcomes, in paroxysmal nocturnal hemoglobinuria (PNH) patients treated with crovalimab within the IPIG registry (Study MO45473).

17.2.8. Etranacogene dezaparvovec – HEMGENIX (CAP) – EMA/PAM/0000248926

Applicant: CSL Behring GmbH

PRAC Rapporteur: Bianca Mulder

Scope: The MAH submitted a PASS protocol (version 1.0), which covers a Healthcare Professional Survey (HCP) to assess the effectiveness of the additional Risk Minimization Measures (aRMM) for Hemgenix (etranacogene dezaparvovec).

17.2.9. Guselkumab – TREMFYA (CAP) – EMA/PAM/0000308163

Applicant: Janssen Cilag International

PRAC Rapporteur: Dirk Mentzer

Scope: Protocol update for PCSIMM001324 - A Retrospective Cohort Study Using Health Administrative Claims Databases to Assess Adverse Pregnancy and Infant Outcomes in Women Who Were Exposed to Guselkumab Versus Other Biologic Therapies During Pregnancy

17.2.10. Human thrombin / Human fibrinogen – TACHOSIL (CAP) – EMA/PAM/0000247840

Applicant: Corza Medical GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Revised protocol for PASS PasTel: Short- and long-term safety evaluation of TachoSil in paediatric population

17.2.11. Miglustat – OPFOLDA (CAP) – EMA/PAM/0000303344

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

Scope: Submission of protocol for POM-005 Registry, a global prospective observational registry of patients with Pompe disease.

17.2.12. Respiratory syncytial virus vaccine (bivalent, recombinant) – ABRYSVO (CAP) – EMA/PAM/0000303298

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Study protocol (Version 2.0) and first progress report for PASS C3671038, a post-authorisation safety study of ABRYSVO in immunocompromised, or renally or hepatically impaired older adults aged 60 years and older in a real world setting in Europe and UK.

17.2.13. Risankizumab – SKYRIZI (CAP) – EMA/PAM/0000309550

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: Protocol amendment for Study P16-751: Pregnancy Exposures and Outcomes in Women with Psoriasis Treated with Risankizumab: A Cohort Study Utilizing Large Electronic Healthcare Databases with Mother-Baby Linkage in the United States.

17.2.14. Risankizumab – SKYRIZI (CAP) – EMA/PAM/0000310075

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: Protocol amendment for study P23-653: Pregnancy Exposures and Outcomes in Women with Inflammatory Bowel Disease Treated with Risankizumab.

17.2.15. Semaglutide – RYBELSUS (CAP) – EMA/PAM/0000301197

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Protocol amendment for study NN9535-4447: 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.

17.2.16. Semaglutide – OZEMPIC (CAP) – EMA/PAM/0000295858

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Protocol amendment for Study NN9535-4447: 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.

17.2.17. 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.

17.2.18. Vutrisiran – AMVUTTRA (CAP) – EMA/PAM/0000301789

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Amendment of the study protocol of Prospective observational study to monitor and assess the safety of Amvuttra® [vutrisiran] in a real-world cohort of ATTR amyloidosis patients Protocol version 2.0 dated 09 September 2025

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

None

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

17.4.1. Adalimumab – IMRALDI (CAP) – EMA/VR/0000282472

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Karin Bolin

Scope: A grouped application comprised of:

Type II (C.I.13): Submission of the final report from study (ARTIS) listed as a category 3 study in the RMP. This is a nation-wide safety monitoring of Imraldi treatment in patients with Rheumatic diseases in Sweden. The RMP version 8.0 has been updated accordingly.

Type II (C.I.13): Submission of the final report from study (BIOBADASER) listed as a category 3 study in the RMP. This is a Spanish register of adverse events with targeted DMARD therapies in rheumatic diseases. The RMP version 8.0 has been updated accordingly.

Type IB (C.I.11) for RMP: Submission of an updated RMP version 8.0 in order to reflect the changes made in the RMP of the reference product Humira.

17.4.2. Arsenic trioxide – TRISENOX (CAP) – EMA/VR/0000281747

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.8 of the SmPC to update the safety information based on the final results from PASS C18477-ONC-50025 listed as a category 3 study in the RMP; this is an observational Post-Authorisation Long-Term Retrospective Safety Cohort Study of Arsenic Trioxide in First Line Low-to-Intermediate-Risk Acute Promyelocytic Leukaemia (APL) Patients. The updated RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4.

[41] In accordance with Article 107p-q of Directive 2001/83/EC
[42] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

17.4.3. COVID-19 mRNA vaccine – SPIKEVAX (CAP) – EMA/VR/0000264109

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: A grouped application consisting of:

C.I.4 Update of section 4.8 of the SmPC in order to update the frequency of the adverse reactions ''Anaphylaxis'' and ''Erythema multiforme'' from ''Not known'' to ''Rare'', based on final results from study mRNA-1273-P904 listed as a category 3 study in the RMP. This is a Non-Interventional, Post-Authorisation Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1273 Vaccine in the EU. The Package leaflet is updated accordingly. An updated RMP (version 11.0) is also included.

C.I.13: Submission of the final report from study mRNA-1273-P905 (Monitoring safety of COVID-19 Vaccine Moderna in pregnancy: an observational study using routinely collected health data in five European countries) listed as a category 3 study in the RMP.

17.4.4. COVID-19 mRNA vaccine – COMIRNATY (CAP) – EMA/VR/0000302705

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the final report, protocol amendment #6 and SAP amendment #5 for the non-interventional study C4591021, listed as a category 3 PASS in the RMP. This is a post conditional approval active surveillance study among individuals in Europe receiving the Pfizer BioNTech Coronavirus Disease 2019 (COVID-19) vaccine. The RMP version 15.1 has also been submitted.

17.4.5. Darbepoetin alfa – ARANESP (CAP) – EMA/VR/0000301503

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study 20190404 listed as a category 3 PASS in the RMP. This is a retrospective, multicentre, observational chart review study to assess the use of erythropoiesis stimulating agents (ESAs) in patients with non-myeloid malignancies receiving myelosuppressive chemotherapy in Europe. The RMP version 11.0 has also been submitted.

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

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

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

17.5.1. Abrocitinib – CIBINQO (CAP) – EMA/PAM/0000310297

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Petar Mas

Scope: Submission of the first progress report for PASSB7451084, entitled 'An Active Surveillance Study to Monitor the Safety of Abrocitinib Among Real-World Patients with Atopic Dermatitis (AD) in the European Union (EU)'

Action: For adoption

17.5.2. Abrocitinib – CIBINQO (CAP) – EMA/PAM/0000310306

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Petar Mas

Scope: Submission of the first progress report for PASS B7451085, entitled 'A Drug Utilization Study to Evaluate the Effectiveness of Risk Minimization Measures (RMMs) for Abrocitinib in the EU Using Electronic Healthcare Data'

17.5.3. Bimekizumab – BIMZELX (CAP) – EMA/PAM/0000302071

Applicant: UCB Pharma

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the first annual recruitment report for PS0036; a Bimekizumab Pregnancy Exposure and Outcome Registry: An OTIS Autoimmune Diseases in Pregnancy Study. The objective of this study is to assess maternal, foetal and infant outcomes among people who become pregnant while exposed to bimekizumab relative to the outcomes in 2 matched comparator populations.

17.5.4. Ciltacabtagene autoleucel – CARVYKTI (CAP) – EMA/PAM/0000286337

Applicant: Janssen Cilag International, ATMP

PRAC Rapporteur: Jo Robays

Scope: Post-authorization Safety Study Survey (Study PCSONCA0014) to Evaluate the Effectiveness of the Ciltacabtagene Autoleucel HCP Educational Program and the Product Handling Training. Submission of first interim report.

17.5.5. COVID-19 mRNA vaccine – SPIKEVAX (CAP) – EMA/PAM/0000309160

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of the fourth interim update for study mRNA-1273-P911 (long-term outcomes of myocarditis following administration of Spikevax) and the responses to the RSI adopted in procedure MEA/066.4 for Spikevax.

17.5.6. 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.

17.5.7. Daratumumab – DARZALEX (CAP) – EMA/PAM/0000310226

Applicant: Janssen Cilag International

PRAC Rapporteur: Carla Torre

Scope: Submission of Erratum PSUR/PBRER report for daratumumab, including data which were inadvertently omitted from the last submitted PSUR/PBRER report covering the period 16 November 2022 to 15 November 2024.

17.5.8. Difelikefalin – KAPRUVIA (CAP) – EMA/PAM/0000307833

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: Development Safety Update Report No.12 (23 August 2024 to 22 August 2025) for study CR845- 310601 - A 2-part, Multicenter, Randomized, Double-blind Study to Evaluate the Efficacy and Safety of Oral Difelikefalin for Moderate-to-Severe Pruritus in Adult Subjects With Notalgia Paresthetica.

This submission concerns DSUR v 12.0.

17.5.9. Dulaglutide – TRULICITY (CAP) – EMA/PAM/0000303057

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: EMEA/H/C/002825/MEA/006 - H9X-MC-B013 - Dulaglutide and Potential Risks of Pancreatic Cancer and Thyroid Cancer: A Non-Interventional Post-Authorisation Safety Study (PASS), 1st interim report

17.5.10. Emicizumab – HEMLIBRA (CAP) – EMA/PAM/0000307773

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: 6th Interim clinical study report (CSR) of Hemlibra (emicizumab) EUHASS registry study, submitted as per the obligation set out in Article 46 of Regulation (EC) No 1901/2006 as a 'standalone' post-authorisation measure (PAM) application.

17.5.11. Enfortumab vedotin – PADCEV (CAP) – EMA/PAM/0000314208

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Final study report: A Non-Interventional Post-Authorization Safety Study (NI-PASS) as an Effectiveness Check of a Patient Card for Padcev™ (ISN: 7465-PV-0002)

17.5.12. Ketoconazole – KETOCONAZOLE ESTEVE (CAP) – EMA/PAM/0000312512

Applicant: Esteve Pharmaceuticals S.A.

PRAC Rapporteur: Petar Mas

Scope: Eighth Interim Annual Report covering the period from 01 September 2018 to 31 August 2025. - Study ERCUSYN

PASS EUPAS21731

Prospective, multi-country, observational registry to collect clinical information on patients with endogenous Cushing's syndrome exposed to Ketoconazole (using the existing European Registry on Cushing's Syndrome (ERCUSYN)), to assess drug utilization pattern and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of Ketoconazole.

17.5.13. Neratinib – NERLYNX (CAP) – EMA/PAM/0000281194

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Bianca Mulder

Scope: Interim report of the NER7402 (NERLYFE) study, a category 3 PASS: a multicentre, multi-country, prospective, observational, post-authorisation safety study to describe the incidence of discontinuation due to diarrhoea within the first 3 months of a treatment with neratinib, in adult breast cancer patients treated in extended adjuvant in a real world setting.

Interim report for the combined NERLYFE/ELEANOR study, a category 3 PASS. The ELEANOR study is a multi-centric, multi-national, prospective, longitudinal, non-interventional study in Austria, Germany and Switzerland conducted with neratinib in patients with HER2+ breast cancer.

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

Applicant: Janssen Cilag International

PRAC Rapporteur: Jan Neuhauser

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

17.5.15. 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

17.5.16. Patisiran – ONPATTRO (CAP) – EMA/PAM/0000306413

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5th Interim study report of Study ALN-TTR02-010

Description: Patisiran-LNP Pregnancy Surveillance Program.

To collect primary data on pregnant women from the US, the United Kingdom (UK), France, Spain, Italy, Portugal and Germany, and other potential countries, who have been exposed to patisiran during the exposure window, defined as 12 weeks prior to their last menstrual period (LMP), or at any time during pregnancy. Establish a worldwide Pregnancy Surveillance Program (PSP) to collect and analyze information pertaining to pregnancy complications and birth outcomes in women exposed to patisiran during pregnancy. The collection and analysis of data should continue for a minimum of 10 years.

17.5.17. Selumetinib – KOSELUGO (CAP) – EMA/PAM/0000302968

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: SOB, PASS category 2, Study number: D1346R00004.

Interim Report and APR3: Post-Authorisation Safety Study of Paediatric Patients Initiating Selumetinib: A Multiple-Country Prospective Cohort Study. As per Koselugo Study milestones listed in the RMP and PASS protocol, the interim report APR3 is due in Q3 2025.

17.5.18. Sutimlimab – ENJAYMO (CAP) – EMA/PAM/0000273920

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Jan Neuhauser

Scope: 3rd Annual interim report for the sutimlimab Cold Agglutinin Disease Real World Evidence Registry (CADENCE, OBS16454) a multinational, multi-center, observational, prospective, longitudinal disease registry; former MEA 003.2.

17.5.19. Upadacitinib – RINVOQ (CAP) – EMA/PAM/0000301869

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Annual progress report for PASS study P21-825: Drug Utilization Study Evaluating the Additional Risk Minimisation Measures for Upadacitinib in the Treatment of Atopic Dermatitis in Europe

17.5.20. Upadacitinib – RINVOQ (CAP) – EMA/PAM/0000301747

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Interim study report for PASS study P19-150: Long-term safety cohort studies of upadacitinib use for the treatment of RA in Europe

17.5.21. Upadacitinib – RINVOQ (CAP) – EMA/PAM/0000301931

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Annual progress report for PASS study P20-390: a cohort study of long-term safety of upadacitinib in the treatment of atopic dermatitis in Denmark and Sweden

17.5.22. Upadacitinib – RINVOQ (CAP) – EMA/PAM/0000303398

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Annual progress report for PASS study P24-344: Drug utilization study evaluating additional risk minimisation measures for upadacitinib in the treatment of Ulcerative Colitis in Europe

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

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

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

17.6. New Scientific Advice

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

17.7. Ongoing Scientific Advice

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

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

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

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

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

18.1. Annual reassessments of the marketing authorisation

18.1.1. Lonafarnib – ZOKINVY (CAP) – EMA/S/0000306613

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.1.2. Metreleptin – MYALEPTA (CAP) – EMA/S/0000302645

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.1.3. Odevixibat – KAYFANDA (CAP) – EMA/S/0000306639

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.1.4. Tocofersolan – VEDROP (CAP) – EMA/S/0000304509

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Andexanet alfa – ONDEXXYA (CAP) – EMA/R/0000308136

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.2. Linvoseltamab – LYNOZYFIC (CAP) – EMA/R/0000306825

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Veronika Macurova

Scope: Conditional renewal of the marketing authorisation

18.2.3. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) – PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) – EMA/R/0000313191

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Conditional renewal of the marketing authorisation

18.2.4. Volanesorsen – WAYLIVRA (CAP) – EMA/R/0000308372

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Azathioprine – JAYEMPI (CAP) – EMA/R/0000296298

Applicant: Lipomed GmbH

PRAC Rapporteur: Karin Erneholm

Scope: 5-year renewal of the marketing authorisation

18.3.2. Bimekizumab – BIMZELX (CAP) – EMA/R/0000304244

Applicant: UCB Pharma

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

18.3.3. Odevixibat – BYLVAY (CAP) – EMA/R/0000306638

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

18.3.4. Pitolisant – OZAWADE (CAP) – EMA/R/0000304208

Applicant: Bioprojet Pharma

PRAC Rapporteur: Terhi Lehtinen

Scope: 5-year renewal of the marketing authorisation

18.3.5. Relugolix / Estradiol / Norethisterone acetate – RYEQO (CAP) – EMA/R/0000304469

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

18.3.6. Roxadustat – EVRENZO (CAP) – EMA/R/0000304810

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Jana Pecherova

Scope: 5-year renewal of the marketing authorisation

18.3.7. Setmelanotide – IMCIVREE (CAP) – EMA/R/0000302063

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Miroslava Gocova

Scope: 5-year renewal of the marketing authorisation

18.3.8. Tralokinumab – ADTRALZA (CAP) – EMA/R/0000288404

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: 5-year renewal of the marketing authorisation

18.3.9. Vericiguat – VERQUVO (CAP) – EMA/R/0000304275

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

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 12-15 January 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	
Krõõt Aab	Alternate	Estonia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Terhi Lehtinen	Member	Finland	No interests declared	
Kimmo Jaakkola	Alternate	Finland	No interests declared	
Tiphaine Vaillant	Member	France	No interests declared	
Martin Huber	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:	6.2.2. EMA/PSUR/0000296525 6.3.8. EMA/PSUR/0000296563
Julia Pallos	Member	Hungary	No participation in discussion, final deliberations and voting on:	15.2.2. EMA/VR/0000288444 15.3.8. EMA/VR/0000282554 15.3.9. EMA/VR/0000309456 15.3.28. EMA/VR/0000282199 15.3.29. EMA/VR/0000304938 15.3.30. EMA/VR/0000303785 15.3.31. EMA/VR/0000291324 16.1.2. EMA/PSUR/0000296576 16.1.44. EMA/PSUR/0000296531

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				16.1.49 EMA/PSUR/0000296528
Melinda Palfi	Alternate	Hungary	No interests declared	
Guðrún Stefánsdóttir	Member	Iceland	No restrictions applicable to this meeting	
Rhea Fitzgerald	Member	Ireland	No interests declared	
Eamon O Murchu	Alternate	Ireland	No interests declared	
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	
Anne-Cecile Vuillemin	Member	Luxembourg	No interests declared	
Magdalena Wielowieyska	Alternate	Luxembourg	No participation in discussion, final deliberations and voting on:	6.2.2. EMA/PSUR/0000296525 15.3.40. EMA/VR/0000255408 16.1.45. EMA/PSUR/0000296562 16.1.54. EMA/PSUR/0000296490
John Joseph Borg	Member	Malta	No restrictions applicable to this meeting	
Benjamin Micallef	Alternate	Malta	No interests declared	
Liana Martirosyan	Member	Netherlands	No interests declared	
Bianca Mulder	Alternate	Netherlands	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
David Olsen	Member	Norway	No participation in discussion, final deliberations and voting on:	4.1.1. X-ray contrast agents - Iobitridol (NAP); Iodixanol (NAP); Iohexol (NAP); Iomeprol (NAP); Iopamidol (NAP); Iopromide (NAP); Ioversol (NAP) 6.3.5. EMA/PSUR/0000296537 6.3.7. EMA/PSUR/0000296588 6.3.8. EMA/PSUR/0000296563 6.3.10. EMA/PSUR/0000296534 14.1.2. Darolutamide – NUBEQA (CAP) 15.3.16. EMA/X/0000248026 15.3.34. EMA/VR/0000312922 16.1.1. EMA/PSUR/0000296585 16.1.38. EMA/PSUR/0000296535 16.3.4. EMA/PSUR/0000296617 17.5.6. EMA/PAM/0000303584 18.3.9. EMA/R/0000304275

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Pernille Harg	Alternate	Norway	No interests declared	
Adam Przybylkowski	Member	Poland	No restrictions applicable to this meeting	
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 restrictions applicable to this meeting	
Polona Golmajer	Member	Slovenia	No interests declared	
Maria del Pilar Rayon	Member	Spain	No interests declared	
Maria Martinez Gonzalez	Alternate	Spain	No interests declared	
Mari Thorn	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin	Alternate	Sweden	No restrictions applicable to this meeting	
Annalisa Capuano	Member	Independent scientific expert	No restrictions applicable to this meeting	
Milou-Daniel Drici	Member	Independent scientific expert	No restrictions applicable to this meeting	
Maria Teresa Herdeiro	Member	Independent scientific expert	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
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	
Yiannoula Koulla	Member	Patients' Organisation Representative	No interests declared	
Michal Rataj	Alternate	Patients' Organisation Representative	No interests declared	
Daniela Philadelphy	Expert	Austria	No interests declared	
Daniela Ljubica	Expert	Croatia	No interests declared	
Nanna Birkmose Rasmussen	Expert	Denmark	No restrictions applicable to this meeting	
Alexander Braathen	Expert	Denmark	No interests declared	
Rita Chan Andersen	Expert	Denmark	No restrictions applicable to this meeting	
Kirsten Egebjerg Juul	Expert	Denmark	No interests declared	
Nicklas Hasselblad Lundstrøm	Expert	Denmark	No interests declared	
Cecilie Louise Pedersen	Expert	Denmark	No participation in discussion, final deliberations and voting on:	14.1.4 Vortioxetine - BRINTELLIX (CAP) 6.1.10. EMA/PSUR/0000296561

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				15.3.37. EMA/X/0000296344 16.1.11. EMA/PSUR/0000296628 16.1.36. EMA/PSUR/0000296618 17.2.4. EMA/PAM/0000276447 17.2.15. EMA/PAM/0000301197 17.2.16. EMA/PAM/0000295858
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	
Per Sindahl	Expert	Denmark	No interests declared	
Thyra Skau	Expert	Denmark	No interests declared	
Badis-Lakhdar Bensaad	Expert	France	No interests declared	
Camille De-Kervasdoue	Expert	France	No interests declared	
Philipp Berg	Expert	Germany	No interests declared	
Dennis Lex	Expert	Germany	No interests declared	
Kerstin Loschcke	Expert	Germany	No interests declared	
Laura Zein	Expert	Germany	No interests declared	
Eleanor Carey	Expert	Ireland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Clare Foley	Expert	Ireland	No interests declared	
Kevin Keohane	Expert	Ireland	No interests declared	
Finbarr Leacy	Expert	Ireland	No interests declared	
Aine McKenna	Expert	Ireland	No interests declared	
Risteard Prendergast	Expert	Ireland	No interests declared	
Maxime Cuijpers	Expert	Netherlands	No restrictions applicable to this meeting	
Helen Gatling	Expert	Netherlands	No interests declared	
Gunnar Rimul	Expert	Norway	No interests declared	
Kristin Thorseng Kvande	Expert	Norway	No interests declared	
Joao Fernandes	Expert	Portugal	No restrictions applicable to this meeting	
Ana Cuñado Moral	Expert	Spain	No restrictions applicable to this meeting	
Charlotte Backman	Expert	Sweden	No interests declared	
Rolf Gedeborg	Expert	Sweden	No restrictions applicable to this meeting	
Jenny Jönsson	Expert	Sweden	No restrictions applicable to this meeting	
Asa Lindh	Expert	Sweden	No interests declared	
Kristina Magnusson Lundqvist	Expert	Sweden	No interests declared	
Observers from Health Canada (Canada) attended the meeting.				
Meeting run with support from relevant EMA staff.				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.

PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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

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

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