21 March 2025
EMA/PRAC/67596/2025 Rev 1[1]
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 13 - 16 January 2025

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).

[1] 6.3.1 Aciclovir - PSUSA/00000048/202406 -amendment of minutes to be in line with the assessment report; 6.2.1 Capecitabine - PSUSA/00000531/202404 – typo in the paragraph related to PSUR frequency; 6.1.16. Tolvaptan - PSUSA/00010395/202405 – amendment of minutes to be in line with the assessment report

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1. Introduction

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

The Chairperson opened the 13-16 January 2025 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 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 Polish presidency of the Council of the European Union (EU).

1.2. Agenda of the meeting on 13-16 January 2025

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

1.3. Minutes of the previous meeting on 25-28 November 2024

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 25-28 November 2024 were published on the EMA website on 10 February 2025 (EMA/PRAC/592992/2024).

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[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. Ciltacabtagene autoleucel – CARVYKTI (CAP)

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Jo Robays

[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

Scope: Signal of immune-mediated enterocolitis

EPITT 20133 – New signal

Background

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

During routine signal detection activities, a signal of immune-mediated enterocolitis was identified by EMA, based on 17 cases retrieved from EudraVigilance. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from case reports in EudraVigilance, PRAC agreed that further evaluation on the signal of immune-mediated enterocolitis is warranted and extended the scope of the signal to the CAR T-cell product class.

PRAC appointed Jo Robays as Rapporteur for the signal.

Summary of recommendation(s)

- The MAHs for Abecma (idecabtagene vicleucel), Breyanzi (lisocabtagene maraleucel), Carvykti (ciltacabtagene autoleucel), Kymriah (tisagenlecleucel), Tecartus (Brexucabtagene autoleucel) and Yescarta (axicabtagene ciloleucel) should submit to EMA, within 60 days, a cumulative review of the signal of immune-mediated enterocolitis/immune effector cell-associated enteritis including an analysis of case reports of MedDRA high level term (HLT) colitis (excluding infective) and selected preferred terms (PTs) from HLT Gastrointestinal inflammatory disorders NEC (autoimmune enteropathy, cryptitis, cuffitis, duodenitis, enteritis, enterocolitis, gastrointestinal inflammation, immune-mediated gastrointestinal disorder), a review of the published literature, data from spontaneous reports and reports from studies. In addition, the MAHs should discuss the need to amend the product information and/or the RMP (e.g. educational material) as well as the need for a direct healthcare professional communication (DHPC), as warranted.
- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.2. Clozapine (NAP)

Applicant: various

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of new aspect of the known risk of neutropenia/agranulocytosis with potential impact on the risk management measures

EPITT 20141 – New signal

Background

Clozapine is an atypical antipsychotic indicated for the treatment of resistant schizophrenic patients or schizophrenic patients intolerant to other antipsychotics, and in psychotic

disorders occurring during the course of Parkinson's disease, in cases where standard treatment has failed.

During routine signal detection activities, a signal of new aspect of the known risk of neutropenia/agranulocytosis with potential impact on the risk management measures was identified by France, based on a literature review and the recommendations from the French clozapine task force[4]. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from the literature, including the recommendations from the French clozapine task force and the European clozapine task force[5], PRAC agreed that further evaluation on the signal of new aspect of the known risk of neutropenia/agranulocytosis with potential impact on the risk management measures is warranted, along with an exploration of additional analyses of data from real-world evidence to complement the assessment.

PRAC appointed Amelia Cupelli as Rapporteur for the signal.

Summary of recommendation(s)

- The MAHs Viatris and Mylan for clozapine-containing medicinal products should submit to EMA, within 90 days, a time to onset (TTO) analysis of clozapine induced neutropenia/agranulocytosis based on spontaneous cases, including all cases in EudraVigilance database, as well as a literature review on the magnitude of the risk of neutropenia and agranulocytosis associated with duration of treatment with clozapine. In addition, the MAHs Viatris and Mylan should discuss if any differences across EU Member States in the rules for monitoring white blood cells (WBC)/absolute neutrophil counts (ANC) and in the criteria that are used for stopping clozapine, along with any changes to the requirements for monitoring ANC/WBC or new recommendations recently implemented by other regulatory authorities, as well as should review available evidence on use of clozapine in patients with benign ethnic neutropenia (BEN). Finally, the MAHs Viatris and Mylan should discuss the need to amend the current recommendations for blood monitoring and consequently any potential amendment to the product information (PI) and/or the risk management plan (RMP), as warranted.
- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.3. Enzalutamide - ENZALUTAMIDE VIATRIS (CAP), XTANDI (CAP); NAP

Applicant(s): Astellas Pharma Europe B.V. (Xtandi), Viatris Limited (Enzalutamide Viatris), various

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Signal of laboratory test interference leading to falsely elevated digoxin plasma levels with enzalutamide

[4] Verdoux H, Lepetit A. Clozapine monitoring: Have the times come for changing the rules? Annales Médico-Psychologiques, Revue Psychiatrique, 2024, ff10.1016/j.amp.2024.09.025ff. ffhal04758445f
[5] Verdoux H, Bittner RA, Hasan A, et al. The time has come for revising the rules of clozapine blood monitoring in Europe. A joint expert statement from the European Clozapine Task Force. *European Psychiatry*. Published online 2025:1-13. doi:10.1192/j.eurpsy.2024.1816

EPITT 20134 – New signal

Background

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

During routine signal detection activities, a signal of laboratory test interference leading to falsely elevated digoxin plasma levels with enzalutamide was identified by EMA, based on literature and 18 cases retrieved from EudraVigilance. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from case reports in EudraVigilance and in the literature, PRAC agreed that further evaluation on the signal of laboratory test interference leading to falsely elevated digoxin plasma levels with enzalutamide is warranted and extended the scope of this signal to include digoxin.

Summary of recommendation(s)

- The MAHs Astellas Pharma Europe B.V for Xtandi (enzalutamide) and Aspen Pharma Trading Limited for digoxin-containing medicinal products should submit to EMA, within 60 days, a cumulative review of all cases of digoxin laboratory test interference with enzalutamide including data from spontaneous reports, published literature, non-clinical and clinical studies, spontaneous reports and reports from studies. In addition, the MAHs should discuss a proposal for amending the product information and/or the RMP as well as a proposal of any safety communication tool as warranted.
- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.2. Signals follow-up and prioritisation

4.2.1. Afatinib - GIOTRIF (CAP) - EMEA/H/C/002280/SDA/009

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Mari Thorn

Scope: Signal of growth of eyelashes

EPITT 19987 – Follow-up to December 2023[6]

Background

For background information, see PRAC minutes December 2023.

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

Discussion

Having considered the available evidence in EudraVigilance, the literature and the cumulative review submitted by the MAH, PRAC concluded that there is sufficient evidence to establish a

[6] Held 27–30 November 2023

causal association for the growth of eyelashes with Giotrif (afatinib). Therefore, the product information should be amended to add aberrant eyelash growth as undesirable effect with a frequency 'uncommon'.

Summary of recommendation(s)

- The MAHs for Giotrif (afatinib) should submit to EMA, within 60 days, a variation to amend the product information[7].

4.2.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/026; Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/SDA/012; Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/SDA/013; Dostarlimab - JEMPERLI (CAP) - EMEA/H/C/005204/SDA/007; Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/SDA/013; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/SDA/049; Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/SDA/058; Nivolumab, relatlimab - OPDUALAG (CAP) - EMEA/H/C/005481/SDA/007; Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/042; Retifanlimab - ZYNYZ (CAP) - EMEA/H/C/006194/SDA/002; Tislelizumab - TEVIMBRA (CAP) - EMEA/H/C/005919/SDA/004; Tremelimumab - IMJUDO (CAP) - EMEA/H/C/006016/SDA/004

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

PRAC Rapporteur: Bianca Mulder

Scope: Signal of thrombotic microangiopathy

EPITT 20090 – Follow-up to July 2024

Background

For background information, see PRAC minutes July 2024.

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

Discussion

Having considered the available evidence in EudraVigilance, clinical studies, spontaneous reports, literature and the responses of the MAHs, PRAC concluded that the current evidence is insufficient to establish a causal relationship between the class of immune checkpoint inhibitors and thrombotic microangiopathy to further warrant an update to the product information and/or risk management plan at this stage.

Summary of recommendation(s)

- The MAHs for Opdivo and Opdualag (nivolumab), Keytruda (pembrolizumab), Imfinzi (durvalumab), Bavencio (avelumab), Tecentriq (atezolizumab), Libtayo (cemiplimab), Jemperli (dostarlimab), Tevimbra (tislelizumab), Yervoy (ipilimumab), Imjudo (tremelimumab) and Zynyz (retifanlimab) should continue to monitor relevant cases of

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

thrombotic microangiopathy and related adverse event terms assessed within the scope of this signal in the next PSUR(s).

4.2.3. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/SDA/021; LENVIMA (CAP) - EMEA/H/C/003727/SDA/024

Applicant: Eisai GmbH

PRAC Rapporteur: Mari Thorn

Scope: Signal of tumour lysis syndrome

EPITT 20108 – Follow-up to September 2024

Background

For background information, see PRAC minutes September 2024.

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

Discussion

Having considered the available evidence in EudraVigilance, the literature, and the cumulative review submitted by the MAH, PRAC concluded that there is sufficient evidence to establish a causal association of tumour lysis syndrome (TLS) with lenvatinib-containing medicinal products. Therefore, the product information should be amended to TLS as a warning and undesirable effect with a frequency 'rare'.

Summary of recommendation(s)

- The MAHs for lenvatinib-containing medicinal products Kisplyx and Lenvima should submit to EMA, within 60 days, a variation to amend the product information[8].

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.

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

5.1.1. Amino acids - (CAP MAA) - EMEA/H/C/005557, Orphan

Applicant: Recordati Rare Diseases

Scope (pre D-180 phase): Treatment of decompensation episodes in MSUD patients

5.1.2. Diflunisal - (CAP MAA) - EMEA/H/C/006248, Orphan

Applicant: AO Pharma AB

Scope (pre D-180 phase): Treatment of ATTR amyloidosis

5.1.3. Ferric citrate coordination complex - (CAP MAA) - EMEA/H/C/006402

Scope (pre D-180 phase): Treatment of iron deficiency anaemia in adult chronic kidney disease (CKD) patients with elevated serum phosphorus levels

5.1.4. Troriluzole - (CAP MAA) - EMEA/H/C/006068, Orphan

Applicant: Biohaven Bioscience Ireland Limited

Scope (pre D-180 phase): Treatment of adult patients with spinocerebellar ataxia genotype 3 (SCA3)

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 Annex I 15.3.

6. Periodic safety update reports (PSURs)

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

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

See also Annex I 16.1.

6.1.1. Apixaban - ELIQUIS (CAP) - PSUSA/00000226/202405

Applicant: Bristol-Myers Squibb / Pfizer EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Eliquis, a centrally authorised medicine containing apixaban 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 Eliquis (apixaban) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include anticoagulant-related nephropathy as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[9].
- In the next PSUR, the MAH should provide a review of all available information on the potential drug-drug interaction between amiodarone and apixaban and discuss whether there is a need to update the product information. The MAH should also evaluate the effectiveness of the existing additional risk minimization measures (guide for healthcare professionals and patient card) and discuss the suitability of continuing or discontinuing of these materials.

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

6.1.2. Atezolizumab - TECENTRIQ (CAP) - PSUSA/00010644/202405

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

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 add lichen disorders as undesirable effect with a frequency 'uncommon' for atezolizumab monotherapy and 'rare' for atezolizumab combination therapy, as well as to add colitis as undesirable effect with a frequency 'common' for atezolizumab combination therapy. Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAH should provide a cumulative review of cases of neutropenia (including neutropenia, neutrophil count decreased, febrile neutropenia, neutropenic infection, neutropenic sepsis, granulocytopenia) for atezolizumab in monotherapy from

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

all available sources, including clinical trial, post-marketing and literature data and discuss the need for update of the product information. In addition, the MAH should continue to closely monitor cases of cardiac arrhythmias and provide any new information on this safety topic.

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

6.1.3. Azacitidine[11] - ONUREG (CAP) - PSUSA/00010935/202405

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Onureg, a centrally authorised medicine containing azacitidine 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 Onureg (azacitidine) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- The MAH should submit to EMA, within 60 days, a cumulative review of cases of differentiation syndrome for azacitidine (oral formulation) together with a causality assessment, as well as a review of cases of pericardial effusion and pericarditis with azacitidine (oral formulation), and discuss the need to update the product information.

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.

6.1.4. Dabrafenib - FINLEE (CAP); TAFINLAR (CAP) - PSUSA/00010084/202405

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

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 its marketing authorisation(s).

Summary of recommendation(s) and conclusions

[11] Oral formulations only

- 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 for Finlee and Tafinlar should be updated to add a warning regarding Vogt-Koyanagi-Harada (VKH)-like uveitis, including that cases of biocular panuveitis or biocular iridocyclitis suggestive of VKH syndrome have been observed. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAH should provide cumulative reviews of cases of 'potentiation of radiation toxicity' together with a causality assessment. The MAH should also provide a cumulative review of cases of possible VKH syndrome, including a causality assessment and discuss the need for update of the product information. The MAH should also provide a cumulative review of cases of cytokine release syndrome, including data from clinical trials, post-marketing setting and literature, and discuss the need for update of product information.

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

6.1.5. Efgartigimod alfa - VYVGART (CAP) - PSUSA/00011014/202406

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Vyvgart, a centrally authorised medicine containing efgartigimod alfa 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 Vyvgart (efgartigimod alfa) in the approved indication(s) remains unchanged.
- Nevertheless, the product information of intravenous (IV) and subcutaneous (SC) formulations should be updated to add nausea as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- In the next PSUR, the MAH should provide a cumulative review of cases of infusion reactions for IV formulation and swelling events for both IV and SC formulations, together with causality assessments and discuss the need for any update of the product information.

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

[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
[13] 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

2001/83/EC. The frequency of submission of the subsequent PSURs should be changed from 6-monthly to yearly and the list of Union reference dates (EURD list) will be updated accordingly.

6.1.6. Entrectinib - ROZLYTREK (CAP) - PSUSA/00010874/202406

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Rozlytrek, a centrally authorised medicine containing entrectinib 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 Rozlytrek (entrectinib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add myocarditis as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[14].

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

6.1.7. Fenfluramine - FINTEPLA (CAP) - PSUSA/00010907/202406

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

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 warning on valvular heart disease and pulmonary arterial hypertension and to add valvular heart disease as an undesirable effect with a frequency 'not known'. In addition, the Annex II-D should be updated to reclassify the important potential risk of valvular heart disease

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

to important identified risk. Therefore, the current terms of the marketing authorisation(s) should be varied[15].

- In the next PSUR, the MAH should revise the PSUR summary of safety concerns to consider valvular heart disease as an important identified risk and closely monitor the risk of medication errors including those related to the preferred terms (PTs) 'accidental overdose', 'extra dose administered' and 'incorrect dose administered'. In addition, the MAH should present and discuss all data available concerning the compliance to the timeline of the required continuous ECHO monitoring as well as any inaccuracy in ECHO monitoring, and should recommend any plan and improvements related to this monitoring.
- The MAH should, within 3 months, submit an updated RMP to reclassify the important potential risk of valvular heart disease as important identified.

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

6.1.8. Hydroxycarbamide[16] - SIKLOS (CAP); XROMI (CAP) - PSUSA/00001692/202406

Applicant: Theravia (Siklos), Nova Laboratories Ireland Limited (Xromi)

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Siklos, Xromi, a centrally authorised medicine containing hydroxycarbamide 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 Siklos, Xromi (hydroxycarbamide) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation of Siklos (hydroxycarbamide) should be maintained, while the product information of Xromi (hydroxycarbamide) should be updated to reflect the interference with continuous glucose monitoring systems. Therefore, the current terms of the marketing authorisation(s) should be varied[17].
- In the next PSUR, the MAH for Xromi (hydroxycarbamide) should characterise the newly identified risk of 'interferences between hydroxycarbamide and continuous glucose monitoring systems leading to spuriously elevated sensor glucose reading'.

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.

[15] Update of SmPC sections 4.4 and 4.8. The package leaflet and Annex II-D are updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[16] For centrally authorised product only
[17] Update of SmPC section 4.5. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

6.1.9. Latanoprost, netarsudil - ROCLANDA (CAP) - PSUSA/00010905/202406

Applicant: Santen Oy

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Roclanda, a centrally authorised medicine containing latanoprost/netarsudil 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 Roclanda (latanoprost/netarsudil) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add reticular epithelial corneal oedema as a warning and as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[18].

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. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - PSUSA/00010848/202405

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Zolgensma, a centrally authorised medicine containing onasemnogene abeparvovec 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 Zolgensma (onasemnogene abeparvovec) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to reflect that routine monitoring of troponin-I levels is not indicated after Zolgensma administration. In addition, the product information should be updated to add infusion-related reactions, including anaphylactic reactions as a warning and as undesirable effects with a frequency 'uncommon' and 'rare' respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[19].

[18] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[19] Update of SmPC sections 4.2, 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

- In the next PSUR, the MAH should continue to closely monitor cases of spinal cord expansivities and haemophagocytic lympohostiocytosis /macrophage activation syndrome, as well as present cases of patients with sensory adverse events including patients receiving intrathecal administration.

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.

6.1.11. Ozanimod - ZEPOSIA (CAP) - PSUSA/00010852/202405

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Zeposia, a centrally authorised medicine containing ozanimod 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 Zeposia (ozanimod) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding immune reconstitution inflammatory syndrome after discontinuation of ozanimod due to progressive multifocal leukoencephalopathy (PML). The following educational materials should also be updated accordingly: healthcare professional checklist and patient/caregiver's guide. Therefore, the current terms of the marketing authorisation(s) should be varied[20].
- In the next PSUR, the MAH should provide cumulative reviews of cases of cerebrovascular accident (CVA), transient ischemic attack (TIA), myocardial infarction (MI), pulmonary embolism, lymphopenia grade IV, and bradycardia after dose escalation. In addition, the MAH should continue to monitor cases of pregnancy-related events and embryofoetal toxicity, atrioventricular block, alopecia and melanoma. The MAH should also provide a comparative review of the cases of basal cell carcinoma (BCC) with the comparator. Finally, the MAH should discuss any update on the product information 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.

6.1.12. Roxadustat - EVRENZO (CAP) - PSUSA/00010955/202406

Applicant: Astellas Pharma Europe B.V.

[20] Update of SmPC section 4.4. The package leaflet and Annex II-D are updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Evrenzo, a centrally authorised medicine containing roxadustat 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 Evrenzo (roxadustat) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add thrombocytopenia as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[21].
- In the next PSUR, the MAH should provide a cumulative review of cases of vaso-occlusive crisis, including from data from post marketing sources, clinical trials and literature and discuss the need to update the product information, 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. The frequency of submission of the subsequent PSURs should be changed from 6-monthly to yearly and the list of Union reference dates (EURD list) will be updated accordingly.

6.1.13. Semaglutide - OZEMPIC (CAP); RYBELSUS (CAP); WEGOVY (CAP) - PSUSA/00010671/202405

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Ozempic, Rybelsus, Wegovy, a centrally authorised medicine 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, Wegovy (semaglutide) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- The MAH should submit to EMA, within 60 days, a review of all cases related to the potential association between semaglutide and non-arteritic anterior ischemic optic neuropathy (NAION), including data from clinical trials, post-marketing setting,

[21] 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

mechanistic studies (if any) and literature, together with a causality assessment, and discuss the need for any potential amendments to the product information and/or the RMP, as warranted.

- In the next PSUR, the MAH should submit a cumulative review of cases of altered skin sensation for Ozempic (semaglutide), including data from clinical trials and post-marketing sources and discuss the need for any potential amendments to the product information as warranted. In addition, the MAH should provide a cumulative review of cases of nephrolithiasis from post-marketing setting and discuss the need for update of the product information, as warranted. Finally, the MAH should discuss the recently available publications on risk of thyroid cancer associated with the use of GLP-1 receptor agonists and on the self-injurious ideation and suicidal ideation.

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.

6.1.14. Sotorasib - LUMYKRAS (CAP) - PSUSA/00010970/202405

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Lumykras, a centrally authorised medicine containing sotorasib 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 Lumykras (sotorasib) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- The MAH should continue to closely monitor cases of 'acute pancreatitis' and include it as an important potential risk in the list of safety concern of the PSURs.

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

6.1.15. Tislelizumab - TEVIMBRA (CAP) - PSUSA/00000136/202406

Applicant: Beigene Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tevimbra, a centrally authorised medicine containing tislelizumab 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 Tevimbra (tislelizumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add haemophagocytic lymphohistiocytosis (HLH) as a warning and as an undesirable effect with a frequency 'not known' for monotherapy and frequency 'rare' for tislelizumab in combination with chemotherapy. In addition, the product information should be updated to add cystitis noninfective as a warning and as an undesirable effect with a frequency 'rare' for tislelizumab monotherapy and '-' for tislelizumab in combination with chemotherapy. Therefore, the current terms of the marketing authorisation(s) should be varied[22].
- In the next PSUR, the MAH should provide a detailed review of cases of immune-mediated neuropathy and encephalitis, as well as a cumulative review of the topic 'safety of tislelizumab in patients with pre-existing autoimmune disease'.

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

6.1.16. Tolvaptan[23] - JINARC (CAP) - PSUSA/00010395/202405

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Jinarc, a centrally authorised medicine containing tolvaptan 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 Jinarc (tolvaptan) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add blood creatine phosphokinase increased as 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 should provide in-depth analyses and causality assessments for the following topics to be kept under monitoring: chest pain, fatal outcome, 'too rapid rise of serum sodium and neurologic sequelae (encephalopathy, osmotic

[22] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[23] Indicated for adults with autosomal dominant polycystic kidney disease (ADPKD)
[24] 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

demyelination) in autosomal dominant polycystic kidney disease (ADPKD) patients', hepatitis, nausea and pulmonary thrombosis or pulmonary embolism.

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.

6.1.17. Trastuzumab deruxtecan - ENHERTU (CAP) - PSUSA/00010894/202406

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Enhertu, a centrally authorised medicine containing trastuzumab deruxtecan 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 Enhertu (trastuzumab deruxtecan) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add pancytopenia as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[25].
- In the next PSUR, the MAH should provide a review of cases of convulsions, including data from literature, together with a WHO-UMC causality assessment. In addition, the MAH should provide a review of cases of 'gastrointestinal inflammatory conditions' (HLGT), including data from post-marketing setting, clinical trials and literature, together with a WHO-UMC causality assessment.

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.

6.1.18. Ublituximab - BRIUMVI (CAP) - PSUSA/00000045/202406

Applicant: Neuraxpharm Pharmaceuticals S.L.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Background

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

[25] 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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Briumvi (ublituximab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add encephalitis, meningitis and meningoencephalitis with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[26].

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.

6.1.19. Vedolizumab - ENTYVIO (CAP) - PSUSA/00010186/202405

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Entyvio, a centrally authorised medicine containing vedolizumab 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 Entyvio (vedolizumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add the liver enzyme increased and hepatitis as undesirable effects with frequency 'common' and 'very rare', respectively. In addition, the product information should be updated to amend the existing warning on hypersensitivity in order to reflect that hypersensitivity reactions have been reported after switching from subcutaneous to intravenous formulation. Therefore, the current terms of the marketing authorisation(s) should be varied[27].

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

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

See also Annex I 16.2.

[26] 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
[27] 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

6.2.1. Capecitabine - CAPECITABINE ACCORD (CAP); CAPECITABINE MEDAC (CAP); ECANSYA (CAP); XELODA (CAP); NAP - PSUSA/00000531/202404

Applicant(s): Accord Healthcare S.L.U. (Capecitabine Accord), medac Gesellschaft fur klinische Spezialpraparate mbH (Capecitabine medac), KRKA, d.d., Novo mesto (Ecansya), CHEPLAPHARM Arzneimittel GmbH (Xeloda), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Background

Capecitabine is a precursor of the cytotoxic moiety 5-fluorouracil (5-FU) and it is indicated for the adjuvant treatment of colon cancer, metastatic colorectal cancer, first-line treatment of advanced gastric cancer, locally advanced or metastatic breast cancer.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Capecitabine Accord, Capecitabine Medac, Ecansya and Xeloda, centrally authorised medicines containing capecitabine, and nationally authorised medicines containing capecitabine 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 capecitabine-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning on phenotyping for dihydropyrimidine dehydrogenase (DPD) deficiency in order to reflect that impaired kidney function is associated with increased uracil levels in blood, that could lead to a false diagnosis of DPD deficiency and subsequently to underdosing of capecitabine. Therefore, the current terms of the marketing authorisations should be varied[28].
- In the next PSUR, the MAH(s) should submit a cumulative review of data regarding the impact of variant c.557A>G on DPD activity and fluoropyrimidine toxicity and discuss the need for update of the product information.

The frequency of PSUR submission should be revised from three 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. Measles, mumps, rubella vaccines (live, attenuated) - M-M-RVAXPRO (CAP); NAP - PSUSA/00001937/202405

Applicant(s): Merck Sharp & Dohme B.V. (M-M-RvaxPro), various

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Background

[28] 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

This vaccine is indicated for simultaneous vaccination against measles, mumps, and rubella in individuals 12 months of age or older.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of M-M-RVAXPRO, (a) centrally authorised medicine(s) and nationally authorised medicines containing measles, mumps, rubella vaccines (live, attenuated), 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 M-M-RVAXPRO in the approved indication(s) remains unchanged, and the current terms of the marketing authorisations should be maintained.
- Based on the review of the data on safety and efficacy, the benefit-risk balance of Priorix (nationally approved medicine) in the approved indication(s) remains unchanged, and the product information should be updated to amend the contraindication related to administration of this vaccine in the presence of immunosuppression. Also, the product information should be amended to update the recommendation for use during pregnancy. Therefore, the current terms of the marketing authorisations should be varied[29].
- In the next PSUR, all MAHs should provide a detailed analysis of all serious and non-serious cases of hypotonic-hyporesponsive episodes (HHE), including a causality assessment, as well as a cumulative review of cases of hemophagocytic lymphohistiocytosis (HLH) and discuss the need for an update of the product information.
- In addition, at the next regulatory opportunity, the MAH Merck Sharp & Dohme should remove 'exposure to M-M-RII/M-M-RVAXPRO during pregnancy' and the MAH GSK should remove 'use in pregnancy' as a safety concern in the RMP.

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

6.2.3. Treprostinil - TREPULMIX (CAP); NAP - PSUSA/00003013/202405

Applicant: SciPharm Sarl, various

PRAC Rapporteur: Zane Neikena

Background

Treprostinil is an analogue of prostacyclin (PGI2) that exerts a direct vasodilation effect on the pulmonary and systemic arterial circulation and inhibits platelet aggregation and it is indicated for treatment of adult patients with WHO Functional Class (FC) III or IV and inoperable chronic thromboembolic pulmonary hypertension (CTEPH), or persistent or recurrent CTEPH after surgical treatment to improve exercise capacity and symptoms of the disease.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Trepulmix, (a) centrally authorised medicine(s) containing treprostinil, and nationally

[29] Update of SmPC sections 4.3 and 4.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

authorised medicines containing treprostinil 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 treprostinil-containing product(s) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisations should be maintained.
- The MAHs for intravenous treprostinil containing medicinal products should submit an updated RMP to remove the additional risk minimisation measures (educational materials for healthcare professionals) aimed to address the 'risk of central venous catheter (CVC)-bloodstream infections (BSIs) and sepsis'.

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

See also Annex I 16.3.

6.3.1. Aciclovir (NAP) - PSUSA/00000048/202406

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Background

Aciclovir is a direct acting antiviral and it is indicated for the treatment of human herpes viruses, including herpes simplex virus (HSV) types 1 and 2, varicella zoster virus, Epstein Barr virus and cytomegalovirus (CMV).

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing aciclovir 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 aciclovir-containing medicinal products (except for those intended for intravenous use) in the approved indication(s) remains unchanged and the current terms of the marketing authorisation(s) should be maintained.
- Based on the review of the data on safety and efficacy, the benefit-risk balance of aciclovir-containing medicinal products intended for intravenous use in the approved indication(s) remains unchanged and the product information should be updated to add/amend the posology regarding dosing of obese and remove (if applicable) warnings regarding dosing of obese patients from the respective section of the product

information. Therefore, the current terms of the marketing authorisation(s) should be varied[30].

- In the next PSUR, all MAHs for aciclovir-containing medicinal products with ophthalmic formulations should provide a review of 'risk of aciclovir resistance in herpetic keratitis' from literature data in both the immunocompromised and immune-competent population and discuss the need for update of the product information and/or other RMMs. In addition, all MAHs for aciclovir-containing medicinal products with systemic formulations should provide a cumulative review of serious cutaneous adverse reactions (SCARs), with a special focus on the most serious types of SCARs (AGEP, DRESS, SJS and TEN), including information from all sources and a causality assessment of all retrieved post-marketing cases preferably using the WHO-UMC causality assessment criteria.

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.

6.3.2. Bismuth subcitrate potassium, metronidazole, tetracycline (NAP) - PSUSA/00010199/202405

Applicant(s): various

PRAC Lead: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

Background

Bismuth subcitrate potassium, metronidazole and tetracycline hydrochloride (Pylera) is a combination medicine indicated for the eradication of *Helicobacter pylori* in combination with omeprazole (quadruple therapy).

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing bismuth subcitrate potassium, metronidazole, tetracycline 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 containing bismuth subcitrate potassium, metronidazole, tetracycline-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add cerebellar syndrome as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[31].
- In the next PSUR, the MAH(s) should provide cumulative reviews of cases of lupus, of drug-induced liver injury, and of psychiatric disorders, including causality assessments and discuss the need for updates of the product information. The MAH(s) should continue to monitor cases of acute generalised exanthematous pustulosis.

[30] Update of SmPC sections 4.2 and 4.4. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position
[31] 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

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

6.3.3. Iobitridol (NAP) - PSUSA/00001761/202404

Applicant(s): various

PRAC Lead: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

Background

Iobitridol is a non-ionic, monomeric tri-iodinated, water-soluble X-ray contrast medium with low osmolality and it is indicated in adults and paediatrics for diagnostic use only and may be used for a large variety of indications.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing iobitridol 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 iobitridol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add contrast encephalopathy as a warning and as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[32].

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. Oxycodone hydrochloride, paracetamol (NAP) - PSUSA/00002256/202407

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Background

Paracetamol is a non-opioid analgesic, while oxycodone is a centrally acting opioid analgesic, with an agonist action on μ and κ receptors. Oxycodone/paracetamol fixed-dose combination is indicated in treatment of moderate to severe degenerative muscle-osteoarticular pain not treated by single administration of non-steroidal anti-inflammatory drugs (NSAIDs)/paracetamol and for the relief of moderate to severe pain in patients with cancer.

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

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing oxycodone/paracetamol 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 oxycodone/paracetamol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add hyperalgesia as an undesirable effect with a frequency 'not known'. In addition, the product information should be updated to amend the existing warning regarding hepatobiliary disorders and to add a new black box warning about the risk of dependence and addiction in the package leaflet. Therefore, the current terms of the marketing authorisation(s) should be varied[33].
- In the next PSUR, the MAH(s) should provide a follow-up trend analysis of oxycodone cases aggregately reported under the SMQ 'drug abuse, dependence and withdrawal', as well as cases reported under the separate MedDRA PTs of 'drug dependence', 'withdrawal syndrome', 'drug withdrawal syndrome', 'drug abuse' and 'overdose', and discuss the need to further actions 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.

6.3.5. Phenylpropanolamine (NAP) - PSUSA/00010483/202406

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Background

Phenylpropanolamine is a sympathomimetic agent indicated for the treatment of allergic and vasomotor rhinitis with mucosal swelling, mild to moderate sensory stress incontinence and urge incontinence and severe stress incontinence in postmenopausal women.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing phenylpropanolamine 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 phenylpropanolamine-containing medicinal products in the approved indication(s) remains unchanged.

[33] 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

- Nevertheless, the product information should be updated to add palpitations as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[34].

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.

6.4. 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. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0052/G, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped application comprising two type II variations as follows:
Type II (C.I.3.b) – Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on rash and to add hypersensitivity to the list of adverse drug reactions (ADRs) with frequency "not known" following the outcome of procedure PSUSA/00010868/202310. The Package Leaflet is updated accordingly.
Type II (C.I.z) – Submission of post-marketing breast-feeding case reports

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 to amend the existing warning on rash, to re-evaluate the existing information regarding hypersensitivity and to update the existing warning on the exposure via breast milk. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

Summary of recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC concluded that the product information should be updated to include additional guidance to the existing information regarding rash, to add hypersensitivity as an undesirable effect with the frequency 'not known', and to update the existing information regarding breastfeeding.

[34] 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

- The wording of the product information agreed by PRAC was not agreed by the Applicant, therefore an RSI was adopted with immediate 30-day timetable.

6.6. Expedited summary safety reviews[35]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[36]

See also Annex I 17.1.

7.1.1. Topiramate (NAP) - EMEA/H/N/PSP/J/0106.1

Applicant: Janssen (on behalf of a consortium)

PRAC Rapporteur: Karin Bolin

Scope: MAH's response to PSP/0106 [DUS to evaluate the effectiveness of the implemented risk minimisation measures, particularly focusing on preventing pregnancies and further characterising the prescribing patterns for topiramate in the target populations for pregnancy prevention] as per the request for supplementary information (RSI) adopted in July 2024

Background

Topiramate is an antiepileptic drug indicated for the treatment of seizures but also prophylaxis of migraine headache, as warranted.

In line with the conclusions of the referral procedures under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1520), finalised in 2023, the MAH Janssen Cilag SA, on behalf of the Topiramate Safety Consortium, was required to conduct a non-interventional post-authorisation safety study (PASS) to evaluate the effectiveness of the implemented risk minimisation measures (RMMs). The initial protocol of the study was presented for review by PRAC in April 2024. For further background, see PRAC minutes July 2024.

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 2.0, in accordance with Article 107n of Directive 2001/83/EC, PRAC considered by consensus that the study is non-interventional and the PASS protocol for topiramate can be endorsed.

7.1.2. Topiramate (NAP) - EMEA/H/N/PSP/J/0107.1

Applicant: Janssen (on behalf of a consortium)

PRAC Rapporteur: Karin Bolin

Scope: MAH's response to PSP/0107 [PASS survey among healthcare professionals and

[35] 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
[36] In accordance with Article 107n of Directive 2001/83/EC

patients to assess their knowledge and behaviour regarding the risks of topiramate use during pregnancy, the measures implemented to prevent pregnancy, and the receipt/use of educational materials as part of the pregnancy prevention program] as per the request for supplementary information (RSI) adopted in July 2024

Background

Topiramate is an antiepileptic drug indicated for the treatment of seizures but also prophylaxis of migraine headache, as warranted.

In line with the conclusions of the referral procedures under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1520), finalised in 2023, the MAH Janssen Cilag SA, on behalf of the Topiramate Safety Consortium, was required to conduct a non-interventional post-authorisation safety study (PASS) to evaluate the knowledge and adherence to the implemented risk minimisation measures (RMMs) via surveys to the health care professional (HCP) and patients/caregivers. The initial protocol of the study was presented for review by PRAC in April 2024. For further background, see PRAC minutes July 2024.

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 2.0, in accordance with Article 107n of Directive 2001/83/EC, PRAC considered by consensus that the study is non-interventional and the PASS protocol for topiramate can be endorsed.
- PRAC also agreed that all changes to the questions in HCP and patient/caregiver surveys assessed in the updated protocol v. 2.0 should in all details be correctly reflected also in the finalised survey questionnaires.

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[37]

See Annex I 17.2.

7.3. Results of PASS imposed in the marketing authorisation(s)[38]

See Annex I 17.3.

7.4. Results of PASS non-imposed in the marketing authorisation(s)[39]

See Annex I 17.4.

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

See Annex I 17.5.

7.6. Others

See Annex I 17.6.

[37] 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
[38] In accordance with Article 107p-q of Directive 2001/83/EC
[39] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1.

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2.

8.3. Renewals of the marketing authorisation

See also Annex I 18.3.

8.3.1. Lefamulin - XENLETA (CAP) - EMEA/H/C/005048/R/0010 (without RMP)

Applicant: Nabriva Therapeutics Ireland DAC

PRAC Rapporteur: Eva Jirsová

Scope: 5-year renewal 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.

Xenleta, a centrally authorised medicine containing lefamulin, was authorised in 2020. The MAH submitted an application for renewal of the marketing authorisation for opinion by CHMP. PRAC is responsible for providing advice to CHMP on this renewal with regard to safety and risk management aspects.

Summary of advice

- Based on the review of the available pharmacovigilance data for Xenleta (lefamulin) and the CHMP Rapporteur's assessment report, PRAC considered that the renewal of the marketing authorisation could be granted with unlimited validity.
- PRAC concluded that no relevant safety concerns had arisen from the assessment of this Xenleta (lefamulin) renewal procedure. PRAC recommended that the MAH continue to submit Xenleta (lefamulin) PSURs.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

10. Other safety issues for discussion requested by CHMP or EMA

10.1. Safety related variations of the marketing authorisation

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

None

10.3. Other requests

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The Chair thanked Sofia Trantza for her contribution as the member for Greece and welcomed Maria Poulianiti who was appointed as the new alternate for Greece replacing Georgia Gkegka who has taken over the role of the member for Greece. The Chair also thanked Zane Stade for her contribution as the alternate for Latvia and welcomed Diana Litenboka as the new Latvian alternate. Finally, the Chair thanked Nadine Petitpain whose mandate as the member for Luxembourg ends on 31 January 2025.

12.1.2. Vote by proxy

Annalisa Capuano gave a proxy to Milou-Daniel Drici to vote on behalf of her on 15 January 2025.

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. Health threats and EMA Emergency Task Force (ETF) activities - update

The EMA Secretariat presented to PRAC an update on monkeypox vaccines and treatment options, on the spread of human infection with avian influenza A(H5N1) virus in USA and Canada and on studies related to treatment of Marburg virus. In addition, PRAC was informed on the European Proactive Adaptive Clinical Trials Network within EU Response: PROACT EU-Response project as well as on the WHO Statement on the antigen composition of COVID-19 vaccines. PRAC noted the information.

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

None

12.8. Planning and reporting

12.8.1. Marketing authorisation applications (MAA) forecast for 2024 – planning update dated Q4 2024

The EMA Secretariat presented for information to PRAC a quarterly updated report on marketing authorisation applications (MAA) planned for submission (the business 'pipeline') in 2025 highlighting the applications without appointed Rapporteur(s). For the latest previous update, see PRAC minutes October 2024.

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 2025, reflecting the PRAC's comments impacting on the data lock point (DLP) and PSUR submission frequencies of the substances/combinations. PRAC endorsed the newly allocated

Rapporteurs for upcoming PSUSAs in accordance with the principles previously endorsed by PRAC (see PRAC minutes April 2013).

Post-meeting note: following the PRAC meeting of January 2025, the updated EURD list was adopted by CHMP and CMDh at their January 2025 meetings and published on the EMA website, see: Home> Human Regulatory>Post-authorisation>Pharmacovigilance>Periodic safety update reports>> List of Union reference dates and frequency of submission of periodic safety update reports (PSURs)

12.11. Signal management

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

PRAC lead: Martin Huber

The EMA Secretariat presented the outcome of the SMART WG discussions on the process optimisation to integrate real-world evidence (RWE) in the signal management process. PRAC agreed that a refinement of the process is needed. The updated proposal will be brought to PRAC for discussion as the decision to conduct a RWE study is anyway to be taken by PRAC.

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. EMA's approach to safety communications

The EMA Secretariat presented to PRAC a summary of EMA's communication activities, which encompass media and public relations, stakeholders engagement, medical and health information, along with the initiatives aimed at enhancing the communication with the

network. The presentation then focused on the communication tools specifically used for PRAC, along with guidance for members on interacting with media and using social media in the context of ongoing safety issues.

12.21.2. Guideline on risk assessment of medicinal products on human reproduction and lactation: from data to labelling – Public consultation comments on concept paper to revise the guideline

PRAC lead: Ulla Wändel Liminga

The EMA Secretariat presented to PRAC the outcome of the assessement of the comments received during the public consultation of the Concept paper revision GL risk assessment human reproduction lactation for PC (europa.eu). For background information, see PRAC minutes April 2024. PRAC agreed with the drafting group proposal to maintain the improved/revised recommendations in labelling/standardised statements to healthcare professionals in the revised guideline to provide more concrete data for decision making, allowing some flexibility for some case-by-case considerations. PRAC noted also the next steps planned for this activity.

12.21.3. Implementation of new fee regulation (EU) 2024/568 from 1 January 2025

The EMA Secretariat presented to PRAC the changes related to the implementation of the new fee regulation focusing on the updates in the parts relevant for the pharmacovigilance procedures. PRAC noted the information.

12.21.4. PRAC Assessors trainings - update

PRAC Lead(s): Liana Martirosyan, Ulla Wändel Liminga

The EMA Secretariat provided the proposed plan for the 2025 PRAC Assessors training with several short webinar sessions scheduled around the year. PRAC welcomed the proposal and noted the information.

12.21.5. Serious cutaneous adverse reactions (SCARs) - PRAC guidance update

PRAC Lead(s): Ulla Wändel Liminga, Zane Neikena

The EMA Secretariat presented to PRAC the initiative to update the PRAC internal assessor's guidance on SCARs along with the next steps that will facilitate sharing the relevant information with the MAHs as needed. PRAC noted the information and endorsed the way forward.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[40]

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[41].

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

14.1.1. Clozapine (NAP)

Applicant(s): various

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of appendicitis

EPITT 20139 – New signal

14.1.2. Omalizumab – OMLYCLO (CAP); XOLAIR (CAP)

Applicant: Celltrion Healthcare Hungary Kft. (Omlyclo), Novartis Europharm Limited (Xolair)

PRAC Rapporteur: Mari Thorn

Scope: Signal of hearing losses

EPITT 20128 – New signal

14.1.3. Sertraline (NAP)

Applicant: various

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of multiple acyl-coenzyme A dehydrogenase deficiency (MADD)

EPITT 20125 – New signal

14.1.4. Sulfamethoxazole, trimethoprim (co-trimoxazole) (NAP)

Applicant: various

PRAC Rapporteur: Barbara Kovačić Bytyqi

Scope: Signal of circulatory shock

EPITT 20135 – New signal

[40] 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

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

14.2. Signals follow-up and prioritisation

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. Trastuzumab - (CAP MAA) - EMEA/H/C/006219

Scope (pre D-180 phase): treatment of metastatic and early breast cancer

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. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/II/0040, Orphan

Applicant: Fondazione Telethon ETS, ATMP

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of an updated RMP version 7.0 in order to propose amendments to the STRIM-005 and STRIM-003 study protocols, as well as revised timelines for completion of both studies. In addition, the Annex II is updated accordingly

15.2.2. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/WS2771/0054; Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/WS2771/0084

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Karin Erneholm

Scope: Submission of an updated RMP version 4.3 for Tecartus and version 11.1 for Yescarta following the PRAC recommendation for the Secondary malignancy of T-cell origin signal (EPITT no: 20040), and of a PASS protocol for a framework for the sampling and testing of secondary malignancies of T-cell origin

15.2.3. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/II/0040, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of an updated RMP version 8.0 in order to remove hyperphosphataemia as an important potential risk and to add a specific adverse drug reaction follow-up form/questionnaire for increased parathyroid hormone levels as a routine pharmacovigilance activity

15.2.4. Cetuximab - ERBITUX (CAP) - EMEA/H/C/000558/II/0103

Applicant: Merck Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of an updated RMP version 19.2 in order to re-classify important identified risks and important potential risks and to remove them from the summary of safety concerns, following the PRAC assessment for PSUSA/00000635/202309

15.2.5. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/II/0034, Orphan,

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: Submission of an updated RMP version 5.2 in order to add a new important identified risk of "Secondary malignancy of T-cell origin", to change the important potential risk of "Second primary malignancies" to "Second primary malignancy except secondary malignancy of T-cell origin", and to include an additional pharmacovigilance activity for testing of secondary malignancies of T-cell origin, following the PRAC recommendation for the Secondary malignancy of T-cell origin signal (EPITT no: 20040)

15.2.6. Conestat alfa - RUCONEST (CAP) - EMEA/H/C/001223/II/0088/G

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of an updated RMP version 19.3 in order to request the early termination of the EU registry study C1 1412, as well as to update safety information based on cumulative data from clinical trials, the EU registry data, post-marketing data and literature. A request for the extension of the due date for the European survey of educational materials for Ruconest is also included

15.2.7. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0028, Orphan

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: Submission of a revised protocol for study EP0218 listed as an obligation in the Annex II of the Product Information. This is a Long-term Registry in approved indications for fenfluramine, with a specific focus on cardiovascular events and growth retardation. The RMP version 4.0 is updated accordingly. In addition, the MAH introduced minor amendments in the targeted follow-up questionnaire for cardiovascular adverse events

15.2.8. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0062

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final report from study COVID-PR (CO-US-540-6127) listed as a category 3 study in the RMP. This is a non-interventional, patient-reporting, postmarketing cohort study designed to collect safety data from pregnant and recently pregnant women treated with monoclonal antibodies or antiviral drugs for mild, moderate, or severe COVID-19 at any time from the first day of the last menstrual period to the end of pregnancy. The RMP version 8.2 is updated accordingly

15.2.9. Zoledronic Acid – ZOLEDRONIC ACID ACCORD (CAP); NAP - EMA/VR/0000226953

Applicant(s): Accord Healthcare S.L.U., various

PRAC Rapporteur: Karin Erneholm

Scope: To align the RMP for Zoledronic Acid Accord with the RMP of the reference product. In addition for the nationally authorised products Zoledronic Acid Accord 4 mg/5 ml, 4 mg/100 ml concentrate for solution for infusion (product reference PT/H/0742/001/DC) the RMP is being merged with the RMP of the centrally authorised product

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. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/II/0028

Applicant: AstraZeneca AB

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Extension of indication to include CALQUENCE in combination with venetoclax with or without obinutuzumab for the treatment of adult patients with previously untreated chronic lymphocytic leukemia (CLL), based on interim results from study AMPLIFY (D8221C00001). This is a Randomized, Multicenter, Open-Label, Phase 3 Study to Compare the Efficacy and Safety of Acalabrutinib in Combination with Venetoclax with and without Obinutuzumab Compared to Investigator’s Choice of Chemoimmunotherapy in Subjects with Previously Untreated Chronic Lymphocytic Leukemia Without del(17p) or TP53 Mutation (AMPLIFY). As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8 of the RMP has also been submitted

15.3.2. Amivantamab - RYBREVANT (CAP) - EMEA/H/C/005454/X/0014

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Extension application to introduce a new pharmaceutical form (solution for

injection), two new strengths of 1600 mg and 2240 mg (160 mg/ml concentration) and a new route of administration (subcutaneous use)

15.3.3. Brexpiprazole - RXULTI (CAP) - EMEA/H/C/003841/II/0015

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Miroslava Gocova

Scope: Extension of indication to include treatment of schizophrenia in adolescent patients aged from 13 years to 17 years for RXULTI, based on results from the following clinical studies: one phase 1 dose-escalation trial (Trial 331-10-233) and two phase 3 clinical trials (Trial 331-10-234 and Trial 331-10-236). In addition, a paediatric extrapolation study was completed (Study 331-201-00185). These studies investigated the efficacy and safety of brexpiprazole in paediatric patients (13-17 years old) with schizophrenia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 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, and to bring the PI in line with the latest QRD template version 10.4

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

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

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

15.3.5. COVID-19 mRNA vaccine - COMIRNATY (CAP) - EMA/VR/0000231586

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of:

C.I.11.b: Submission of an updated RMP version 13.1 in order to include Protocol amendment no. 5 where the study design and objectives were revised for an interventional study C4591048, a master phase 1/2/3 protocol to investigate the safety, tolerability, and immunogenicity of bivalent BNT162b2 RNA- based vaccine candidate(s) in healthy children, listed as a category 3 study in the RMP.

C.I.13: Submission of the final report from study C4591044 listed as a category 3 study in the RMP. This is an interventional randomized, active controlled, Phase 2/3 Study to Investigate the Safety, Tolerability, and Immunogenicity of Bivalent BNT162b RNA-Based Vaccine Candidates as A Booster Dose In COVID-19 Vaccine–Experienced Healthy Individuals. The RMP version 13.1 has also been submitted

15.3.6. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0084

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report from study CRZ-NBALCL listed as a category 3 study in the RMP. This is a phase I/II study to evaluate the adverse effects of ocular toxicity and bone toxicity and impaired bone growth associated with crizotinib in paediatric and young adult patients with recurrent/refractory anaplastic lymphoma kinase-positive anaplastic large cell lymphoma or neuroblastoma. The RMP version 9.2 is updated accordingly

15.3.7. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/II/0034

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment and prophylaxis of bleeding in previously treated patients ≥7 years of age with haemophilia A for JIVI, based on integrated analysis results from Part A of the Alfa-PROTECT study (21824) and PROTECT Kids main study (15912). Alfa-PROTECT is a Phase 3, single-group treatment, open-label study to evaluate the safety of BAY 94-9027 infusions for prophylaxis and treatment of bleeding in previously treated children aged 7 to <12 years with severe hemophilia A. PROTECT Kids is a multi-center, Phase 3, non-controlled, open-label trial to evaluate the pharmacokinetics, safety, and efficacy of BAY 94-9027 for prophylaxis and treatment of bleeding in previously treated children (age <12 years) with severe haemophilia A. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 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. Furthermore, the PI is brought in line with the latest QRD template version 10.4

15.3.8. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/X/0033/G

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to add a new strength of Jivi 4000 UI powder and solvent for solution for injection for treatment and prophylaxis of bleeding in previously treated patients ⩾ 12 years of age with haemophilia A (congenital factor VIII deficiency).
Version 3.1 of the RMP has also been submitted.
In addition, the MAH has taken the opportunity to align the product information with the pre-specified language from the updated EC Excipient Guideline.

B.III.2.b
B.II.b.2.a

15.3.9. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[42]) - EMEA/H/W/002168/II/0027

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include reducing the risk of HIV-1 infection via vaginal intercourse in HIV-uninfected women 16 years and older for Dapivirine Vaginal Ring 25 mg, based on final results from study MTN-034 (REACH) listed as a category 3 study in the RMP; this is a Phase 2a crossover trial evaluating the safety of and adherence to a vaginal matrix ring containing dapivirine and oral emtricitabine/tenofovir disoproxil fumarate in an adolescent and young adult female population. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 1.5 of the RMP has also been submitted

15.3.10. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0076, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Carla Torre

Scope: Extension of indication for Darzalex in combination with bortezomib, lenalidomide and dexamethasone for the treatment of newly diagnosed multiple myeloma, to include also adult patients who are not eligible for stem cell transplant (SCT), based on the results of the final PFS analysis from Study CEPHEUS (54767414MMY3019), a randomised, open-label, active-controlled, multicenter phase 3 study in adult participants, comparing the clinical outcome of D-VRd with VRd in participants with untreated multiple myeloma for whom stem cell transplant is not planned as initial therapy, in terms of the primary endpoint of MRD negativity rate in participants with CR or better rate and major secondary endpoints of CR or better rate, PFS and sustained MRD negativity.
As a consequence, SmPC sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 are updated and the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Package Leaflet.
An updated RMP version 11.1 has also been submitted

15.3.11. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0024

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include in combination with androgen deprivation therapy (ADT) the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) for NUBEQA, based on final results from study 21140 (ARANOTE); this is a randomized, double-blind, placebo-controlled Phase 3 study of darolutamide to demonstrate the superiority of darolutamide in addition to ADT over placebo plus ADT in patients with mHSPC. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce

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

minor editorial changes to the PI and update the Package Leaflet to more patient friendly wording based on patient council feedback

15.3.12. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0073

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include IMFINZI in combination with cisplatin-based chemotherapy as neoadjuvant treatment, followed by IMFINZI as monotherapy adjuvant treatment after radical cystectomy, for the treatment of adults with muscle invasive bladder cancer (MIBC), based on an ongoing pivotal study D933RC00001 (NIAGARA); this is a phase 3, randomized, open-label, multi-center, global study to determine the efficacy and safety of durvalumab in combination with gemcitabine+cisplatin for neoadjuvant treatment followed by durvalumab alone for adjuvant treatment in patients with muscle-invasive bladder cancer. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version 13 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes and update the PI according to the Excipients Guideline

15.3.13. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/II/0020, Orphan

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) with active disease despite treatment with corticosteroids or immunoglobulins for VYVGART, based on final results from study ARGX-113-1802; this is a pivotal study to investigate the efficacy, safety and tolerability of efgartigimod PH20 SC in adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP); and based on interim results from study ARGX-113-1902; this is an open-label extension study of the ARGX-113-1802 trial to investigate the long-term safety, tolerability and efficacy of efgartigimod PH20 SC in patients with (CIDP).
As a consequence, sections 4.1, 4.2. 4.4, 4.8, 5.1 and 5.2 of the SmPC has been updated. The Package Leaflet has been updated in accordance with the SmPC. In addition, the MAH took the opportunity to implement editorial changes to the SmPC

15.3.14. Faricimab - VABYSMO (CAP) - EMEA/H/C/005642/II/0016

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Update of section 5.1 of the SmPC to reflect the long-term safety profile of faricimab in patients with diabetic macular edema (DME) based on the final results from study GR41987 (Rhone-X) listed as a category 3 study of the RMP. Rhone-X was a phase III interventional, multicenter, open-label extension study to evaluate the long-term safety and tolerability of faricimab in patients with diabetic macular edema. The RMP version 7.0 has also been submitted

15.3.15. Formoterol, glycopyrronium bromide, budesonide - RILTRAVA AEROSPHERE (CAP) - EMEA/H/C/005311/WS2780/0017; Formoterol, glycopyrronium bromide, budesonide - TRIXEO AEROSPHERE (CAP) - EMEA/H/C/004983/WS2780/0024

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Type II var - B.II.a.3.b.2
The change is reflected in the PI and it is supported by non clinical and clinical data. The RMP version 2 has also been submitted.

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Extension of indication to include in combination with gemcitabine and oxaliplatin the treatment of adult patients with relapse or refractory diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS) who are not candidates for autologous stem cell transplant (ASCT) for COLUMVI, based on results of primary and updated analyses from study GO41944 (STARGLO) listed as a Specific Obligation in the Annex II of the Product Information, as well supportive data from the Phase Ib study GO41943. Study GO41944 (STARGLO) is a Phase III, open-label, multicenter, randomized study of glofitamab in combination with GemOx (Glofit-GemOx) vs. rituximab in combination with GemOx (R-GemOx) in patients with R/R DLBCL. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and update the list of local representatives in the Package Leaflet. As part of the application, the MAH is requesting a 1-year extension of the market protection

15.3.17. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) - EMA/VR/0000235389

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of sections 4.4 and 5.1 of the SmPC to include the final results of study ZOSTER-062, listed as a category 3 study in the RMP. This is a phase III, randomized, observer-blind, placebo controlled, multicenter clinical trial to assess Herpes Zoster recurrence and the reactogenicity, safety and immunogenicity of Shingrix when administered intramuscularly on a 0 and 2 month schedule to adults $\geqslant$ 50 years of age with a prior episode of Herpes Zoster. The RMP version 9.0 has also been submitted. In addition, the MAH took the opportunity to implement a minor editorial change to Annex II of the PI

15.3.18. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/II/0076

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of sections 4.8 and 5.1 of the SmPC to include the final results of study ZOSTER-049, listed as a category 3 study in the RMP. This is a Phase 3b, open label, multi-country, long-term follow-up study that assessed the prophylactic efficacy, safety, and immunogenicity persistence of Shingrix in adults ≥50 years of age at the time of primary vaccination in studies ZOSTER 006 and ZOSTER-022. The study also assessed 1 or 2 additional doses of Shingrix on a 0 or 0, 2-month schedule in two subgroups of older adults. The updated RMP version 8.0 is also included. In addition, the MAH took the opportunity to implement editorial changes to the SmPC, Labelling and Package Leaflet; and to bring the PI in line with the latest QRD template version 10.4

15.3.19. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2717/0146; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2717/0115

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: A Worksharing application for OPDIVO and YERVOY, as follows:

Extension of indication to include a new indication for OPDIVO in combination with ipilimumab as first line treatment of adult patients with unresectable or advanced hepatocellular carcinoma (HCC) based on study CA2099DW. This is a phase 3 randomised, multi-centre, open label study of Nivolumab in combination with Ipilimumab compared to Sorafenib or Lenvatinib as first-line treatment in participants with advanced HCC. 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 41.0 of the RMP has also been submitted.

Extension of indication to include a new indication for YERVOY in combination with ipilimumab as first line treatment of adult patients with unresectable or advanced hepatocellular carcinoma (HCC) based on study CA2099DW. This is a phase 3 randomised, multi-centre, open label study of Nivolumab in combination with Ipilimumab compared to Sorafenib or Lenvatinib as first-line treatment in participants with advanced HCC. 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 44.0 of the RMP has also been submitted

15.3.20. Iptacopan - FABHALTA (CAP) - EMEA/H/C/005764/II/0001, Orphan

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Lina Seibokiene

Scope: Extension of indication to include, in combination with a renin-angiotensin system (RAS) inhibitor, the treatment of adult patients with complement 3 glomerulopathy (C3G) for FABHALTA, based on interim analysis results from study CLNP023B12301 (APPEAR-C3G) and supported by additional evidence of efficacy and safety data from Phase II study CLNP023X2202 (X2202) and Phase IIIb study CLNP023B12001B (C3G-REP). APPEAR-C3G is a Phase 3, multicenter, randomized, double-blind, parallel arm, placebo-controlled study to evaluate the efficacy and safety of iptacopan in patients with C3G. The study included a 6-month blinded, placebo-controlled period, followed by a 6-month period in which all patients receive open-label iptacopan (total study duration of 12 months). As a consequence,

sections 4.1, 4.2, 4.4, 4.6, 4.8 and 5.1 of the SmPC are being updated. The Annex II and Package Leaflet are updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI

15.3.21. Lenacapavir - SUNLENCA (CAP) - EMEA/H/C/005638/II/0022/G

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouping of two type II variations:
- Update of section 5.1 of the SmPC to include efficacy and resistance data based on week 156 interim data from Study GS-US-200-4625; a phase 2/3 study to evaluate the safety and efficacy of long-acting capsid inhibitor GS-6207 in combination with an optimized background regimen in heavily treatment experienced people living with HIV-1 infection with multidrug resistance (category 3 study in the RMP). Additionally, upon request by the CHMP following the assessment of II/0013, the MAH proposes to update section 4.8 of the SmPC to include information related to injection site nodules and induration that were non-resolved at the end of follow-up.
- Provision of the final study report of Study GS-US-200-4334: a phase 2 randomized, open label, active controlled study evaluating the safety and efficacy of long-acting capsid inhibitor GS-6207 in combination with other antiretroviral agents in people living with HIV (category 3 study in the RMP).

An updated RMP version 2.1 was included as part of the application

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

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: A grouped application consisting of:

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

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

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

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

15.3.23. Lutetium (^{177}Lu) vipivotide tetraxetan - PLUVICTO (CAP) - EMEA/H/C/005483/II/0022

Applicant: Novartis Europharm Limited

PRAC Rapporteur: John Joseph Borg

Scope: Update of section 4.8 of the SmPC in order to update safety information based on final results from study PSMA-617-01 (CAAA617A12301 – VISION) listed as a category 3 study in the RMP; this is an international, prospective, open-label, multicenter, randomized Phase 3 study of 177Lu-PSMA-617 in the treatment of patients with progressive PSMA-positive metastatic castration-resistant prostate cancer. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI

15.3.24. Melatonin - SLENYTO (CAP) - EMEA/H/C/004425/II/0028

Applicant: RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include treatment of insomnia in children and adolescents aged 2-18 with Attention-Deficit Hyperactivity Disorder (ADHD), where sleep hygiene measures have been insufficient, based on results from phase III study NEU_CH_7911 and literature. As a consequence, sections 4.1 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

15.3.25. Mercaptamine - CYSTADROPS (CAP) - EMEA/H/C/003769/II/0032, Orphan

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include treatment of children from 6 months of age for CYSTADROPS, based on final results from study CYT-C2-001. This is an Open-label, Single-arm, Multicenter Study to Assess the Safety of Cystadrops in Pediatric Cystinosis Patients from 6 Months to Less Than 2 Years Old. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update Annex II of the PI and the list of local representatives in the Package Leaflet

15.3.26. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/X/0144

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (600 mg) and a new route of administration (subcutaneous use). Version 40.0 of the RMP has also been submitted

15.3.27. Nusinersen - SPINRAZA (CAP) - EMEA/H/C/004312/II/0034/G, Orphan

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Karin Bolin

Scope: A grouped application consisting of:
C.I.4: Update of sections 5.1 and 5.2 of the SmPC based on final results from study CS11 (SHINE) listed as a PAES in the Annex II. The Annex II and the RMP v12.1 are updated accordingly. SHINE is a phase III, open-label extension study for patients with Spinal Muscular Atrophy (SMA) who previously participated in investigational studies of ISIS 396443.
C.I.4: Update of section 5.1 of the SmPC based on interim results from study CS5 (NURTURE, 232SM201). NURTURE is a Phase II, open-label study to assess the efficacy, safety, tolerability, and pharmacokinetics of multiple doses of nusinersen delivered intrathecally to patients with genetically diagnosed and presymptomatic SMA.
C.I.4: Update of section 5.1 of the SmPC in order to relocate the updated information regarding immunogenicity from SmPC section 4.8 to section 5.1 as per applicable CHMP guidance. The data has been revised based on an updated integrated analysis across several studies.
C.I.4: Update of section 5.1 of the SmPC based on the outcome of a systematic literature review (SLR) and Natural History data from an International SMA registry (ISMAR)

15.3.28. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/II/0022/G, Orphan

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application including two type II variations:
- Update of sections 4.2, 4.4, 4.8, and 5.1 of the SmPC based on the clinical study report for the completed 72 weeks of Study A4250-008; an open-label, phase III study to evaluate the long-term efficacy and safety of odevixibat in children with PFIC (category 3 study in the RMP; MEA 002).
The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and the Package Leaflet. An updated RMP version 6.1 is included in this submission.
- Submission of the clinical study report for Study A4250-J001; a Phase I PK study in healthy Japanese adult male patients

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

Applicant: Sanofi B.V.

PRAC Rapporteur: Martin Huber

Scope: A grouped application consisting of:
C.I.4: Update of sections 4.4 and 4.8 of the SmPC in order to update safety information based on final results from study DFI12712 ASCEND, listed as a category 3 study in the RMP; this is a Phase 2/3, multicenter, randomised, double-blinded, placebo-controlled, repeat-dose study to evaluate the efficacy, safety, pharmacodynamics and pharmacokinetics of olipudase alfa in patients with AMSD. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4 and to implement editorial changes to the SmPC.

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

15.3.30. Omalizumab - OMLYCLO (CAP) - EMEA/H/C/005958/II/0004/G

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Mari Thorn

Scope: - to introduce a new alternative delivery device in addition to the already authorised pre-filled syringe (PFS), (Type II - B.II.e.1.b.2);
(Type IAIN - B.II.e.5.a.1);
(Type IAIN - B.II.e.5.a.1)

15.3.31. Pegcetacoplan - ASPAVELI (CAP) - EMEA/H/C/005553/II/0028, Orphan

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.8 of the SmPC in order to add urticaria/hives to the list of adverse drug reactions (ADRs) with frequency "common" and to add anaphylactic reaction and anaphylactic shock to the list of ADRs with frequency "uncommon", based on post-marketing data and literature; the Package Leaflet is updated accordingly. The RMP version 3.1 has also been submitted

15.3.32. Pegunigalsidase alfa - ELFABRIO (CAP) - EMEA/H/C/005618/II/0007

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Update of sections 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC in order to introduce an alternative posology regimen based on results from study PB-102-F50 (BRIGHT) and interim results from its extension study CLI-06657AA1-03 (formerly presented as PB-102-F51), as well as results of the observational patient reporting outcome study CLI-06657AA1-05. CLI-06657AA1-03 is an Open-Label Extension Study to Evaluate the Long-Term Safety and Efficacy of Pegunigalsidase Alfa (PRX-102) 2 mg/kg Administered by Intravenous Infusion Every 4 Weeks in Patients with Fabry Disease. The Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.4

15.3.33. Pirtobrutinib - JAYPIRCA (CAP) - EMEA/H/C/005863/II/0002

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adult patients with chronic lymphocytic leukemia (CLL) who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor for JAYPIRCA, based on interim results from study LOXO-BTK-20020 (BRUIN CLL-321); this is a phase 3 open-label, randomized study of LOXO-305 versus investigator's choice of idelalisib plus rituximab or bendamustine plus rituximab in BTK inhibitor pretreated CLL/SLL.
As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.
As part of the application the MAH is requesting a 1-year extension of the market protection

15.3.34. Pyronaridine, artesunate - PYRAMAX (Art 58[43]) - EMEA/H/W/002319/II/0036

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of sections 4.4 and 4.6 of the SmPC with revised recommendations for treatment during pregnancy. The Package Leaflet has been updated accordingly. An updated RMP version 18 was provided as part of the application

15.3.35. Ranibizumab - RANIBIZUMAB MIDAS (CAP) - EMEA/H/C/006528/II/0002/G

Applicant: MIDAS Pharma GmbH

PRAC Rapporteur: Karin Bolin

Scope: Type II - B.II.e.1.b.2
2x Type II (B.II.b.1.c)
Type II (B.II.b.3.c)
Type IB - B.II.b.1.z
4x Type IB (B.II.b.2.a)
Type IB (B.II.d.2.a)
6x Type IA (B.II.d.1.c)
Type IAIN (B.II.e.6.a)
Type IAIN (B.II.f.1.a.1)
The product information and the RMP (version 2.0) is updated consequentially

15.3.36. Ranibizumab - RANIVISIO (CAP) - EMEA/H/C/005019/II/0017/G

Applicant: Midas Pharma GmbH

PRAC Rapporteur: Karin Bolin

Scope: Type II - B.II.e.1.b.2

2x Type II (B.II.b.1.c)

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

Type II (B.II.b.3.c)
Type IB - B.II.b.1.z
4x Type IB (B.II.b.2.a)
Type IB (B.II.d.2.a)
6x Type IA (B.II.d.1.c)
Type IAIN (B.II.e.6.a)
Type IAIN (B.II.f.1.a.1)

The product information and the RMP (version 2.0) is updated consequentially

15.3.37. Sparsentan - FILSPARI (CAP) - EMEA/H/C/005783/II/0002, Orphan

Applicant: Vifor France

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.8, and 5.1 of the SmPC in order to amend the frequency of the adverse drug reactions (ADRs) based on final results from study 021IGAN17001 (PROTECT) listed as a specific obligation in the Annex II; this is a randomized, multicenter, double-blind parallel-group, active control study of the efficacy and safety of sparsentan for the treatment of immunoglobulin A nephropathy. The Package Leaflet is updated accordingly. The RMP version 1.0 has also been submitted. In addition, the MAH took the opportunity to update Annex II and to bring the PI in line with the latest QRD template version 10.4. Consequently, the MAH proposes a switch from conditional marketing authorisation to full marketing authorisation

15.3.38. Tasimelteon - HETLIOZ (CAP) - EMEA/H/C/003870/II/0040, Orphan

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include the treatment of nighttime sleep disturbances in adults with Smith Magenis Syndrome (SMS) for HETLIOZ, based on results from study VP-VEC-162-2401. This is a double-blind, randomized, two-period crossover study evaluating the effects of tasimelteon vs. placebo on sleep disturbances of individuals with Smith-Magenis Syndrome (SMS). As a consequence, sections 4.1, 4.5, 5.1, 5.2 and 5.3 of the SmPC are updated. The Labelling and Package Leaflet are updated in accordance. The RMP version 5.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.4. As part of the application, the MAH is requesting a 1-year extension of the market protection

15.3.39. Tedizolid phosphate - SIVEXTRO (CAP) - EMEA/H/C/002846/II/0054

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include treatment of paediatric patients aged from birth to less than 12 years for SIVEXTRO, based on final results from studies MK-1986-013, MK-

1986-014 and MK-1986-018. MK-1986-013 is a single-dose trial to evaluate pharmacokinetics (PK) and safety of oral and intravenous (IV) administration of tedizolid phosphate in patients from 2 years to <12 years of age; MK-1986-014 is an open-label, multicentre, 2-part, single and multiple dose study to assess the PK of tedizolid phosphate and its active metabolite, tedizolid, and the safety of tedizolid phosphate following single and multiple dose IV and single oral dose. MK-1986-018 is a randomised, active controlled, investigator-blind, multicentre trial to evaluate safety and efficacy in patients from birth to less than 12 years of age; As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.1 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 and to implement minor editorial corrections

15.3.40. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/II/0092, Orphan,

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 4.2 of the SmPC in order to update the 'monitoring after infusion' recommendations, based on existing clinical trial data as well as literature references reporting real word experience. The Package Leaflet is updated accordingly. The RMP version 8.0 has also been submitted. In addition, the MAH took the opportunity to introduce a minor change to the HCP educational programme in the Annex II in order to enhance readability

15.3.41. Tislelizumab - TEVIMBRA (CAP) - EMEA/H/C/005919/II/0016

Applicant: Beigene Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include first-line treatment of adult patients with extensive-stage Small Cell Lung Cancer (SCLC) for Tevimbra in combination with etoposide and platinum chemotherapy based on final results from study BGB-A317-312; a phase 3, randomized, double-blind, placebo-controlled study of platinum plus etoposide with or without tislelizumab in patients with untreated extensive-stage small cell lung cancer. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The MAH also took the opportunity to make editorial changes to the SmPC, Annex II and Package Leaflet.
The supportive studies BGB-A317-309 and BGB-A317-315 are provided for the purpose of updating the safety data package as well as updated data (latest CSR versions with new data cut-off) from the monotherapy pool (tislelizumab used at 200mg Q3W) consisting of the studies 001, 102, 203, 204, 208, 209, 301, 302, and 303 and from the combination with chemotherapy pool consisting of the studies 205, 206, 304, 305, 306, 307 and 312. Version 2.4 of the RMP has also been submitted

15.3.42. Ustekinumab - OTULFI (CAP) - EMEA/H/C/006544/II/0001/G

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Type II - B.II.e.1.b.2
Type II - B.II.b.3.c
Type IB - B.II.d.1.z
Type IAIN - B.II.b.1.a
The product information and the RMP (v 1.0) is updated consequentially

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

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Type II B.IV.1.c

Type IB C.I.2.a To update section 4.6 Fertility, Pregnancy and lactation of the SmPC to update information on pregnancy following assessment of the same change for the reference product Stelara (EMEA/H/C/000958).

An updated RMP (version 4.0) is provided

15.3.44. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0108

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include treatment of moderately to severely active Crohn's disease in paediatric patients weighing at least 40 kg, who have had an inadequate response to, or were intolerant to either conventional or biologic therapy or have medical contraindications to such therapies for STELARA, based on final results from study CNTO1275CRD3004. This is a Phase 3 Study of the Efficacy, Safety, and Pharmacokinetics of Ustekinumab as Open label Intravenous Induction Treatment Followed by Randomized Double blind Subcutaneous Ustekinumab Maintenance in Pediatric Participants with Moderately to Severely Active Crohn’s Disease. 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 29.1 of the RMP has also been submitted

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

Applicant: Amgen Technology (Ireland) Unlimited Company

PRAC Rapporteur: Rhea Fitzgerald

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

15.3.46. Vutrisiran - AMVUTTRA (CAP) - EMEA/H/C/005852/II/0015, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Extension of indication to include treatment of wild-type or hereditary transthyretin-mediated amyloidosis in adult patients with cardiomyopathy (ATTR-CM), based on primary

analysis results from study HELIOS-B (ALN-TTRSC02-003); a Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Vutrisiran in Patients With Transthyretin Amyloidosis With Cardiomyopathy (ATTR Amyloidosis With Cardiomyopathy). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. An updated version 1.3 of the RMP has also been submitted. As part of the application the MAH applied for +1 year of additional market protection.

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

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

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

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

16.1.1. Abiraterone - ABIRATERONE MYLAN (CAP); ZYTIGA (CAP) - PSUSA/00000015/202404

Applicant: Mylan Pharmaceuticals Limited (Abiraterone Mylan), Janssen-Cilag International N.V. (Zytiga)

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

16.1.2. Adagrasib - KRAZATI (CAP) - PSUSA/00000214/202406

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

16.1.3. Alpelisib - PIQRAY (CAP) - PSUSA/00010871/202405

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.4. Amivantamab - RYBREVANT (CAP) - PSUSA/00010977/202405

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.5. Arpraziquantel - ARPRAZIQUANTEL (Art 58[44]) - EMEA/H/W/004252/PSUV/0001

Applicant: Merck Europe B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUR procedure

16.1.6. Avatrombopag - DOPTELET (CAP) - PSUSA/00010779/202405

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

16.1.7. Azacitidine - VIDAZA (CAP) - PSUSA/00000274/202405

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.8. Basiliximab - SIMULECT (CAP) - PSUSA/00000301/202404

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.9. Binimetinib - MEKTOVI (CAP) - PSUSA/00010717/202406

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

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

16.1.10. Budesonide[45] - KINPEYGO (CAP) - PSUSA/00011007/202406

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.1.11. Cannabidiol[46] - EPIDYOLEX (CAP) - PSUSA/00010798/202406

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.1.12. Cefepime, enmetazobactam - EXBLIFEP (CAP) - PSUSA/00000305/202406

Applicant: Advanz Pharma Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.13. Cholera vaccine, oral, live - VAXCHORA (CAP) - PSUSA/00010862/202406

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.1.14. Delafloxacin - QUOFENIX (CAP) - PSUSA/00010822/202406

Applicant: A. Menarini Industrie Farmaceutiche Riunite s.r.l.

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

16.1.15. Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/202406

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

16.1.16. Elacestrant - ORSERDU (CAP) - PSUSA/00000120/202406

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

[45] For centrally authorised products indicated for primary immunoglobulin A nephropathy only
[46] For centrally authorised products only

16.1.17. Eladocagene exuparvovec - UPSTAZA (CAP) - PSUSA/00011004/202406

Applicant: PTC Therapeutics International Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.18. Encorafenib - BRAFTOVI (CAP) - PSUSA/00010719/202406

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

16.1.19. Etranacogene dezaparvovec - HEMGENIX (CAP) - PSUSA/00011037/202405

Applicant: CSL Behring GmbH, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.20. Fexinidazole - FEXINIDAZOLE WINTHROP (Art 58[47]) - EMEA/H/W/002320/PSUV/0020

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUR procedure

16.1.21. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP); REVINTY ELLIPTA (CAP) - PSUSA/00010099/202405

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

16.1.22. Formoterol fumarate dihydrate, glycopyrronium bromide, budesonide - RILTRAVA AEROSPHERE (CAP); TRIXEO AEROSPHERE (CAP) - PSUSA/00010908/202406

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

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

16.1.23. Galsulfase - NAGLAZYME (CAP) - PSUSA/00001515/202405

Applicant: BioMarin International Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.1.24. Givosiran - GIVLAARI (CAP) - PSUSA/00010839/202405

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.25. Imatinib - GLIVEC (CAP) - PSUSA/00001725/202405

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

16.1.26. Indacaterol, glycopyrronium, mometasone - ENERZAIR BREEZHALER (CAP); ZIMBUS BREEZHALER (CAP) - PSUSA/00010861/202407

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.27. Indacaterol, mometasone furoate - ATECTURA BREEZHALER (CAP); BEMRIST BREEZHALER (CAP) - PSUSA/00010850/202405

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.28. Inebilizumab - UPLIZNA (CAP) - PSUSA/00010996/202406

Applicant: Horizon Therapeutics Ireland DAC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.29. Insulin lispro - HUMALOG (CAP); INSULIN LISPRO SANOFI (CAP); LIPROLOG (CAP); LYUMJEV (CAP) - PSUSA/00001755/202404

Applicant: Eli Lilly Nederland B.V. (Humalog, Liprolog, Lyumjev), Sanofi Winthrop Industrie (Insulin lispro Sanofi)

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.30. Interferon beta-1a[48] - AVONEX (CAP) - PSUSA/00010725/202405

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

16.1.31. Iptacopan - FABHALTA (CAP) - PSUSA/00011054/202406

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure

16.1.32. Laronidase - ALDURAZYME (CAP) - PSUSA/00001830/202404

Applicant: Sanofi B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.1.33. Larotrectinib - VITRAKVI (CAP) - PSUSA/00010799/202405

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

16.1.34. Lonafarnib - ZOKINVY (CAP) - PSUSA/00011005/202405

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.35. Lumacaftor, ivacaftor - ORKAMBI (CAP) - PSUSA/00010455/202405

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.1.36. Luspatercept - REBLOZYL (CAP) - PSUSA/00010860/202406

Applicant: Bristol-Myers Squibb Pharma EEIG

[48] Intramuscular use

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

16.1.37. Maribavir - LIVTENCITY (CAP) - PSUSA/00011024/202405

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.38. Migalastat - GALAFOLD (CAP) - PSUSA/00010507/202405

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.39. Mosunetuzumab - LUNSUMIO (CAP) - PSUSA/00010999/202406

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.40. Nusinersen - SPINRAZA (CAP) - PSUSA/00010595/202405

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.1.41. Obeticholic acid - OCALIVA (CAP) - PSUSA/00010555/202405

Applicant: Advanz Pharma Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.42. Octreotide[49] - MYCAPSSA (CAP) - PSUSA/00011036/202406

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

[49] For centrally authorised products only

16.1.43. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - PSUSA/00010501/202405

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

16.1.44. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP) - PSUSA/00002281/202405

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.45. Pegzilarginase - LOARGYS (CAP) - PSUSA/00000222/202406

Applicant: Immedica Pharma AB

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.46. Pentosan polysulfate sodium[50] - ELMIRON (CAP) - PSUSA/00010614/202406

Applicant: bene-Arzneimittel GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.1.47. Pertuzumab - PERJETA (CAP) - PSUSA/00010125/202406

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.1.48. Pertuzumab, trastuzumab - PHESGO (CAP) - PSUSA/00010906/202406

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.49. Piflufolastat (^{18}F) - PYLCLARI (CAP) - PSUSA/00000097/202405

Applicant: Curium Pet France

PRAC Rapporteur: Kimmo Jaakkola

[50] For centrally authorised product

Scope: Evaluation of a PSUSA procedure

16.1.50. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - PREVENAR 20 (CAP) - PSUSA/00010981/202406

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.1.51. Polatuzumab vedotin - POLIVY (CAP) - PSUSA/00010817/202406

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.52. Quizartinib - VANFLYTA (CAP) - PSUSA/00000176/202406

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

16.1.53. Radium-223 dichloride - XOFIGO (CAP) - PSUSA/00010132/202405

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

16.1.54. Relugolix, estradiol, norethisterone acetate - RYEQO (CAP) - PSUSA/00010942/202405

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.55. Respiratory syncytial virus vaccine (bivalent, recombinant) - ABRYSVO (CAP) - PSUSA/00000102/202405

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.56. Rilpivirine[51] - EDURANT (CAP) - PSUSA/00009282/202405

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.57. Ritlecitinib - LITFULO (CAP) - PSUSA/00000133/202406

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.58. Rozanolixizumab - RYSTIGGO (CAP) - PSUSA/00000216/202406

Applicant: UCB Pharma

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

16.1.59. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - PSUSA/00010972/202406

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.60. Satralizumab[52] - ENSPRYNG (CAP) - PSUSA/00010944/202405

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.61. Setmelanotide - IMCIVREE (CAP) - PSUSA/00010941/202405

Applicant: Rhythm Pharmaceuticals Netherlands B.V.,

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

16.1.62. Sildenafil[53] - REVATIO (CAP) - PSUSA/00002700/202405

Applicant: Upjohn EESV

PRAC Rapporteur: Bianca Mulder

[51] For oral use only
[52] For centrally authorised products only
[53] Indicated for the treatment of pulmonary hypertension

Scope: Evaluation of a PSUSA procedure

16.1.63. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/202406

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

16.1.64. Tolvaptan[54] - SAMSCA (CAP) - PSUSA/00002994/202405

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.65. Tralokinumab - ADTRALZA (CAP) - PSUSA/00010937/202406

Applicant: LEO Pharma A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

16.1.66. Trametinib - MEKINIST (CAP); SPEXOTRAS (CAP) - PSUSA/00010262/202405

Applicant: Novartis Europharm Limited

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

16.1.67. Turoctocog alfa pegol - ESPEROCT (CAP) - PSUSA/00010782/202406

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.68. Vadadustat - VAFSEO (CAP) - PSUSA/00011050/202406

Applicant: Medice Arzneimittel Pütter GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

16.1.69. Vutrisiran - AMVUTTRA (CAP) - PSUSA/00011021/202406

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Liana Martirosyan

[54] Indicated for adults with hyponatraemia secondary to syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Scope: Evaluation of a PSUSA procedure

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

16.2.1. 5-aminolevulinic acid[55] - AMELUZ (CAP); NAP - PSUSA/00010006/202406

Applicant(s): Biofrontera Bioscience GmbH (Ameluz), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.2.2. Brinzolamide, timolol - AZARGA (CAP); NAP - PSUSA/00000433/202404

Applicant(s): Novartis Europharm Limited (Azarga), various

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.2.3. Linagliptin, metformin hydrochloride - JENTADUETO (CAP); linagliptin - TRAJENTA (CAP); NAP - PSUSA/00010427/202405

Applicant(s): Boehringer Ingelheim International GmbH (Jentadueto, Trajenta), various

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.2.4. Naloxone[56] - NYXOID (CAP); NAP - PSUSA/00010657/202405

Applicant(s): Mundipharma Corporation (Ireland) Limited (Nyxoid), various

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.2.5. Olopatadine - OPATANOL (CAP); NAP - PSUSA/00002211/202404

Applicant: Novartis Europharm Limited, various

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.2.6. Ulipristal[57] - ELLAONE (CAP); NAP - PSUSA/00003074/202405

Applicant(s): Laboratoire HRA Pharma (ellaOne), various

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

[55] For treatment of keratosis only
[56] For use in non-medical settings
[57] For female emergency contraception only

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

16.3.1. Acemetacin (NAP) - PSUSA/00000026/202405

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

16.3.2. Alginic acid, aluminium oxide hydrated, sodium hydrogen carbonate (NAP); alginic acid, aluminium hydroxide, calcium carbonate, sodium carbonate (NAP) - PSUSA/00000123/202406

Applicant(s): various

PRAC Lead: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

16.3.3. Biclotymol (NAP) - PSUSA/00000408/202405

Applicant(s): various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

16.3.4. Buspirone (NAP) - PSUSA/00000463/202404

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.3.5. Cefuroxime sodium[58] (NAP) - PSUSA/00010206/202405

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

16.3.6. Cidofovir (NAP) - PSUSA/00010558/202406

Applicant(s): various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

[58] For intracameral use only

16.3.7. Daunorubicin (NAP) - PSUSA/00000936/202406

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

16.3.8. Deoxycholic acid (NAP) - PSUSA/00010525/202404

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.3.9. Dienogest, estradiol[59] (NAP) - PSUSA/00010443/202406

Applicant(s): various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.3.10. Enalapril maleate, lercanidipine (NAP) - PSUSA/00001215/202406

Applicant(s): various

PRAC Lead: Carla Torre

Scope: Evaluation of a PSUSA procedure

16.3.11. Ferucarbotran (NAP) - PSUSA/00001382/202406

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.3.12. Flunarizine (NAP) - PSUSA/00001416/202405

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.3.13. Human hemin (NAP) - PSUSA/00001629/202405

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

[59] Hormone replacement therapy (HRT) indication(s) only

16.3.14. Hydrochlorothiazide, zofenopril (NAP) - PSUSA/00003148/202405

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.3.15. Indocyanine green (NAP) - PSUSA/00001737/202405

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.3.16. Iodine (^{131}i) iobenguane (NAP) - PSUSA/00001764/202405

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.3.17. Isoniazid, rifampicin (NAP) - PSUSA/00001792/202405

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.3.18. Loperamide (NAP); loperamide, simeticone (NAP) - PSUSA/00010665/202405

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.3.19. Loteprednol (NAP) - PSUSA/00001913/202405

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.3.20. Metyrapone (NAP) - PSUSA/00002046/202406

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

16.3.21. Olodaterol, tiotropium (NAP) - PSUSA/00010489/202405

Applicant(s): various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.3.22. Praziquantel (NAP) - PSUSA/00002503/202404

Applicant(s): various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

16.3.23. Ranitidine (NAP) - PSUSA/00002610/202405

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.3.24. Tafluprost (NAP) - PSUSA/00002843/202404

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.3.25. Terlipressin (NAP) - PSUSA/00002905/202404

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.3.26. Tolperisone (NAP) - PSUSA/00002991/202406

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

16.3.27. Yohimbine (NAP) - PSUSA/00003136/202405

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.4. Follow-up to PSUR/PSUSA procedures

None

16.5. Variation procedure(s) resulting from PSUSA evaluation

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

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

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

16.5.2. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/II/0026, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of section 4.8 of the SmPC in order to add 'granuloma' to the list of adverse drug reactions (ADRs) with frequency 'unknown', based on post marketing data; the Package Leaflet is updated accordingly

16.6. Expedited summary safety reviews[60]

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)[61]

17.1.1. Axicabtagene ciloleucel – YESCARTA (CAP) - EMEA/H/C/PSA/S/0118

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Karin Erneholm

Scope: Substantial amendment to a protocol for a long-term, non-interventional study of recipients of Yescarta for treatment of relapsed or refractory Diffuse Large B-cell Lymphoma and Primary Mediastinal B-cell Lymphoma

[60] 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

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

17.1.2. Ciltacabtagene autoleucel – CARVYKTI (CAP) - EMEA/H/C/PSA/S/0116

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: Substantial amendment to a PASS Study 68284528MMY4004 Protocol submission: An Observational Post-authorization Safety Study to Evaluate the Safety of Multiple Myeloma Patients Treated with Ciltacabtagene Autoleucel

17.1.3. Dinutuximab beta – QARZIBA (CAP) - EMEA/H/C/PSA/S/0117

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Substantial amendment to a patient registry of patients with high-risk neuroblastoma being treated with the monoclonal antibody dinutuximab beta to assess:

• Pain severity and use of analgesics during treatment

• Incidence of neurotoxicity, visual impairment, capillary leak syndrome, cardiovascular events and hypersensitivity reactions.

• Long term safety

17.1.4. Pegzilarginase – LOARGYS (CAP) - EMEA/H/C/PSP/S/0105.2

Applicant: Immedica Pharma AB

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/0105.1 [A European, non-interventional, multicentre, registry-based post-authorisation safety study to evaluate the long-term safety of Loargys treatment in arginase 1 deficiency patients in standard clinical care] as per the request for supplementary information (RSI) adopted in September 2024

17.1.5. Tofersen – QALSODY (CAP) - EMEA/H/C/PSP/S/0109

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: An observational registry-based study utilising data from two disease registry networks pecision ALS and ALS/MND NHC to evaluate the long-term safety of tofersen in people with SOD1-ALS

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[62]

17.2.1. Anifrolumab - SAPHNELO (CAP) - EMEA/H/C/004975/MEA 001.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Martirosyan

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

Scope: From Initial MAA:
Revised Protocol for PASS No. D3461R00028 (non-imposed)
Title: A multiple database study of the use (and safety) of anifrolumab in women with SLE during pregnancy

17.2.2. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 002.5

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: ***Revised Protocol / PS0038***- Version 3.0, amendment #3
Bimekizumab real-world outcomes study:
The goal of this study is to evaluate any potential increase in the risk of safety outcomes of interest in bimekizumab exposed PSO, PsA, AS or HS patients compared to PSO, PsA, AS or HS patients exposed to other biologics (eg, anti TNF, anti-IL-23, but not anti IL 17).
The PAM is fulfilled.

17.2.3. Capivasertib - TRUQAP (CAP) - EMEA/H/C/006017/MEA 001.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: From initial MAA
Protocol / Study D3612R00020 (CAPIseid)
A database study of the safety and effectiveness of TRUQAP (capivasertib) + fulvestrant in patients with advanced breast cancer and type 1 or type 2 diabetes. (NINI; RMP)

17.2.4. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/MEA 007.3

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: ***Protocol amendment / PASS study PCSONCA0014***(v. 1)
Post-authorization Safety Study Survey to Evaluate the Effectiveness of the Ciltacabtagene Autoleucel HCP Educational Program and the Product Handling Training

17.2.5. Deucravacitinib - SOTYKTU (CAP) - EMEA/H/C/005755/MEA 001.3

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: MAH Response to MEA 001.2 [Revised Protocol No. IM011194] as adopted in September 2024:
Long-term, observational cohort study of adults with plaque psoriasis, who are new users of deucravacitinib, non-TNFi (tumor necrosis factor inhibitor) biologics, TNFi biologics, or non-biologic systemic therapy in the real-world clinical setting (IM011194). To evaluate the long-term safety of deucravacitinib in patients with psoriasis in the real-world setting

17.2.6. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 006.7

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 006.6 [***REVISED PROTOCOL / H9X-MC-B013***] RSI as adopted in September 2024.

17.2.7. Enfortumab vedotin - PADCEV (CAP) - EMEA/H/C/005392/MEA 003.2

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: ***Updated Study Protocol / Study no.: 7465-PV-0002*** version 3.0
To evaluate patients understanding and awareness of the content of the patient card related to risks of skin reactions and patients behaviours to minimise the risks

17.2.8. Hydroxycarbamide - XROMI (CAP) - EMEA/H/C/004837/MEA 006.1

Applicant: Nova Laboratories Ireland Limited

PRAC Rapporteur: Jo Robays

Scope: MAH Response to MEA 006 [Study No. NOVVD-001]as adopted in September 2024:

17.2.9. Netarsudil - RHOKIINSA (CAP) - EMEA/H/C/004583/MEA 001.5

Applicant: Santen Oy

PRAC Rapporteur: Maria del Pilar Rayon

Scope: ***Updated Protocol / Study AR-13324-OBS02***
Non-interventional, observational post-authorisation safety study (PASS) cohort study to investigate the long-term safety of netarsudil beyond 12 months treatment

17.2.10. Pegcetacoplan - ASPAVELI (CAP) - EMEA/H/C/005553/MEA 002.2

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: ***Updated PASS Protocol / Study Sobi.PEGCET-301***
MAH's response to include the appropriate reference group, once the use of internal reference group from the IPIG registry has been further explored and agreed with the IPIG registry holder

17.2.11. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 009.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: ***Protocol Amendment / PASS study P23-653 v2.0***
Pregnancy Exposures and Outcomes in Women with Inflammatory Bowel Disease Treated

with Risankizumab.

17.2.12. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 010.4

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: ***Protocol Amendment / PASS study P23-654*** v3.0
Comparative Cohort Study of Long-term Safety Outcomes of Risankizumab Compared to Biologic Treatments for Ulcerative Colitis and Crohn's Disease in a Real-world Setting in Sweden and Denmark.

17.2.13. Spesolimab - SPEVIGO (CAP) - EMEA/H/C/005874/MEA 003.2

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: ***Updated PASS Protocol / Study no.: 1368-0128*** (version 2.0)
A 5-year active surveillance, post-authorisation safety study to characterise the safety of spesolimab for flare treatment in patients with GPP. Objectives: To evaluate the risks serious or opportunistic infections, systemic hypersensitivity reaction, malignancy, and peripheral neuropathy in adult patients (aged ≥18 years) experiencing a GPP flare who are treated with spesolimab or other treatments in the routine clinical care setting.
PROTOCOL

17.2.14. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/MEA 002.3

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: ***Revised Protocol*** and MAH's responses to MEA 002.2 [I8B-MC-B011] RSI as adopted in June 2024:

17.2.15. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/MEA 005.3

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: ***Revised Protocol*** and MAH's responses to MEA 005.2 [(IBF-MC-B014 (formerly IBF-MC-B013)] RSI adopted in June 2024:

17.2.16. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 047.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: ***MAH's responses and Updated Study Protocol – SWIBREG*** (Version 6.0) Amendment 2
An Observational Post-authorization Safety Study to Describe The Safety of Ustekinumab and Other Biologic Treatments in a Cohort of Patients With Ulcerative Colitis or Crohn's

Disease Using Compulsory Swedish Nationwide Healthcare Registers and the Independent Swedish National Quality Register for Inflammatory Bowel Disease.

17.3. Results of PASS imposed in the marketing authorisation(s)[63]

17.3.1. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSR/S/0051

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: Final study report for a non-interventional post-authorisation safety study to investigate the risk of mortality in multiple sclerosis patients treated with alemtuzumab (Lemtrada) relative to comparable multiple sclerosis patients using other disease modifying therapies: a cohort study

17.3.2. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSR/S/0049

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Final study report for a post-authorisation, non-interventional, retrospective, drug-utilisation study to describe the pattern of use of lenalidomide in patients with myelodysplastic syndromes (MDS)

17.4. Results of PASS non-imposed in the marketing authorisation(s)[64]

17.4.1. Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/MEA 002.6

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Linked to WS/2794:
Post-authorisation safety study to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents
FINAL STUDY REPORT / Study number: MK8835-062

17.4.2. Ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/MEA 002.6

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Linked to WS/2794:

Post-authorisation safety study to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with

[63] In accordance with Article 107p-q of Directive 2001/83/EC
[64] 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

other antihyperglycemic agents

FINAL STUDY REPORT / Study number: MK8835-062

17.4.3. Ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/WS2794/0026; Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/WS2794/0025; Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/WS2794/0029

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Submission of the final report from study 8835-062 listed as a category 3 study in the RMP for Steglatro, Steglujan and Segluromet. This is a non-interventional post-authorization safety study (PASS) to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents. The RMP version 2.3 have also been submitted

17.4.4. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/MEA 002.6

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Linked to WS/2794:

Post-authorisation safety study to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents.
FINAL STUDY REPORT / Study number: MK8835-062

17.4.5. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/II/0255

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to remove information regarding the Patient Card, based on final results from study B1801309 (BSR Register of Anti-TNF Treated Patients and Prospective Surveillance Study for Adverse Events: Enbrel). This is a non-interventional PASS study listed as a category 3 study in the RMP. The Annex II and Package Leaflet are updated accordingly. The RMP version 7.7 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial and formatting changes to the PI as well as to update the list of local representatives in the Package Leaflet and align the PI with the QRD version 10.4

17.4.6. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0045

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report from study 67896049PAH0002 (EXTRACT) and interim

report for study AC-065A401 (EXPOSURE), listed as a category 3 study in the RMP. EXTRACT is a Retrospective Medical Chart Review of Patients with PAH newly treated with either Uptravi (selexipag) or any other PAH-specific therapy. EXPOSURE is an observational cohort study of PAH patients newly treated with either Uptravi (selexipag) or any other PAH-specific therapy, in clinical practice

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

17.5.1. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 007

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: From RMP:
Interim Study Report / Study AS0014
Title: A multicenter, open-label extension study to assess the long-term safety, tolerability, and efficacy of bimekizumab in the treatment of study participants with active axial spondyloarthritis, ankylosing spondylitis, and nonradiographic axial spondyloarthritis.

17.5.2. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 002.5

Applicant: Merck Europe B.V.

PRAC Rapporteur: Carla Torre

Scope: From Initial MAA:
Study MS 700568-0002:
Long-term PASS (categ. 3 study) - prospective, observational cohort study evaluating the safety profile, in terms of incidence of adverse events of special interest, in patients with highly active relapsing multiple sclerosis (RMS) newly started on oral cladribine.
Second Interim Study Report, Study MS 700568-0002

17.5.3. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 006.4

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: From Initial MAA:
Study 2019nCoV-404:
US Post-authorisation safety study to evaluate the pooled of risk of selected AESI within specified time periods after vaccination with Nuvaxovid using a claim and/or EHR database.
Second Interim Report, Study 2019nCoV-404

17.5.4. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/ANX 001.4

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: ***THIRD INTERIM REPORT***

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' (HA-SAFE). The HA-SAFE study is a post-authorisation measure defined in Annex II.D of the Jivi EU PI.The study protocol was agreed with EMA/PRAC in Nov 2019 (outcome letter); the date of FPFV was 14 May 2021 (impacted by the Covid-19 pandemic). As Annex to the first interim report also the statistical analysis plan is submitted

17.5.5. Difelikefalin - KAPRUVIA (CAP) - EMEA/H/C/005612/MEA 002.2

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: From initial MAA RMP Category 3
Study CR845- 310301
A Multicenter, Randomized, Double-blind, Placebo-controlled 12-Week Study to Evaluate the Safety and Efficacy of Oral Difelikefalin in Advanced Chronic Kidney Disease Subjects With Moderate-to-Severe Pruritus and Not on Dialysis With an up to 52-Week Long-term Extension
INTERIM REPORT

17.5.6. Difelikefalin - KAPRUVIA (CAP) - EMEA/H/C/005612/MEA 003.2

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: From initial MAA RMP Category 3
Study CR845- 310302
A Multicenter, Randomized, Double-blind, Placebo-controlled 12-Week Study to Evaluate the Safety and Efficacy of Oral Difelikefalin in Advanced Chronic Kidney Disease Subjects With Moderate-to-Severe Pruritus and Not on Dialysis With an up to 52-Week Long-term Extension
INTERIM REPORT

17.5.7. Difelikefalin - KAPRUVIA (CAP) - EMEA/H/C/005612/MEA 004.2

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: From initial MAA RMP Category 3
Study CR845- 310501
A Two-part, Multicenter, Randomized, Double-blind Study to Evaluate the Efficacy and Safety of Oral Difelikefalin as Adjunct Therapy to a Topical Corticosteroid for Moderate-to-Severe Pruritus in Adult Subjects With Atopic Dermatitis
INTERIM REPORT

17.5.8. Diroximel fumarate - VUMERITY (CAP) - EMEA/H/C/005437/MEA 002.4

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH Response to MEA 002.3 [***Annual Progress Report / Study 272MS403***] as adopted in July 2024. In addition, a proposal is made to terminate Study 272MS403.
Title: An observational study utilising data from big MS data registries to evaluate the long-term safety of Vumerity and Tecfidera.

17.5.9. Drospirenone, estetrol - DROVELIS (CAP) - EMEA/H/C/005336/MEA 001.5

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: MAH Response to MEA 001.4 [PASS No. INAS-NEES] RSI as adopted in September 2024.

17.5.10. Drospirenone, estetrol - LYDISILKA (CAP) - EMEA/H/C/005382/MEA 001.5

Applicant: Estetra SRL

PRAC Rapporteur: Martin Huber

Scope: MAH Response to MEA 001.4 [PASS No. INAS-NEES] RSI as adopted in September 2024:

17.5.11. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 066.4

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Study mRNA-1273-P911 Long-term outcomes of myocarditis following administration of Spikevax (COVID-19 vaccine mRNA).
Third Interim Report, study P911 and updated Protocols and SAP for study mRNA-1273-P911

17.5.12. Etanercept - NEPEXTO (CAP) - EMEA/H/C/004711/MEA 001.2

Applicant: Biosimilar Collaborations Ireland Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: The MAH is asked to provide subsequent biannual interim reports until final study reports are available.
*** First Biannual Interim Report***

17.5.13. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 002.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: ***Fourth annual progress report / Study I5Q-MC-B003***
Observational Cohort Study of Exposure to Galcanezumab during Pregnancy. From 28 September 2018 through 31 March 2024.

17.5.14. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 003.3

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: ***Annual progress report / Study I5Q-MC-B002***
A retrospective cohort study to assess drug utilisation and long-term safety of galcanezumab in European patients in the course of routine clinical care.

17.5.15. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 004.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: ***Third Annual Progress Report / Study I5Q-MC-B001***
A Cohort Study to Assess Drug Utilisation and Long-Term Safety of Galcanezumab in US Patients in the Course of Routine Clinical Care.
Galcanezumab US Drug Utilization and Safety Outcomes Study (Planned).
- To describe, in real-world clinical practice, the utilization of galcanezumab in the US, and the incidence of important safety outcomes such as serious hypersensitivity and long-term safety including serious cardiovascular events, and malignancies. Another objective is to understand the risk of specified safety events in patients receiving galcanezumab relative to adult patients who initiated treatment with another prophylactic migraine medication.

17.5.16. Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/ANX 002.12

Applicant: HRA Pharma Rare Diseases

PRAC Rapporteur: Petar Mas

Scope: ***Seventh Annual Interim Report***
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

17.5.17. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/MEA 003.4

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Prospective Registry-Based Study of the Long-Term Safety of Odevixibat in Subjects with Progressive Familial Intrahepatic Cholestasis (PFIC). (First Annual Report Version 1.0)
FIRST INTERIM REPORT / Study Number: A4250-019

17.5.18. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 003.7

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: ***Fourth Interim study report*** / Study no.: 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.

17.5.19. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[65]) - EMEA/H/W/002300/MEA 015.2

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's responses to questions related to MEA 015.1 [Statistical Analysis Plan (SAP) and Interim Report / Study EPI-MAL-010] as adopted in April 2024.
A phase IV, longitudinal, cross-sectional, retrospective, ancillary epidemiology study of the EPI-MAL-005 study to evaluate the genetic diversity in the Plasmodium falciparum parasite circumsporozoite sequences before and after the implementation of the RTS,S/AS01E vaccine in malaria-positive subjects ranging from 6 months to less than 5 years of age.

17.5.20. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 005.9

Applicant: Teva B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to MEA 005.8 [Study number C38072-AS-50027] RSI as adopted in September 2024.
Assessment of Potential Risk of Malignancy in Patients with Severe Asthma Treated with Reslizumab: A cohort Study using Secondary Administrative Healthcare Data.

17.5.21. Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/MEA 007.5

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: From Initial MAA:
Study BN42833 (Risdiplam Pregnancy Surveillance Study):
A Phase IV, non-interventional surveillance study.
Third Interim Progress Report

17.5.22. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/MEA 049.5

Applicant: Bayer AG

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

PRAC Rapporteur: Mari Thorn

Scope: Xarelto Paediatric VTE PASS Drug Utilization Study: An observational, longitudinal, multi-source drug utilization safety study to evaluate the drug use patterns and safety of rivaroxaban oral suspension in children under two years with venous thromboembolism (XAPAEDUS)".
Second Progress Report

17.5.23. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 024.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: An Active Surveillance, Post-Authorization Study to Characterize the Safety of Tofacitinib in Patients with Moderately to Severely Active Ulcerative Colitis in the Real-World Setting Using Data from a US Administrative Healthcare Claims Database.
Second Interim Study Result; Updated Protocol with responses / PASS Study A3921347

17.5.24. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 016.3

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: ***First Annual Progress Report / PASS study P24-344***
Title: Drug Utilization Study for Evaluation of the Effectiveness of Additional Risk Minimisation Measures for Upadacitinib in the Treatment of Ulcerative Colitis in Sweden and Denmark.

17.5.25. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 048.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: ***SECOND PROGRESS REPORT and SAP*** including a response document and updated study protocol to address the limitations as identified in the Assessment Report for MEA 048.4.
An observational post-authorisation safety study (PASS) to describe the safety of ustekinumab and other ulcerative colitis treatments in a cohort of patients with ulcerative colitis using SNDS PCSIMM002659.

17.6. Others

17.6.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.18

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: ***Feasibility assessment / Study (PASS) OBS13434***
Submission a feasibility assessment of study A prospective, multicenter, observational, post-authorization safety study (PASS) to evaluate the long-term safety profile of

LEMTRADA (alemtuzumab) treatment in patients with relapsing forms of multiple sclerosis (RMS)

17.7. 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.

17.8. Ongoing Scientific Advice

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

17.9. 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) - EMEA/H/C/005271/S/0012 (without RMP)

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.1.2. Metreleptin - MYALEPTA (CAP) - EMEA/H/C/004218/S/0039 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.1.3. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/S/0023 (without RMP)

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/R/0049 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

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

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Conditional renewal of the marketing authorisation

18.2.3. Lorlatinib - LORVIQUA (CAP) - EMEA/H/C/004646/R/0040 (with RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Conditional renewal of the marketing authorisation

18.2.4. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) - EMEA/H/C/003963/R/0074 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: Conditional renewal of the marketing authorisation

18.2.5. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted, prepared in cell cultures) - INCELLIPAN (CAP) - EMEA/H/C/006051/R/0002 (without RMP)

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.2.6. Volanesorsen - WAYLIVRA (CAP) - EMEA/H/C/004538/R/0029 (without RMP)

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. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/R/0050 (with RMP)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: 5-year renewal of the marketing authorisation

18.3.2. Caffeine citrate - GENCEBOK (CAP) - EMEA/H/C/005435/R/0012 (without RMP)

Applicant: Gennisium Pharma

PRAC Rapporteur: Sonja Hrabcik

Scope: 5-year renewal of the marketing authorisation

18.3.3. Ebola vaccine (rDNA, replication-incompetent) - MVABEA (CAP) - EMEA/H/C/005343/R/0023 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

18.3.4. Ebola vaccine (rDNA, replication-incompetent) - ZABDENO (CAP) - EMEA/H/C/005337/R/0022 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

18.3.5. Fingolimod - FINGOLIMOD ACCORD (CAP) - EMEA/H/C/005191/R/0011 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.6. Glasdegib - DAURISMO (CAP) - EMEA/H/C/004878/R/0015 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

18.3.9. Insulin aspart - INSULIN ASPART SANOFI (CAP) - EMEA/H/C/005033/R/0020 (without RMP)

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.10. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/R/0059 (without RMP)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

18.3.12. Paliperidone - BYANNLI (CAP) - EMEA/H/C/005486/R/0008 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Karin Bolin

Scope: 5-year renewal of the marketing authorisation

18.3.13. Teriparatide - LIVOGIVA (CAP) - EMEA/H/C/005087/R/0015 (with RMP)

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.14. Trastuzumab - ZERCEPAC (CAP) - EMEA/H/C/005209/R/0039 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Gabriele Maurer

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 13-16 January PRAC meeting, which was held remotely.

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

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Kimmo Jaakkola	Alternate	Finland	No interests declared	
Tiphaine Vaillant	Member	France	No interests declared	
Zoubida Amimour	Alternate	France	No participation in discussion, final deliberations and voting on:	4.2.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/026; Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/SDA/012; Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/SDA/013; Dostarlimab - JEMPERLI (CAP) - EMEA/H/C/005204/SDA/007; Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/SDA/013; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/SDA/049; Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/SDA/058; Nivolumab, relatlimab - OPDUALAG (CAP) - EMEA/H/C/005481/SDA/007; Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/042; Retifanlimab - ZYNYZ (CAP) - EMEA/H/C/006

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				194/SDA/002; Tislelizumab - TEVIMBRA (CAP) - EMEA/H/C/005919/SDA/004; Tremelimumab - IMJUDO (CAP) - EMEA/H/C/006016/SDA/004 6.1.1. Apixaban - ELIQUIS (CAP) - PSUSA/00000226/202405 6.1.3. Azacitidine - ONUREG (CAP) - PSUSA/00010935/202405 6.1.11. Ozanimod - ZEPOSIA (CAP) - PSUSA/00010852/202405 15.3.19. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2717/0146; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2717/0115 15.3.22. Lisocabtagene maraleucel, lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/II/0043 /G

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				15.3.26. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/X/0144 16.1.2. Adagrasib - KRAZATI (CAP) - PSUSA/00000214/202406 16.1.7. Azacitidine - VIDAZA (CAP) - PSUSA/00000274/202405 16.1.36. Luspatercept - REBLOZYL (CAP) - PSUSA/00010860/202406 17.2.5. Deucravacitinib - SOTYKTU (CAP) - EMEA/H/C/005755/MEA 001.3 17.3.2. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSR/S/0049 18.3.11. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/R/0028 (without RMP)
Gabriele Maurer	Alternate	Germany	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Georgia Gkegka	Member	Greece	No interests declared	
Maria Poulianiti	Alternate	Greece	No restrictions applicable to this meeting	
Julia Pallos	Member	Hungary	No participation in discussion, final deliberations and voting on:	4.2.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/026; Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/SDA/012; Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/SDA/013; Dostarlimab - JEMPERLI (CAP) - EMEA/H/C/005204/SDA/007; Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/SDA/013; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/SDA/049; Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/SDA/058; Nivolumab, relatlimab - OPDUALAG (CAP) - EMEA/H/C/005481/SDA/007; Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/042; Retifanlimab -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				ZYNYZ (CAP) - EMEA/H/C/006194/SDA/002; Tislelizumab - TEVIMBRA (CAP) - EMEA/H/C/005919/SDA/004; Tremelimumab - IMJUDO (CAP) - EMEA/H/C/006016/SDA/004 6.1.1. Apixaban - ELIQUIS (CAP) - PSUSA/00000226/202405 6.1.3. Azacitidine - ONUREG (CAP) - PSUSA/00010935/202405 6.1.11. Ozanimod - ZEPOSIA (CAP) - PSUSA/00010852/202405 15.3.19. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2717/0146; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2717/0115 15.3.22. Lisocabtagene maraleucel, lisocabtagene maraleucel - BREYANZI

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				(CAP) - EMEA/H/C/004731/II/0043 /G 15.3.26. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/X/0144 16.1.2. Adagrasib - KRAZATI (CAP) - PSUSA/00000214/202406 16.1.7. Azacitidine - VIDAZA (CAP) - PSUSA/00000274/202405 16.1.36. Luspatercept - REBLOZYL (CAP) - PSUSA/00010860/202406 17.2.5. Deucravacitinib - SOTYKTU (CAP) - EMEA/H/C/005755/MEA 001.3 17.3.2. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSR/S/0049 18.3.11. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/R/0028 (without RMP)
Rhea Fitzgerald	Member	Ireland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Eamon O'Murchu	Alternate	Ireland	No interests declared	
Amelia Cupelli	Member	Italy	No interests declared	
Emilio Clementi	Alternate	Italy	No interests declared	
Zane Neikena	Member	Latvia	No interests declared	
Diana Litenboka	Alternate	Latvia	No interests declared	
Rugile Pilviniene	Member	Lithuania	No interests declared	
Lina Seibokiene	Alternate	Lithuania	No restrictions applicable to this meeting	
Nadine Petitpain	Member	Luxembourg	No restrictions applicable to this meeting	
John Joseph Borg	Member	Malta	No interests declared	
Liana Martirosyan	Member	Netherlands	No interests declared	
Bianca Mulder	Alternate	Netherlands	No interests declared	
David Olsen	Member	Norway	No participation in discussion, final deliberations and voting on:	15.3.7. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/II/0034 15.3.8. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/X/0033/G 15.3.11. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0024 16.1.33.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				Larotrectinib - VITRAKVI (CAP) - PSUSA/00010799/202405 16.1.53. Radium-223 dichloride - XOFIGO (CAP) - PSUSA/00010132/202405 16.3.9. Dienogest, estradiol (NAP) - PSUSA/00010443/202406 16.3.22. Praziquantel (NAP) - PSUSA/00002503/202404 17.5.4. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/ANX 001.4 17.5.22. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/MEA 049.5
Pernille Harg	Alternate	Norway	No interests declared	
Adam Przybylkowski	Member	Poland	No interests declared	
Katarzyna Ziolkowska	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins	Member	Portugal	No interests declared	
Carla Torre	Alternate	Portugal	No interests declared	
Roxana Dondera	Member	Romania	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Irina Sandu	Alternate	Romania	No interests declared	
Anna Mareková	Member	Slovakia	No interests declared	
Miroslava Gocova	Alternate	Slovakia	No interests declared	
Polona Golmajer	Member	Slovenia	No interests declared	
Monica Martinez Redondo	Alternate	Spain	No interests declared	
Mari Thorn	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin	Alternate	Sweden	No interests declared	
Annalisa Capuano	Member	Independent scientific expert	No interests declared	
Milou-Daniel Drici	Member	Independent scientific expert	No interests declared	
Maria Teresa Herdeiro	Member	Independent scientific expert	No interests declared	
Patricia McGettigan	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark	Member	Independent scientific expert	No interests declared	
Hedvig Marie Egeland Nordeng	Member	Independent scientific expert	No interests declared	
Roberto Frontini	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Salvatore Antonio Giuseppe Messana	Alternate	Healthcare Professionals' Representative	No interests declared	
Marko Korenjak	Member	Patients' Organisation Representative	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Michal Rataj	Alternate	Patients' Organisation Representative	No interests declared	
Flora Musuamba Tshinanu	Expert	Belgium	No restrictions applicable to this meeting	
Maja Puklek	Expert	Croatia	No interests declared	
Zvjezdana Rehorovic	Expert	Croatia	No restrictions applicable to this meeting	
Nicklas Hasselblad Lundstrøm	Expert	Denmark	No interests declared	
Frederikke Hillebrand Laustsen	Expert	Denmark	No restrictions applicable to this meeting	
Kristina Laursen	Expert	Denmark	No interests declared	
Aynur Sert	Expert	Denmark	No interests declared	
Dennis Lex	Expert	Germany	No interests declared	
Anne-Catherine Redeker	Expert	Germany	No interests declared	
Laura Zein	Expert	Germany	No interests declared	
Aine McKenna	Expert	Ireland	No interests declared	
Magdalena Wielowieyska	Expert	Luxembourg	No restrictions applicable to this meeting	
Talip Eroglu	Expert	Netherlands	No interests declared	
Dennis van Eijl	Expert	Netherlands	No interests declared	
Lucia Kuráková	Expert	Slovakia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Maria Martínez	Expert	Spain	No interests declared	
Charlotte Backman	Expert	Sweden	No interests declared	
Kristina Magnusson-Lundqvist	Expert	Sweden	No interests declared	
Karin Nylén	Expert	Sweden	No interests declared	
Representatives from the European Commission attended the meeting.				
Observers from Health Canada (Canada) and WHO attended the meeting.				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a comprehensive knowledge of a medicine's benefits and risks.
The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the

patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.
The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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