10 December 2024
EMA/PRAC/532125/2024
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 30 September - 03 October 2024

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).

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Table of contents

1. Introduction

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

The Chair opened the meeting by welcoming all participants. The meeting was held 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).

1.2. Agenda of the meeting on 30 September – 03 October 2024

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 02 – 05 September 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 02 – 05 September 2024 were published on the EMA website on 28 October 2024 (EMA/PRAC/468455/2024).

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

3.1.1. Dutasteride (NAP); dutasteride, tamsulosin (NAP); finasteride (NAP); finasteride, tadalafil (NAP); finasteride, tamsulosin (NAP) – EMEA/H/A-31/1539

Applicant(s): various

PRAC Rapporteur: Jana Lukačišinová; PRAC Co-rapporteur: Martin Huber

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

Background

Finasteride and dutasteride belong to the class of 5α-reductase inhibitors (5-ARIs). In the EU, finasteride is indicated at different strengths for the treatment of the early stages of androgenic alopecia in men aged 18 to 41 years, for the treatment and control of benign prostatic hyperplasia (BPH) as well as for the prevention of urologic events. Dutasteride is indicated for the symptomatic treatment of BPH and the reduction in the risk of acute urinary retention (AUR) and surgery in patients with moderate to severe symptoms of BPH.

The French Medicines Agency (ANSM) sent a letter of notification dated 13 September 2024 triggering a referral under Article 31 of Directive 2001/83/EC for the review of finasteride- and dutasteride-containing products following concerns regarding suicidal ideation and suicide.

Considering the above, ANSM referred the matter to PRAC in the interest of the Union for further evaluation, requesting the Committee to assess the impact of the above concerns on the benefit-risk balance of finasteride- or dutasteride-containing products and to give its recommendation as to whether the marketing authorisation(s) for these medicinal products should be maintained, varied, suspended or revoked across the EU.

Discussion

PRAC noted the notification letter from the ANSM.

PRAC appointed Jana Lukačišinová as Rapporteur and Martin Huber as Co-Rapporteur for the procedure.

PRAC discussed the lists of questions (LoQ) to be addressed during the procedure together with a timetable for conducting the review. PRAC also discussed the need for a public hearing.

Summary of recommendation(s)/conclusions

- The Committee adopted a LoQ to the MAHs (EMA/PRAC/414467/2024) and a timetable for the procedure (EMA/PRAC/414468/2024).

- PRAC discussed the option to conduct a public hearing in the context of the current procedure according to the pre-defined criteria set out in the rules of procedure (EMA/11523/2023 Rev.2). It was agreed by the Committee that at this stage in the assessment, in light of the currently available data and the need to determine the suitable approach to stakeholder engagement, a public hearing would not be appropriate. PRAC can reconsider this at a later stage of the procedure as needed.
- PRAC supported the possibility to conduct a study via the DARWIN EU framework and to explore its feasibility.

See the EMA press release (EMA/452263/2024) entitled 'EMA starts safety review of medicines containing finasteride and dutasteride'.

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

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

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

See Annex I 14.1.

4.2. Signals follow-up and prioritisation

4.2.1. Eptinezumab - VYEPTI (CAP) - EMEA/H/C/005287/SDA/007; Erenumab - AIMOVIG (CAP) - EMEA/H/C/004447/SDA/006; Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/SDA/009; Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/SDA/006

Applicant: Eli Lilly Nederland B.V. (Emgality), H. Lundbeck A/S (Vyepti), Novartis

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

Europharm Limited (Aimovig), TEVA GmbH (Ajovy)

PRAC Rapporteur: Terhi Lehtinen

Scope: Signal of erectile dysfunction

EPITT 20074 – Follow-up to May 2024

Background

For background information, see the PRAC minutes May 2024.

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

Discussion

Having considered the available data in EudraVigilance, the literature and the responses of the MAHs, PRAC has concluded that the current evidence is insufficient to establish a causal relationship between galcanezumab, erenumab, fremanezumab or eptinezumab and erectile dysfunction to warrant an update to the product information and/or risk management plan at present.

Summary of recommendation(s)

- The MAHs of Emgality (galcanezumab), Aimovig (erenumab), Ajovy (fremanezumab) and Vyepti (eptinezumab) should continue to monitor cases of erectile dysfunction as part of routine pharmacovigilance.

4.3. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

5.1.1. Beremagene geperpavec (CAP MAA) - EMEA/H/C/006330, PRIME, Orphan

Applicant: Krystal Biotech Netherlands B.V., ATMP

Scope (pre D-180 phase): Treatment of patients from birth with dystrophic epidermolysis bullosa (DEB) with mutation(s) in the collagen type VII alpha 1 chain (COL7A1) gene

5.1.2. Chikungunya virus virus-like particle (CAP MAA) - EMEA/H/C/005470, PRIME, Article 28

Scope (accelerated assessment): Prevention of disease caused by chikungunya (CHIKV) virus

5.1.3. Clascoterone (CAP MAA) - EMEA/H/C/006138

Scope (pre D-180 phase): Indicated for the topical treatment of acne vulgaris in adults and adolescents

5.1.4. Delandistrogene moxeparvovec (CAP MAA) - EMEA/H/C/005293, Orphan

Applicant: Roche Registration GmbH, ATMP

Scope (pre D-120 phase): Treatment of ambulatory patients aged 3 to 7 years old with Duchenne muscular dystrophy

5.1.5. Dorocubicel, Allogeneic umbilical cord-derived CD34- cells, non-expanded (CAP MAA) - EMEA/H/C/005772, PRIME, Orphan

Applicant: Cordex Biologics International Limited, ATMP

Scope (accelerated assessment): Treatment of adult patients with haematological malignancies

5.1.6. Imetelstat (CAP MAA) - EMEA/H/C/006105, Orphan

Applicant: Geron Netherlands B.V.

Scope (pre D-180 phase): For the treatment of transfusion-dependent anaemia in adults with low- to intermediate-1 risk myelodysplastic syndromes (MDS), for the treatment of transfusion-dependent anaemia in adults with low- to intermediate-1 risk myelodysplastic syndromes (MDS)

5.1.7. Ivermectin, albendazole (Art 58[3] MAA) - EMEA/H/W/005186

Scope (pre D-180 phase): Prevention and treatment of lymphatic filariasis, and soil-transmitted helminths infections

5.1.8. Linvoseltamab (CAP MAA) - EMEA/H/C/006370

Scope (pre D-180 phase): Monotherapy for the treatment of adult patients with relapsed or refractory multiple myeloma

5.1.9. Nemolizumab (CAP MAA) - EMEA/H/C/006149

Scope (pre D-180 phase): For the treatment of moderate-to-severe atopic dermatitis and for the treatment of prurigo nodularis

[3] 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)

5.1.10. Seladelpar lysine dihydrate (CAP MAA) - EMEA/H/C/004692, PRIME, Orphan

Applicant: CymaBay Ireland, Ltd

Scope (pre D-180 phase): Treatment of primary biliary cholangitis (PBC) including pruritus in adults without cirrhosis or with compensated cirrhosis (Child-Pugh A) in combination with ursodeoxycholic acid (UDCA) who have an inadequate response to UDCA alone, or as monotherapy in those unable to tolerate UDCA

5.1.11. Tiratricol (CAP MAA) - EMEA/H/C/005220, Orphan

Applicant: Rare Thyroid Therapeutics International ABScope (pre D-180 phase): Treatment of monocarboxylate transporter 8 (MCT8) deficiency

5.1.12. Tisotumab vedotin (CAP MAA) - EMEA/H/C/005363

Scope (pre D-180 phase): Treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after systemic therapy

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

See Annex I 15.2.

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

See also Annex I 15.3.

5.3.1. Levetiracetam - KEPPRA (CAP); NAP - EMEA/H/C/000277/WS2529/0200

Applicant(s): UCB Pharma S.A.

PRAC Rapporteur: Jo Robays

Scope: Type II - B.IV.1.a.3 - To replace the CE marked oral dosing syringes and press-in bottle adaptor used in the Keppra 100 mg/ml oral solution (EU/1/00/146/027, 031, 032) with dosing syringes and press-in bottle adaptor from a new manufacturer. The 3 ml oral dosing syringe used in the Keppra 100 mg/ml oral solution (EU/1/00/146/031) is replaced with a 5 ml oral dosing syringe. An updated RMP version 10.0 and a DHPC are proposed. In addition, the Applicant has taken the opportunity to include the change in the local representatives of the Marketing Authorisation Holder in Estonia, Latvia, and Lithuania

Background

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

CHMP is evaluating a work sharing procedure containing a type II variation for Keppra (levetiracetam) a centrally authorised product, and nationally authorised products containing levetiracetam of the same MAH, to replace the CE marked oral dosing syringes and press-in bottle adaptor. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure. For further background, see the PRAC minutes July 2024.

Summary of advice

- The RMP for Keppra (levetiracetam) and for the levetiracetam-containing medicinal products in the context of this work sharing procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 10.2 is submitted.
- PRAC considered that the risk of medication error following the switch from a 3ml oral syringe to a 5ml oral syringe with the levetiracetam oral solution intended for children aged 6-48 months was low, temporary, and insufficiently significant to include a new important potential risk in the RMP and thus all parts of the RMP should be updated to remove the information relating to this safety concern. PRAC highlighted that the recommendation regarding the proposed temporary modifications of the packaging/labelling to warn about the new dosing device, lies with CHMP. In case CHMP will approve the temporary related modifications on the packaging/labelling, PRAC recommended that the modified packaging/labelling should only be implemented during the period where both presentations of the levetiracetam oral solution are available in a member state (MS). Furthermore, PRAC considered that routine pharmacovigilance was considered sufficient to mitigate the risk and thus the MAH(s) should not submit any specific document after 12 months, assessing the reports of medication errors relating to confusion between the original 3ml and new 5ml syringes. Finally, PRAC agreed that a DHPC alerting healthcare professionals on the switch of the syringe is needed but proposed further modification of the DHPC content, and highlighted that the decision to the DHPC distribution should be taken at national level, as the concerned presentation of the oral solution is not commercially available in some MSs.

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 16.2.

6.1.1. Agomelatine - VALDOXAN (CAP) - PSUSA/00000071/202402

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Pernille Harg

Scope: Evaluation of a PSUSA procedure

Background

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

- Nevertheless, in light of the measures to prevent hepatotoxicity implemented in clinical guidelines/practice and product information, along with the contraindication related to the concomitant use of potent CYP1A2 inhibitors stated in the product information, and considering the declining incidence of cases associated with this contraindication, Annex II-D should be updated to remove the additional risk minimisation measures (physician's guide and patient booklet). Therefore, the current terms of the marketing authorisation(s) should be varied.

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.

6.1.2. Cabotegravir[4] - APRETUDE (CAP) - PSUSA/00000116/202403

Applicant: ViiV Healthcare B.V.

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 Apretude, a centrally authorised medicine containing cabotegravir 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 Apretude (cabotegravir) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include Stevens-Johnsons syndrome/toxic epidermal necrolysis (SJS/TEN) as undesirable effects with a frequency 'very rare' and a warning regarding severe cutaneous adverse reactions (SCARs). In addition, the product information should be updated to add gait disturbance (as a consequence of injection site reactions) as an undesirable effect with a frequency 'rare'. Therefore, the current terms of the marketing authorisation(s) should be varied[5].
- In the next PSUR, the MAH should provide reviews of cases of psychosis, mood disorders, rhabdomyolysis, seizure and SCARs.

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. Cabotegravir[6]- VOCABRIA (CAP) - PSUSA/00010900/202403

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

[4] Indicated for pre-exposure prophylaxis of HIV-1 infection
[5] 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] Indicated for treatment of human immunodeficiency virus type 1 (HIV-1))

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Vocabria, a centrally authorised medicine containing cabotegravir 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 Vocabria (cabotegravir) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include Stevens-Johnsons syndrome/toxic epidermal necrolysis (SJS/TEN) as undesirable effects with a frequency 'very rare' and a warning regarding severe cutaneous adverse reactions (SCARs). In addition, the product information should be updated to add gait disturbance (as a consequence of injection site reactions) as an undesirable effect with a frequency 'rare'. Therefore, the current terms of the marketing authorisation(s) should be varied[7].
- In the next PSUR, the MAH should provide reviews of cases of weight gain, sleep disorders, anxiety, completed suicide, bipolar disorder, psychosis, mood disorders, injection site reactions, rhabdomyolysis, seizure, hyperglycaemia, SCARs, myocardial infarction.

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

6.1.4. COVID-19 vaccine (Ad26.COV2-S [recombinant]) - JCOVDEN (CAP)8 - PSUSA/00010916/202402

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Mari Thörn

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Jcovden, a centrally authorised medicine containing COVID-19 vaccine (Ad26.COV2-S [recombinant]).

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, PRAC is of the view that the reported data does not warrant an update to the product information.
- The MAH should present the safety data gathered from the DLP of this PSUR (24th February 2024) up to the expiry date in end of September 2024 in an ad-hoc PSUR to be assessed by PRAC. This should be submitted before the end of 2024.

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

[8] European Commission decision for withdrawal of marketing authorisation for Jcovden (COVID-19 Vaccine Janssen (Ad26.COV2.S)) in the European Union (EU) is dated 26 July 2024. The withdrawal was at the request of the marketing authorisation holder, Janssen-Cilag International N.V., which notified the European Commission of its decision to permanently discontinue the marketing of the product for commercial reasons.

- However, no PRAC recommendation was adopted due to the withdrawal of the marketing authorisation of Jcovden (COVID-19 vaccine (Ad26.COV2-S [recombinant)])).

6.1.5. Epcoritamab - TEPKINLY (CAP) - PSUSA/00000107/202403

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tepkinly, a centrally authorised medicine containing epcoritamab 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 Tepkinly (epcoritamab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include progressive multifocal leukoencephalopathy (PML) as a warning. Additionally, the product information should be updated to add the frequency of 'uncommon' to the previously added Grade 3-4 immune effector cell-associated neurotoxicity syndrome (ICANS) and to update the influence of epcoritamab on the ability to drive and use machines due to symptoms related to ICANS from minor influence to major influence. Therefore, the current terms of the marketing authorisation(s) should be varied[9].

- In the next PSUR, the MAH should provide a cumulative review of cases related to streptococcal infections and cytomegalovirus infections. Additionally, the MAH should provide cumulative reviews of cases of Guillain-Barré syndrome and of hemophagocytic lymphohistiocytosis (HLH), including data from clinical trials, post-marketing and literature. Regarding further monitoring of cases of ICANS, the MAH should assess the clinical symptoms reported and discuss whether they correspond with the description included in the PI and propose any amendments to the PI, if warranted. Based on the data, the MAH should also provide a discussion on whether epcoritamab should be permanently discontinued or treatment should be withheld, in case of Grade 3 ICANS. In addition, the MAH should further discuss cases of serious infections with fatal outcome.

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

6.1.6. Esketamine[10] - SPRAVATO (CAP) - PSUSA/00010825/202403

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

[9] Update of SmPC sections 4.4, 4.7 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[10] For centrally authorised product only

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Spravato, a centrally authorised medicine containing esketamine 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 Spravato (esketamine) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include bradycardia and seizure with a frequency 'uncommon' and 'rare', respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[11].
- In the next PSUR, the MAH should provide a review of data regarding use in pregnancy/lactation.

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

6.1.7. Gadopiclenol - ELUCIREM (CAP); VUEWAY (CAP) - PSUSA/00000232/202403

Applicant: Guerbet (Elucirem), Bracco Imaging S.p.A. (Vueway)

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 Elucirem and Vueway, centrally authorised medicines containing gadopiclenol and issued a recommendation on their marketing authorisation(s).

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Elucirem and Vueway (gadopiclenol) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing wording regarding data from use of gadopiclenol in pregnant women and anticipated effects on the infant. Additionally, the product information should be updated to add a warning against intrathecal administration of gadopiclenol. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAHs should provide a cumulative review of cases of acute pancreatitis, including data from post-marketing setting and literature and discuss whether there is a need to update the product information. Moreover, the MAH should provide an overview of the implementation of the targeted follow-up questionnaire regarding potential long-term symptoms, accompanied by an evaluation on its effectiveness to gather more detailed information on relevant cases. Depending on the

[11] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[12] Update of SmPC section 4.4 and 4.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

outcome of this evaluation, the MAH should discuss the usefulness of continuation of the follow-up questionnaire or the need for any improvements, as appropriate. Additionally, Kounis syndrome and hypersensitivity/anaphylactic reactions with cardiovascular events should be monitored as a topic of special interest in future PSURs and the MAH should evaluate available data or state the lack of new information. 'Safety in children' should be added as missing information to the list of safety concerns in the next PSUR.

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

6.1.8. Lonapegsomatropin - SKYTROFA (CAP) - PSUSA/00010969/202402

Applicant: Ascendis Pharma Endocrinology Division A/S

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 Skytrofa, a centrally authorised medicine containing lonapegsomatropin 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 Skytrofa (lonapegsomatropin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include the risk of osteonecrosis as a warning. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- In the next PSUR, the MAH should provide a comprehensive analysis of risk of medication errors, including an analysis of the reporting rate over time. In addition the MAH should closely monitor the risk of osteonecrosis and provide a detailed review.

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

6.1.9. Nalmefene - SELINCRO (CAP) - PSUSA/00010120/202402

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Background

[13] 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

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Selincro, a centrally authorised medicine containing nalmefene 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 Selincro (nalmefene) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should continue to closely monitor the risk of 'product dispensing error'. All new relevant data should be presented, together with a detailed risk analysis of potential risk factors from post-marketing cases and literature. Moreover, the list of safety concerns in the next PSUR should include 'product dispensing error' as an important potential risk.

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. Nivolumab, relatlimab - OPDUALAG (CAP) - PSUSA/00011018/202403

Applicant: Bristol-Myers Squibb Pharma EEIG

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 Opdualag, a centrally authorised medicine containing nivolumab/relatlimab 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 Opdualag (nivolumab/relatlimab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include serositis and pleural effusion as undesirable effects with frequency 'rare' and 'uncommon', respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[14].
- In the next PSUR, the MAH should provide a cumulative review on the safety of Opdualag (nivolumab/relatlimab) in patients with pre-existing autoimmune diseases, including a thorough discussion of immune-mediated adverse events and discuss the need for any potential amendment to the PI and/or RMP as warranted.

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

[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

6.1.11. Ribociclib - KISQALI (CAP) - PSUSA/00010633/202403

Applicant: Novartis Europharm Limited

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 Kisqali, a centrally authorised medicine containing ribociclib 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 Kisqali (ribociclib) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.

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. Spesolimab - SPEVIGO (CAP) - PSUSA/00011033/202403

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Spevigo, a centrally authorised medicine containing spesolimab 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 Spevigo (spesolimab) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should follow-up on cases of systemic hypersensitivity reactions carefully, particularly cases of anaphylactic reactions and infusion related reactions, and provide any relevant 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.

6.1.13. Vildagliptin - GALVUS (CAP); JALRA (CAP); XILIARX (CAP); metformin, vildagliptin - EUCREAS (CAP); ICANDRA (CAP); ZOMARIST (CAP) - PSUSA/00003113/202402

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thörn

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Galvus, Jalra, Xiliarx, centrally authorised medicines containing vildagliptin and of Eucreas, Icandra, Zomarist, centrally authorised medicines containing vildagliptin/metformin 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 the products above in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide more details about the cases of rhabdomyolysis reported during the PSUR period (e.g. time to onset (TTO), information on dechallenge/rechallenge, concomitant medication and medical history) and present any new cases of rhabdomyolysis.
- The MAH should submit to EMA, within 60 days, a cumulative review of all cases of Severe Cutaneous Adverse Reactions MedDRA SMQ broad level, with DRESS, SJS and TEN cases associated with vildagliptin, including data from published literature, from spontaneous reports and reports from studies, as well as a discussion on possible biological plausibility and mechanism of this association, as well as a causality assessment using the WHO-UMC causality assessment criteria. The MAH should also discuss the need for any potential amendment to the PI and/ or 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. PSUR single assessment (PSUSA) procedures including centrally authorised products (CAPs) and nationally authorised products (NAPs)

See also Annex I 16.3.

6.2.1. Cladribine[15] - LITAK (CAP); NAP - PSUSA/00000787/202402

Applicant(s): Lipomed GmbH (Litak), various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Background

Cladribine is an antineoplastic purine analogue and it is indicated for treatment of hairy cell leukaemia (HCL) and for patients with B-cell chronic lymphocytic leukaemia (CLL), who have

[15] Apart from product(s) with multiple sclerosis indication

not responded to treatment or whose disease has progressed during or after treatment with at least 1 standard alkylating agent-containing regimen.

Based on the assessment of the PSURs, PRAC reviewed the benefit-risk balance of Litak, a centrally authorised medicine containing cladribine, and nationally authorised medicines containing cladribine and issued a recommendation on their marketing authorisations.

Summary of recommendations and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of cladribine-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing wording on breastfeeding to reflect that limited data from case reports have shown that cladribine is excreted in human milk after oral administration. Therefore, the current terms of the marketing authorisations should be varied[16].
- In the next PSUR, the MAHs should discuss the findings on the interaction with nucleoside transporters from the publication by *Hermann et al.*[17]. In addition, the MAHs should provide a cumulative review regarding medicinal products with a clinically significant inhibitory effect on nucleoside transporters, including a discussion on the potential implications for cladribine efficacy, using data from clinical trials, post-marketing setting and literature and discuss whether an update of the product information is warranted.
- In the next PSUR, both MAHs are requested to submit updated cumulative reviews on the association between drug-induced liver injury and cladribine use.

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.

6.2.2. Pemetrexed - ALIMTA (CAP); ARMISARTE (CAP); PEMETREXED ACCORD (CAP); PEMETREXED FRESENIUS KABI (CAP); NAP - PSUSA/00002330/202402

Applicants: Accord Healthcare S.L.U. (Pemetrexed Accord), Actavis Group PTC ehf. (Armisarte), Eli Lilly Nederland B.V. (Alimta), Fresenius Kabi Deutschland GmbH (Pemetrexed Fresenius Kabi), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Background

Pemetrexed is a multi-targeted anti-cancer antifolate agent that and it is indicated as second-line monotherapy or first-line with cisplatin in the treatment of locally advanced or metastatic non-squamous non-small cell lung cancer. It is also used as maintenance monotherapy in patients whose disease has not progressed after platinum-based first-line chemotherapy. Pemetrexed is also used with cisplatin in the first line treatment of unresectable malignant pleural mesothelioma.

[16] Update of SmPC section 4.6. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[17] Hermann R, Krajcsi P, Fluck M, Seithel-Keuth A, Bytyqi A, Galazka A, Munafo A. Cladribine as a Potential Object of Nucleoside Transporter-Based Drug Interactions. Clin Pharmacokinet. 2022 Feb;61(2):167-187. doi: 10.1007/s40262-021-01089-9. Epub 2021 Dec 11. PMID: 34894346; PMCID: PMC8813788

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Alimta, Armisarte, Pemetrexed Accord, Pemetrexed Fresenius Kabi, centrally authorised medicines containing pemetrexed, and nationally authorised medicines containing pemetrexed 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 pemetrexed-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include the drug-drug interaction between proton pump inhibitors and pemetrexed. Therefore, the current terms of the marketing authorisations should be varied[18].
- In the next PSUR, the MAHs should provide reviews of cases of posterior reversible encephalopathy syndrome (PRES), cardiomyopathy and of capillary leak syndrome (CLS) that occurred during the reporting period and discuss whether an update of the product information is warranted. Additionally, the MAHs should provide cumulative reviews of cases of SCARs not listed in the product information (in particular DRESS, AGEP and exfoliative dermatitis), together with a discussion on the need to update the product information.

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.

6.2.3. Rivastigmine – EXELON (CAP); PROMETAX (CAP); RIVASTIGMINE 1A PHARMA (CAP); RIVASTIGMINE HEXAL (CAP); RIVASTIGMINE SANDOZ (CAP); NAP - PSUSA/00002654/202401

Applicants: 1 A Pharma GmbH (Rivastigmine 1A Pharma), Almirall S.A. (Prometax), Hexal AG (Rivastigmine HEXAL), Novartis (Exelon), Sandoz GmbH (Rivastigmine Sandoz), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Background

Rivastigmine is a cholinesterase inhibitor and it is indicated for the symptomatic treatment of patients with Alzheimer's disease and Parkinson's disease.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Exelon, Prometax, Rivastigmine 1A Pharma, Rivastigmine HEXAL, Rivastigmine Sandoz, centrally authorised medicines containing rivastigmine, and nationally authorised medicines containing rivastigmine 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 rivastigmine-containing product(s) in the approved indication(s) remains unchanged.

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

- Nevertheless, the product information should be updated to include pleurothotonus (Pisa syndrome) as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisations should be varied[19].
- In the next PSUR, the MAHs should continue to closely monitor the important identified risks and important potential risks listed as safety concerns in the PSUR. In addition, the MAH should provide a specific in-depth analysis concerning the risk of pemphigoid, including data from clinical trials, post-marketing setting and literature and discuss whether there is a need to update the product information. The MAH should also provide a review on the risk of medication errors, as part of the dedicated PSUR safety concern, including a separate review with respect to the twice weekly formulation (transdermal patches). Finally, the MAH should continue to closely monitor the risks of off-label use, overdose and drug abuse/misuse.

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.

6.2.4. Sugammadex - BRIDION (CAP); NAP - PSUSA/00002799/202401

Applicant(s): Merck Sharp & Dohme B.V. (Bridion), various

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

Background

Sugammadex is a reversal agent for the neuromuscular blocking agents rocuronium and vecuronium and it is indicated for reversal of neuromuscular blockade induced by rocuronium or vecuronium in patients 2 years of age and older.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Bridion, (a) centrally authorised medicine(s) containing sugammadex, and nationally authorised medicines containing sugammadex 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 sugammadex-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add information about hypersensitivity reactions reported following the use of sugammadex and sugammadex-rocuronium complex. Therefore, the current terms of the marketing authorisations should be varied[20].

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.

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

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

See also Annex I 16.3.1.

6.3.1. Mesalazine (NAP) - PSUSA/00001990/202402

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Background

Mesalazine (5-aminosalicylic acid) is an intestinal anti-inflammatory agents indicated for the treatment of mild to moderate ulcerative colitis, both in the acute phase and in the prevention of recurrence, treatment of Crohn's disease both in the acute (active) phase and for the prevention of recurrence as long as the disease is restricted to the colon.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicines containing mesalazine 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 mesalazine-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include idiopathic intracranial hypertension as a warning and as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisations should be varied[21].
- In the next PSUR, the MAH should provide cumulative reviews of cases of bradycardia and of decreased foetal and neonatal renal function, including data from clinical trials, post-marketing setting and literature, together with a discussion on the need to update the product information.

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

6.4. Follow-up to PSUR/PSUSA procedures

See also Annex I 16.4.1.

6.4.1. Delafloxacin - QUOFENIX (CAP) - EMEA/H/C/004860/LEG 004.1

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

PRAC Rapporteur: Petar Mas

Scope: MAH's responses to LEG 004 [Cumulative review on spontaneously reported cases of

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

prolonged, potentially irreversible, serious suspected adverse drug reactions to fluoroquinolones] RSI as adopted in June 2024.

The MAH should comment on the proposed PI amendments updating the existing information in section 4.8, to reflect the new aspects of prolonged, disabling and potentially irreversible adverse drug reactions

Background

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

As a consequence of the Article 31 referral procedure concluded in November 2018 and following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit further data on prolonged, potentially irreversible, serious suspected adverse drug reactions to fluoroquinolones. The responses were assessed by the Rapporteur for further PRAC advice. See also section 11.1 in the current Agenda. For further background, see PRAC minutes June 2024.

Summary of advice/conclusion(s)

- Based on the review of the available information, PRAC maintained the position adopted during the June 2024 plenary meeting and considered that, although the available evidence is limited, information on newly identified aspects of neuropsychiatric reactions should be added to the existing information under the Description of selected adverse drug reactions in the SmPC section 4.8 (and corresponding section in the package leaflet) to include anxiety, suicidal ideation, panic attack, neuralgia and concentration impairment as potential aspects of fluoroquinolone induced long-lasting and disabling adverse drug reactions.

6.4.2. Levofloxacin - QUINSAIR (CAP) - EMEA/H/C/002789/LEG 006.1

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: MAH's responses to LEG 006 [***5-year Cumulative Safety Review***(from 1 January 2017 - 31 December 2022)
Regarding long-lasting, disabling and potentially irreversible side effect.] RSI as adopted in June 2024.

The MAH should comment on the proposed PI amendments updating the existing information in section 4.8, to reflect the new aspects of prolonged, disabling and potentially irreversible adverse drug reactions

Background

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

As a consequence of the Article 31 referral procedure concluded in November 2018 and following the evaluation of the most recently submitted PSUR(s) for the above-mentioned

medicine(s), PRAC requested the MAH to submit further data on prolonged, potentially irreversible, serious suspected adverse drug reactions to fluoroquinolones. The responses were assessed by the Rapporteur for further PRAC advice. See also section 11.1 in the current Agenda. For further background, see PRAC minutes June 2024.

Summary of advice/conclusion(s)

- Based on the review of the available information, PRAC maintained the position adopted during the June 2024 plenary meeting and considered that, although the available evidence is limited, information on newly identified aspects of neuropsychiatric reactions should be added to the existing information under the Description of selected adverse drug reactions in the SmPC section 4.8 (and corresponding section in the package leaflet) to include anxiety, suicidal ideation, panic attack, neuralgia and concentration impairment as potential aspects of fluoroquinolone induced long-lasting and disabling adverse drug reactions.

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0063

Applicant: Orexigen Therapeutics Ireland Limited

Scope: Re-examination of variation II/63 concluded with negative PRAC recommendation in July 2024

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 recommendation for refusal of the variation EMEA/H/C/003687/II/0063 to the terms of the Marketing Authorisation adopted by PRAC in July 2024 (see PRAC minutes July 2024), the MAH submitted a request for re-examination on 09 August 2024, followed by the submission of the scientific grounds for re-examination on 25 September 2024. 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)

- PRAC adopted the revised timetable for the re-examination procedure and the LoQ for the AHEG meeting scheduled for 18 October 2024.

6.6. Expedited summary safety reviews[22]

None

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

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[23]

None

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

See Annex I 17.2.

7.3. Results of PASS imposed in the marketing authorisation(s)[25]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[26]

See also Annex I 17.4.

7.4.1. Denosumab - PROLIA (CAP) - EMEA/H/C/001120/II/0100

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report from the postmarketing observational study 20090522, listed as a category 3 study in the RMP. This is a denosumab global safety assessment among women with postmenopausal osteoporosis (PMO), men with osteoporosis, and men and women who receive Prolia with glucocorticoid exposure in multiple observational databases

Background

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

As stated in the RMP of Prolia (denosumab), the MAH conducted a non-imposed non-interventional PASS to evaluate the incidence of adverse events of special interest (AESI) in postmenopausal women using Prolia (denosumab). The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI). For further background, see the PRAC minutes January 2024, April 2024 and June 2024.

Summary of advice

- Based on the available data, the MAH's responses to the RSI and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be recommended for approval.

[23] In accordance with Article 107n of Directive 2001/83/EC
[24] 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
[25] In accordance with Article 107p-q of Directive 2001/83/EC
[26] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

- PRAC agreed to update the product information[27] to amend the existing wording on osteonecrosis of the jaw to reflect the study results.

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

See Annex I 17.4.1.

7.6. Others

See Annex I 17.5.1.

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 18.2.

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2.1.

8.3. Renewals of the marketing authorisation

See Annex I 18.3.1.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

[27] Update of SmPC section 4.8

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

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.

10.1.1. Alectinib – ALECENSA (CAP) - EMEA/H/C/004164/II/0048

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: PRAC consultation on a direct healthcare professional communication (DHPC) in the context of a type II variation to update sections 4.4 and 4.6 of the SmPC and the package leaflet to amend the duration of the period for which female patients of child-bearing potential must use highly effective contraceptive methods following the last dose of Alecensa, and must be informed of potential harm to the foetus in the event of pregnancy, from 3 months to 5 weeks based on the latest guidelines on contraception requirements for drugs with aneugenic potential, on request of CHMP

Background

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

A type II variation proposing to update the product information of Alecensa in line with the latest guidelines on contraception requirements for drugs with aneugenic potential is under evaluation at CHMP. PRAC was requested to provide advice on the need for a DHPC to inform health care professionals about the use of highly effective contraception in male patients.

Summary of advice

- Based on the review of the available information, PRAC considered that a distribution of a DHPC informing healthcare professionals about the need for the use of highly effective contraception in male patients is not adequate. PRAC highlighted that the proposed updates of the product information are related to the release of revised SWP/NcWP recommendations on the duration of contraception following the end of treatment with a genotoxic drug and are not due to new (non) clinical data. PRAC also acknowledged that information about the contraception requirements for male patients is not new for the class of ALK inhibitors and that oncology is a highly specialised area where

fertility/contraception aspects are a very well known topic. Reference was also made to the expected median age of patients treated for non-small cell lung cancer (60-70 years of age) and expected low number of patients affected by this product information amendment. Therefore, PRAC considered that there is no need for a DHPC in this topic and that risk minimisation measures, namely the update of the product information are sufficient.

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

11.1.1. Fluoroquinolones for systemic and inhalation use: ciprofloxacin (NAP); levofloxacin (NAP); lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin (NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP) - CZ/H/PSUFU/A31/1452/202210

Applicant: various

PRAC Lead: Eva Jirsová

Scope: PRAC consultation on a PSUR follow-up procedure regarding risk minimisation measures following submission of cumulative reviews of spontaneously reported cases of prolonged, potentially irreversible, serious suspected adverse drug reactions, in accordance to the outcome of the referral procedure under Article 31 of Directive 2001/83/EC (EMEA/H/A-31/1452) concluded in 2019, on request of Czech Republic (follow up to the advice adopted by PRAC in June 2024)

Background

As a follow-up to the PRAC advice adopted in June 2024 (see the PRAC minutes June 2024), the MAHs provided their comments on the proposed amendments to the product information. Czech Republic requested PRAC a second PRAC advice on the final amendments of the product information.

Summary of advice

- Based on the review of the available information, PRAC maintained the position adopted during the June 2024 plenary meeting and considered that, although the available

evidence is limited, information on newly identified aspects of neuropsychiatric reactions should be added to the existing information under the Description of selected adverse drug reactions in the SmPC section 4.8 (and corresponding section in the package leaflet) to include anxiety, suicidal ideation, panic attack, neuralgia and concentration impairment as potential aspects of fluoroquinolone induced long-lasting and disabling adverse drug reactions.

11.1.2. Human plasma protein - OCTAPLASLG - SE/H/1866/01-02/II/99

Applicant: Octapharma AB

PRAC Lead: Mari Thorn

Scope: PRAC consultation on a type II variation procedure to amend the product information section 4.8 in order to add TRALI (transfusion-related acute lung injury) as an adverse reaction (as a follow up of the request made by PRAC in the PSUSA/00001635/202302 concluded in November 2023), on request of Sweden

Background

OctaplasLG is a solvent/detergent plasma product that has the same content and distribution of plasma proteins as the raw material of pooled fresh frozen plasma (FFP) and it is indicated in complex deficiencies of coagulation factors and therapeutic plasma exchange procedures.

In the context of the evaluation of a type II variation procedure on amendment of the product information section 4.8 in order to add TRALI (transfusion-related acute lung injury) as an adverse reaction, Sweden requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, and cumulative review provided by the MAH, PRAC supported the proposed amendments to the product information to add transfusion-related acute lung injury as an undesirable effect with a frequency 'not known'.

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

At the organisational, regulatory and methodological matters (ORGAM) meeting on 17 October 2024, the PRAC Chair welcomed Karin Bolin as the new Alternate for Sweden, replacing Mari Thörn who has taken over the role of the Member for Sweden following the PRAC Chair elections.

12.1.2. Vote by proxy

None

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 the monkeypox virus cases in Africa as well as on the latest developments of the relevant vaccines and treatments. In addition, PRAC was updated on influenza and long COVID-19 research, as well as several potential outbreaks and warnings released globally by relevant authorities. 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 Q3 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 2024 highlighting the applications without appointed Rapporteur(s).

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)

PRAC lead: Jana Lukacisinova

The EMA Secretariat provided to PRAC an update on GPAG activities.

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 October 2024, 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 October 2024, the updated EURD list was adopted by CHMP and CMDh at their October 2024 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

None

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Specific adverse drug reaction (ADR) follow-up questionnaire (FUQ) drafting group – update on the activities

PRAC lead: Tiphaine Vaillant

At the organisational, regulatory and methodological matters (ORGAM) meeting on 17 October 2024, the PRAC Lead presented to the Committee the consolidated comments for the Specific ADR FUQ which had been released for public consultation in December 2023. For background information, see PRAC minutes September 2023. PRAC members were invited to provide comments in writing before its final endorsement.

12.12.3. Additional monitoring

None

12.12.4. 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. ADEPT study (Antiepileptic Drugs Exposure and Pregnancy and neonaTal outcomes research) – protocol and study deliverables

The EMA secretariat presented to PRAC the protocol for the objective 1 (describe the utilisation of antiseizure medication in individuals of childbearing age, pregnant, and male individuals) of the ADEPT study, as well as the study timelines including those for the objective 2 (assess feasibility of estimating the risk of adverse outcomes). For background information, please see the PRAC minutes July 2023. PRAC was invited to provide comments and express their interest to be involved in the study.

12.21.2. Committees' timetables and deadlines around the end of year holiday period

PRAC Lead(s): Liana Martirosyan, Bianca Mulder

The EMA Secretariat will explore further solutions to address the points raised regarding the deadlines around the end of the year holiday period and provide an update in the following period.

12.21.3. CHMP AR template – Revamp Project

PRAC Lead(s): Ulla Wändel Liminga

The EMA secretariat presented to PRAC briefly the new CHMP AR/Overview template, following the call for written comments. For background information, please see the PRAC minutes September 2024. PRAC endorsed the final version of the CHMP AR/Overview template and was reminded of the upcoming training sessions on the new process.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[28]

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[29].

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

14.1.1. Adagrasib – KRAZATI (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of thrombocytopenia

EPITT 20112 – New signal

14.1.2. Mogamulizumab – POTELIGEO (CAP)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of colitis

EPITT 20113 – New signal

14.1.3. Oxytetracycline hydrochloride, hydrocortisone acetate, polymyxin B sulfate (ear/eye drops/suspension/ointment) (NAP)

Applicant(s): various

[28] 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

[29] 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

PRAC Rapporteur: Jo Robays

Scope: Signal of hearing and vestibular disorders

EPITT 20120 – New signal

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. Denosumab EMEA/H/C/006424

Scope (pre D-180 phase): Treatment of osteoporosis and bone loss

15.1.2. Denosumab EMEA/H/C/006468

Scope (pre D-180 phase): Prevention of skeletal related events with advanced malignancies and treatment of giant cell tumour of bone

15.1.3. Guanfacine EMEA/H/C/006312

Scope (pre D-180 phase): Treatment of attention deficit hyperactivity disorder (ADHD) in children and adolescents 6-17 years old

15.1.4. Methylphenidate hydrochloride EMEA/H/C/005975, PUMA[30]

Scope (pre D-180 phase): Treatment of Attention Deficit Hyperactivity Disorder (ADHD) in children aged 6 years of age and over

15.1.5. Pegfilgrastim EMEA/H/C/006348, PUMA[31]

Scope (pre D-180 phase): Treatment of neutropenia in paediatric patients

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

Applicant: Kyowa Kirin Holdings B.V.

[30] Paediatric use marketing authorisation(s)
[31] Paediatric use marketing authorisation(s)

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

15.2.2. 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

15.2.3. Covid-19 Vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/II/0082

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission an updated RMP version 5.1 in order to include the safety and effectiveness data available from the non-clinical studies and post-authorisation usage regarding the JN.1 variant strain

15.2.4. Rotavirus vaccine (live, oral) - ROTARIX (CAP) - EMEA/H/C/000639/II/0135

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of an updated RMP version 24 in order to remove missing information related to long term genetic stability of the vaccine virus strain.

15.2.5. Saxagliptin, metformin hydrochloride - KOMBOGLYZE (CAP) - EMEA/H/C/002059/WS2743/0060; Saxagliptin - ONGLYZA (CAP) - EMEA/H/C/001039/WS2743/0061

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an updated RMP version 18.1 in order to remove the previously classified important potential risk serious cutaneous adverse reactions (SCAR)

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. Adalimumab - HUKYNDRA (CAP) - EMEA/H/C/005548/X/0026

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Mari Thorn

Scope: Extension application to add a new strength of 20 mg for adalimumab solution for injection in the pre-filled syringe administered by subcutaneous use

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. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0075/G, Orphan

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Karin Erneholm

Scope: Grouped application comprising two type II variations as follows:
C.I.13 - Submission of the final report from study KTE-C19-101 (ZUMA-1) listed as a category 3 study in the RMP. This is a Phase 1/2 Multicenter Study Evaluating The Safety And Efficacy Of Kte-C19 In Subjects With Refractory Aggressive Non-Hodgkin Lymphoma.
C.I.13 - Submission of the final report from study KTE-C19-106 (ZUMA-6) listed as a category 3 study in the RMP. This is a Phase 1-2 Multi-Center Study Evaluating The Safety And Efficacy Of Kte-C19 In Combination With Atezolizumab In Subjects With Refractory Diffuse Large B-Cell Lymphoma (Dlbcl).
The RMP version 9.2 has also been submitted

15.3.4. Baloxavir marboxil - XOFLUZA (CAP) - EMEA/H/C/004974/II/0021

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Extension of indication to include treatment of patients aged 3 weeks and above for Xofluza, based on final results from study CP40559 (MiniSTONE-1); this was a global Phase 3, multicenter, single-arm, open-label study to assess the safety, PK, and efficacy of baloxavir marboxil in OwH pediatric patients from birth to < 1 year with influenza-like symptoms. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.4

15.3.5. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/II/0133

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of paediatric patients from 5 years of age with active, autoantibody-positive systemic lupus erythematosus (SLE) for BENLYSTA, based on final results from study 200908; this is a worldwide population pharmacokinetic analysis of subcutaneous administered belimumab plus standard therapy to pediatric patients aged 5-17 years with systematic lupus erythematous (SLE), which was aimed to describe the pharmacokinetic (PK) analysis of belimumab to support an appropriate weight-based dosing regimen for subcutaneous administration in paediatric patients aged 5-17 years with SLE. 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 46.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.4

15.3.6. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0056, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Lukacisinova

Scope: Extension of indication to include treatment as part of consolidation therapy for the treatment of patients with Philadelphia chromosome negative CD19 positive B-cell precursor ALL for BLINCYTO. The proposed indication is supported by efficacy data from Studies E1910, 20120215, and AALL1331, safety data for Studies E1910, 20120215, AALL1331, MT103-202, and MT103-203, and Pharmacokinetic data for Studies 20120215, AALL1331, MT103-202, MT103-203, and 20190360. 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 18.0 of the RMP has also been submitted

15.3.7. 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

15.3.8. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0029

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to include information on maintenance treatment and to update efficacy and safety information based on final results from studies CRTH258A2303 (TALON) and CRTH258A2303E1 (TALON Extension). TALON is a 64-week, two-arm, randomized, double-masked, phase IIIb study assessing the efficacy and safety of brolucizumab 6 mg compared to aflibercept 2 mg in a treat-to-control regimen in patients with neovascular age-related macular degeneration. TALON Extension is a 56-week phase IIIb/IV, open-label, one-arm extension study to assess the efficacy and safety of brolucizumab 6 mg in a Treat-to-Control regimen with maximum treatment intervals up to 20 weeks for the treatment of subjects with neovascular age-related macular degeneration who have completed the CRTH258A2303 (TALON) study.
The Package Leaflet is updated accordingly. The RMP version 12.0 has also been submitted

15.3.9. Bulevirtide - HEPCLUDEX (CAP) - EMEA/H/C/004854/II/0031, Orphan

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of chronic hepatitis delta virus (HDV) infection in paediatric patients 3 years of age and older weighing at least 10 kg with compensated liver disease for Hepcludex, based on a modelling and simulation study and an extrapolation study to evaluate the use of Bulevirtide for the treatment of chronic hepatitis D infection in children from 3 to less than 18 years of age. As a consequence, sections 4.1, 4.2, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet has been updated accordingly. Version 4.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI

15.3.10. Darunavir, Cobicistat - REZOLSTA (CAP) - EMEA/H/C/002819/X/0054/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Extension application to introduce a new strength (675 mg/150 mg film-coated tablets) grouped with an extension of indication (C.I.6.a) to include, treatment of HIV-1 infected paediatric patients (aged 6 years and older with body weight at least 25 kg) for REZOLSTA, based on the 48-week ad hoc interim results from study GS-US-216-0128 (Cohort 2); this is a Phase II/III, muticenter, open-label, multicohort interventional study evaluating efficacy, safety, and pharmacokinetics of cobicistat-boosted darunavir in HIV-1 infected children. As a consequence, sections 1, 2, 3, 4.1,4.2, 4.4, 4.8, 5.1, 5.2, 6.1, 6.3, 6.5 and 8 of the SmPC and Annex II are updated. The Package Leaflet and Labelling are updated in accordance. Version 7.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.4

15.3.11. Decitabine, cedazuridine - INAQOVI (CAP) - EMEA/H/C/005823/II/0002

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped application consisting of:
C.I.6: Extension of indication to include treatment of adult patients with myelodysplastic

syndromes (MDS) for INAQOVI.

C.I.6: Extension of indication to include treatment of adult patients with chronic myelomonocytic leukaemia (CMML) for INAQOVI.

Based on final results from studies ASTX727-01, ASTX727-02, ASTX727-04, E7727-01, and E7727-02. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.
Furthermore, the PI is brought in line with the latest QRD template version 10.3. As part of the application the MAH is requesting a 1-year extension of the market protection

15.3.12. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0069

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include treatment of adults with limited-stage small cell lung cancer (LS-SCLC) whose disease has not progressed following platinum-based chemoradiation therapy for IMFINZI, based on final results from study D933QC00001 (ADRIATIC); this is a phase III, randomized, double-blind, placebo-controlled, multi-centre, global study to assess the efficacy and safety of durvalumab monotherapy and durvalumab in combination with tremelimumab compared to placebo as consolidation treatment in patients with LS-SCLC whose disease had not progressed following definitive platinum-based chemoradiation therapy (ADRIATIC). 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 12,s1 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 editorial changes to Annex II. Furthermore, the PI is brought in line with the latest QRD template version 10.4

15.3.13. Eliglustat - CERDELGA (CAP) - EMEA/H/C/003724/X/0036/G, Orphan

Applicant: Sanofi B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension application to introduce a new strength (21 mg capsule, hard) grouped with an extension of indication (C.I.6.a) to include treatment of paediatric patients with GD1 who are 6 years and older with a minimum body weight of 15 kg, who have been previously treated with enzyme replacement therapy (ERT), and who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs) for Cerdelga, based on interim results from study EFC13738 (Open label, two cohort (with and without imiglucerase), multicenter study to evaluate pharmacokinetics, safety, and efficacy of eliglustat in pediatric patients with Gaucher disease type 1 and type 3). 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. The RMP version 8.0 has also been submitted. In addition, the MAH took this opportunity to introduce editorial changes to the PI

15.3.14. Fedratinib - INREBIC (CAP) - EMEA/H/C/005026/II/0020, Orphan

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to update information regarding thiamine levels based on a review of the primary results of the study FEDR-MF-002. This is a Phase 3, multicenter, open-label, randomized study to evaluate the efficacy and safety of fedratinib compared with BAT in subjects with DIPSS intermediate-2 or high-risk primary MF, post-PV MF, or post-ET MF and previously treated with ruxolitinib. The RMP version 3 has also been submitted

15.3.15. 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

15.3.16. 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

15.3.17. Isatuximab - SARCLISA (CAP) - EMEA/H/C/004977/II/0030

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Monica Martinez Redondo

Scope: Extension of indication to include in combination with bortezomib, lenalidomide, and dexamethasone the treatment of adult patients with newly diagnosed active multiple myeloma who are not eligible for autologous stem cell transplant (ASCT) or with no intent for ASCT as initial therapy for Sarclisa, based on results from EFC12522 (IMROZ) pivotal phase III study and the supportive TCD13983 phase 1b/2 study. EFC12522 is an ongoing prospective, multicenter, international, randomized, open-label, 2-arm parallel group study to assess the clinical benefit of VRd (control group) versus IVRd (active group) for the treatment of participants with NDMM who are not eligible for ASCT. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.7, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

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

15.3.19. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0154

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include in combination with pemetrexed and platinum chemotherapy the first-line treatment of adults and adolescents aged 12 years and older with unresectable advanced or metastatic malignant pleural mesothelioma for Keytruda, based on final results from study KEYNOTE-483; this is a multicenter, open-label, Phase 2/3 randomized study to evaluate the efficacy and safety of pembrolizumab in combination with pemetrexed/platinum chemotherapy in participants with unresectable advanced or metastatic malignant pleural mesothelioma (MPM). As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 47.1 of the RMP has also been submitted

15.3.20. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/X/0041

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (0.15 mg/ml granules for oral suspension) for the Pulmonary arterial hypertension (PAH) paediatric indication. As a consequence, the film coated tablets presentations are updated to accommodate the new pharmaceutical form. In addition, contact details for local representatives of Belgium, Luxembourg, Greece and Ireland, have also been updated.

15.3.21. Ruxolitinib - JAKAVI (CAP) - EMEA/H/C/002464/X/0070/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (5 mg/ml oral solution) and a new route of administration (gastric use), indicated for the treatment of Graft versus host disease (GvHD) in patients aged 28 days or older.

The above line extension is grouped with a type II variation:
- C.I.6.a - To include treatment of paediatric patients aged 28 days to less than 18 years old in acute and chronic Graft versus Host Disease for JAKAVI, based on final results from studies REACH4 (CINC424F12201) and REACH5 (Study CINC424G12201). REACH4 is a Phase I/II open-label, single-arm, multi-center study of ruxolitinib added to corticosteroids in pediatric patients with grade II-IV acute graft vs. host disease after allogeneic hematopoietic stem cell transplantation; while REACH5 is a Phase II open-label, single-arm, multi-center study of ruxolitinib added to corticosteroids in pediatric subjects with moderate and severe chronic graft vs. host disease after allogeneic stem cell transplantation (both for oral solution and already approved tablets presentations). As a consequence, sections 4.1,4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance.

The RMP (version 16) is updated in accordance. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to implement editorial changes to Annex II

15.3.22. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2738/0065; Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/WS2738/0062

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Karin Erneholm

Scope: Update of sections 4.8 and 5.3 of the SmPC in order to update information on long-term data in paediatric patients, based on final results from study CLCZ696B2319E1 (PANAROMA-HF OLE) listed as a category 3 study in the RMP (MEA/009); this is a phase 3, multicenter, uncontrolled study to evaluate long-term safety and tolerability of open label sacubitril/valsartan in pediatric patients with heart failure due to systemic left ventricle systolic dysfunction who have completed study CLCZ696B2319 (PANORAMA-HF); the RMP version 8 has also been submitted

15.3.23. Semaglutide - RYBELSUS (CAP) - EMEA/H/C/004953/II/0041

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Update of section 4.6 of the SmPC in order to update information on breast-feeding based on final results from study NN9924-4669. This was an open-label, single-armed, multiple-dose, multi-centre study evaluating the semaglutide and SNAC concentrations in breastmilk from healthy lactating women dosed once daily with oral semaglutide for 10 days (3 mg for 5 days followed by 7 mg for 5 days). The primary endpoints were evaluated during a 24 hours pharmacokinetic (PK) sampling period after the 10th dose. The package leaflet is updated accordingly. The RMP version 9.0 has also been submitted

15.3.24. 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

15.3.25. Sugammadex - BRIDION (CAP) - EMEA/H/C/000885/II/0047

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Extension of indication to include treatment of paediatric patients from birth to less than 2 years of age for Bridion based on final results from paediatric study PN169 (MK-8616-P169); this is a Phase 4 double-blinded, randomized, active comparator-controlled clinical trial to study the efficacy, safety, and pharmacokinetics of sugammadex (MK-8616) for reversal of neuromuscular blockade in pediatric participants aged birth to <2 years. 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 8.1 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, to implement minor editorial corrections and to update the information intended for healthcare professionals (HCPs) at the end of the Package Leaflet

15.3.26. 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

15.3.27. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/II/0027

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include, as an adjunct to diet and exercise, the treatment of moderate to severe obstructive sleep apnoea (OSA) in adults with obesity for MOUNJARO based on final results from studies I8F-MC-GPI1 and I8F-MC-GPI2; these are multicenter, randomized, parallel-arm, double-blind, placebo-controlled studies investigating the effects of tirzepatide compared with placebo in adult participants with moderate-to-severe OSA and obesity. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted

15.3.28. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/II/0056

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Extension of indication to include treatment of giant cell arteritis (GCA) in adult patients for RINVOQ based on final results from study M16-852. This is a phase 3, global, multicenter, randomized, double-blind, PBO-controlled study evaluating the efficacy and safety of upadacitinib in subjects with GCA. 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 15.0 of the RMP has also been submitted

15.3.29. 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

15.3.30. Ustekinumab - UZPRUVO (CAP) - EMEA/H/C/006101/X/0001

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (130 mg concentrate for solution for infusion) and a new route of administration (intravenous use). The RMP version 1.1 is updated in accordance

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).

16.1.1. Abrocitinib - CIBINQO (CAP) - PSUSA/00010976/202403

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

16.1.2. Atazanavir, cobicistat - EVOTAZ (CAP) - PSUSA/00010404/202401

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.1.3. Baloxavir marboxil - XOFLUZA (CAP) - PSUSA/00010895/202402

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

16.1.4. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/202403

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.5. Bempedoic acid - NILEMDO (CAP); bempedoic acid, ezetimibe - NUSTENDI (CAP) - PSUSA/00010841/202402

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

16.1.6. Bimekizumab - BIMZELX (CAP) - PSUSA/00010953/202402

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.7. Brimonidine[32] - MIRVASO (CAP) - PSUSA/00010093/202402

Applicant: Galderma International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

16.1.8. Burosumab - CRYSVITA (CAP) - PSUSA/00010669/202402

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.9. Ciclosporin[33] - IKERVIS (CAP); VERKAZIA (CAP) - PSUSA/00010362/202403

Applicant: Santen Oy

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.10. Ciltacabtagene autoleucel - CARVYKTI (CAP) - PSUSA/00011000/202402

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

16.1.11. Cipaglucosidase alfa - POMBILITI (CAP) - PSUSA/00011047/202403

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

[32] Centrally authorised product only
[33] Topical use only

Scope: Evaluation of a PSUSA procedure

16.1.12. Dengue tetravalent vaccine (live, attenuated) - DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (Art 58[34]) - EMEA/H/W/005362/PSUV/0014

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUR procedure

16.1.13. Dengue tetravalent vaccine[35] (live, attenuated) - QDENGA (CAP) - PSUSA/00011034/202402

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.14. Deucravacitinib - SOTYKTU (CAP) - PSUSA/00011046/202403

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.15. Difelikefalin - KAPRUVIA (CAP) - PSUSA/00010995/202402

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.16. Elosulfase alfa - VIMIZIM (CAP) - PSUSA/00010218/202402

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

16.1.17. Eptinezumab - VYEPTI (CAP) - PSUSA/00010966/202402

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

[34] 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)

[35] Dengue virus, serotype 2, expressing Dengue virus, serotype 1, surface proteins, live, attenuated / Dengue virus, serotype 2, expressing Dengue virus, serotype 3, surface proteins, live, attenuated / Dengue virus, serotype 2, expressing Dengue virus, serotype 4, surface proteins, live, attenuated, Dengue virus, serotype 2, live, attenuated

16.1.18. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/202402

Applicant: Holostem S.r.l., ATMP

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.1.19. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/202402

Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.20. Fosdenopterin - NULIBRY (CAP) - PSUSA/00011017/202402

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.21. Ganaxolone - ZTALMY (CAP) - PSUSA/00000093/202403

Applicant: Marinus Pharmaceuticals Emerald Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.22. Glycerol phenylbutyrate - RAVICTI (CAP) - PSUSA/00010454/202401

Applicant: Immedica Pharma AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.23. Hepatitis B (rDNA[36]) vaccine (adjuvanted, adsorbed) - FENDRIX (CAP) - PSUSA/00001598/202402

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.1.24. Imlifidase - IDEFIRIX (CAP) - PSUSA/00010870/202402

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Bianca Mulder

[36] Recombinant deoxyribonucleic acid

Scope: Evaluation of a PSUSA procedure

16.1.25. Influenza vaccine (surface antigen, inactivated, adjuvanted) - FLUAD TETRA (CAP); - PSUSA/00010300/202403

Applicant(s): Seqirus Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.1.26. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - FLUCELVAX TETRA (CAP) - PSUSA/00010737/202403

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.27. Lenacapavir - SUNLENCA (CAP) - PSUSA/00011012/202402

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.1.28. Lenvatinib - KISPLYX (CAP); LENVIMA (CAP) - PSUSA/00010380/202402

Applicant: Eisai GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.29. Lorlatinib - LORVIQUA (CAP) - PSUSA/00010760/202403

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

16.1.30. Miglustat[37] - OPFOLDA (CAP) - PSUSA/00000077/202403

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.31. Mitapivat - PYRUKYND (CAP) - PSUSA/00011025/202402

Applicant: Agios Netherlands B.V.

[37] For treatment of Pompe disease only

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.32. Momelotinib - OMJJARA (CAP) - PSUSA/00000263/202403

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.33. Nilotinib - TASIGNA (CAP) - PSUSA/00002162/202401

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.1.34. Omaveloxolone - SKYCLARYS (CAP) - PSUSA/00000245/202402

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.35. Oritavancin - TENKASI (CAP) - PSUSA/00010368/202403

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.36. Ospemifene - SENSHIO (CAP) - PSUSA/00010340/202402

Applicant: Shionogi B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

16.1.37. Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/202401

Applicant: Rayner Surgical (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.38. Pirfenidone - ESBRIET (CAP) - PSUSA/00002435/202402

Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

16.1.39. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[38]) - EMEA/H/W/002300/PSUV/0083

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUR procedure

16.1.40. Pomalidomide - IMNOVID (CAP) - PSUSA/00010127/202402

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

16.1.41. Ponesimod - PONVORY (CAP) - PSUSA/00010940/202403

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.42. Pralsetinib - GAVRETO (CAP) - PSUSA/00010961/202403

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.43. Prasugrel - EFIENT (CAP) - PSUSA/00002499/202402

Applicant: Substipharm

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.1.44. Reslizumab - CINQAERO (CAP) - PSUSA/00010523/202402

Applicant: Teva B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.45. Rezafungin - REZZAYO (CAP) - PSUSA/00000221/202403

Applicant: Mundipharma GmbH

[38] 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: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.46. Omaveloxolone - SKYCLARYS (CAP) - PSUSA/00000245/202402

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.47. Oritavancin - TENKASI (CAP) - PSUSA/00010368/202403

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.48. Ospemifene - SENSHIO (CAP) - PSUSA/00010340/202402

Applicant: Shionogi B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

16.1.49. Phenylephrine, ketorolac - OMIDRIA (CAP) - PSUSA/00010419/202401

Applicant: Rayner Surgical (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.50. Pirfenidone - ESBRIET (CAP) - PSUSA/00002435/202402

Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

16.1.51. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[39]) - EMEA/H/W/002300/PSUV/0083

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUR procedure

[39] 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)

16.1.52. Pomalidomide - IMNOVID (CAP) - PSUSA/00010127/202402

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

16.1.53. Ponesimod - PONVORY (CAP) - PSUSA/00010940/202403

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.54. Pralsetinib - GAVRETO (CAP) - PSUSA/00010961/202403

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.55. Prasugrel - EFIENT (CAP) - PSUSA/00002499/202402

Applicant: Substipharm

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.1.56. Reslizumab - CINQAERO (CAP) - PSUSA/00010523/202402

Applicant: Teva B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.57. Rezafungin - REZZAYO (CAP) - PSUSA/00000221/202403

Applicant: Mundipharma GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.58. Rilpivirine[40] - REKAMBYS (CAP) - PSUSA/00010901/202403

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

[40] For intramuscular use only

16.1.59. Rimegepant - VYDURA (CAP) - PSUSA/00010997/202402

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.60. Ruxolitinib - JAKAVI (CAP) - PSUSA/00010015/202402

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.61. Ruxolitinib[41] - OPZELURA (CAP) - PSUSA/00011052/202403

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.62. Samarium (^{153}Sm) lexidronam - QUADRAMET (CAP) - PSUSA/00002682/202402

Applicant: CIS BIO International

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.63. Sodium thiosulfate - PEDMARQSI (CAP) - PSUSA/00000066/202403

Applicant: Norgine B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.64. Solriamfetol - SUNOSI (CAP) - PSUSA/00010831/202403

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure

16.1.65. Teclistamab - TECVAYLI (CAP) - PSUSA/00011010/202402

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

[41] For non-segmental vitiligo only

16.1.66. Telotristat - XERMELO (CAP) - PSUSA/00010639/202402

Applicant: SERB S.A.S.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.67. Tildrakizumab - ILUMETRI (CAP) - PSUSA/00010720/202403

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.68. Tolcapone - TASMAR (CAP) - PSUSA/00002985/202403

Applicant: Viatris Healthcare Limited

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.1.69. Trastuzumab emtansine - KADCYLA (CAP) - PSUSA/00010136/202402

Applicant: Roche Registration GmbH

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.70. Valoctocogene roxaparvovec - ROCTAVIAN (CAP) - PSUSA/00011009/202402

Applicant: BioMarin International Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.71. Velaglucerase alfa - VPRIV (CAP) - PSUSA/00003103/202402

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.72. Vismodegib - ERIVEDGE (CAP) - PSUSA/00010140/202401

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.73. Vosoritide - VOXZOGO (CAP) - PSUSA/00010952/202402

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

16.1.74. Zanamivir[42] - DECTOVA (CAP) - PSUSA/00010763/202401

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

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

16.2.1. Atosiban - TRACTOCILE (CAP); NAP - PSUSA/00000264/202401

Applicant(s): Ferring Pharmaceuticals A/S (Tractocile), various

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.2.2. Dexrazoxane - SAVENE (CAP); NAP - PSUSA/00001001/202402

Applicant(s): Cnx Therapeutics Ireland Limited (Savene), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.2.3. Voriconazole - VFEND (CAP); NAP - PSUSA/00003127/202402

Applicant(s): Pfizer Europe MA EEIG (Vfend), various

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

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

16.3.1. Ampicillin, sulbactam (NAP) - PSUSA/00000197/202402

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

[42] Centrally authorised products only

16.3.2. Aprotinin (NAP) - PSUSA/00000230/202402

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.3.3. Argatroban (NAP) - PSUSA/00009057/202401

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.3.4. Calcium chloride, histidine, magnesium chloride, mannitol, potassium chloride, sodium chloride, tryptophan, oxogluric acid (NAP) - PSUSA/00000002/202401

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.3.5. Chlormadinone (NAP) - PSUSA/00000677/202401

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.3.6. Chlormadinone acetate, ethinylestradiol (NAP) - PSUSA/00000679/202401

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.3.7. Cilazapril (NAP); cilazapril, hydrochlorothiazide (NAP) - PSUSA/00000749/202402

Applicant(s): various

PRAC Lead: Carla Torre

Scope: Evaluation of a PSUSA procedure

16.3.8. Dobutamine (NAP) - PSUSA/00001151/202403

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.3.9. Dorzolamide, timolol (NAP) - PSUSA/00001166/202402

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.3.10. Flubendazole (NAP) - PSUSA/00001400/202402

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.3.11. Galantamine (NAP) - PSUSA/00001512/202403

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.3.12. Human coagulation factor VIII (inhibitor bypassing fraction) (NAP) - PSUSA/00009174/202402

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

16.3.13. Hydroxyethyl starch (NAP) - PSUSA/00001694/202403

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.3.14. Iloprost[43] (NAP) - PSUSA/00009190/202401

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.3.15. Influenza vaccine[44] (split virion, inactivated) (NAP) - PSUSA/00010298/202403

Applicant(s): various

PRAC Lead: Gabriele Maurer

[43] Intravenous (IV)use only
[44] Non centrally authorised products

Scope: Evaluation of a PSUSA procedure

16.3.16. Influenza vaccine (surface antigen, inactivated) (NAP) - PSUSA/00001744/202403

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.3.17. Lisdexamfetamine (NAP) - PSUSA/00010289/202402

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.3.18. Nafarelin (NAP) - PSUSA/00002105/202402

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

16.3.19. Nomegestrol (NAP) - PSUSA/00002181/202401

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.3.20. Octenidine dihydrochloride, 1-propanol, 2-propanol (NAP) - PSUSA/00010417/202401

Applicant(s): various

PRAC Lead: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

16.3.21. Ondansetron (NAP) - PSUSA/00002217/202402

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

16.3.22. Sterculia (NAP); Frangula, Sterculia (NAP) - PSUSA/00010428/202402

Applicant(s): various

PRAC Lead: Gudrun Stefansdottir

Scope: Evaluation of a PSUSA procedure

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

16.4.1. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/LEG 064

Applicant: Alexion Europe SAS

PRAC Rapporteur: Monica Martinez Redondo

Scope: MAH response to PSUR#19 (EMEA/H/C/PSUSA/00001198/202310) as adopted in 16 May 2024.
The MAH for Soliris is requested to provide cumulative data from all the available sources in a tabulated format for all the hepatotoxicity cases (irrespective of whether, according to the MAH, they have alternative aetiologies) with transaminases elevation and clinical consequences, reported with eculizumab until de DLP of this PSUR

16.5. Follow-up to PSUR/PSUSA procedures

None

16.6. Variation procedure(s) resulting from PSUSA evaluation

None

16.7. Expedited summary safety reviews[45]

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)[46]

None

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[47]

17.2.1. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 002.4

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

[45] 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
[46] In accordance with Article 107n of Directive 2001/83/EC
[47] 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:
Amendment 2 of protocol v.3.0 for PASS No. PS0038
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 patients compared to PSO patients exposed to other biologics (eg, anti TNF, anti-IL-23, but not anti IL 17)

17.2.2. Danicopan - VOYDEYA (CAP) - EMEA/H/C/005517/MEA 002

Applicant: Alexion Europe

PRAC Rapporteur: Martin Huber

Scope: ***Draft Study Protocol / ALX-PNH-502***
Title: An observational cohort study to assess long-term safety of danicopan add-on therapy in patients with paroxysmal nocturnal hemoglobinuria: analysis of IPIG-registry data

17.2.3. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 005.5

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: ***Protocol amendment (version 5.1) / Study (EP0219 [former ZX008-2102])***
Post Authorisation Safety Study (PASS): A Drug Utilisation Study of Fenfluramine In Europe (DUS)

17.2.4. Glofitamab - COLUMVI (CAP) - EMEA/H/C/005751/MEA 004.1

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: MAH's response to MEA 004 [***PASS No BO43309***] RSI as adopted in May 2024.
Evaluation of the Effectiveness of the Additional Risk Minimisation Measures for Glofitamab - A Survey Among Healthcare Professionals in 10 Countries in the European Economic Area

17.2.5. Omaveloxolone - SKYCLARYS (CAP) - EMEA/H/C/006084/MEA 002.1

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's answers to questions regarding MEA/002 [Protocol 296FA401 (408-C-2301)] as adopted in June 2024.
An observational, multinational, post-marketing registry of omaveloxolone-treated patients with Friedreich's ataxia

17.2.6. Respiratory syncytial virus vaccine (bivalent, recombinant) - ABRYSVO (CAP) - EMEA/H/C/006027/MEA 003.1

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Updated protocol for Study C3671026 and MAH's responses to MEA 003 [**PROTOCOL FOR PASS NO. C3671026**] RSI as adopted in June 2024

17.2.7. Respiratory syncytial virus vaccine (bivalent, recombinant) - ABRYSVO (CAP) - EMEA/H/C/006027/MEA 004.1

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: MAH's response to MEA 004 [*PROTOCOL PASS NO. C3671038*] RSI as adopted in June 2024.

- Section 9.5 protocol/section 2.4.5. of this AR shall be addressed
- It is assumed that the background rates used for the study size calculation (Willame C et al. Vaccine. 2023) is also applicable for the population at issue (i.e. immunocompromised, renally impaired, hepatically impaired). The MAH is asked to confirm.
- The MAH is expected to provide regular updates regarding enrollment (e.g. in the PSURs) and timely notify the Rapporteur in case of delays

17.2.8. Ritlecitinib - LITFULO (CAP) - EMEA/H/C/006025/MEA 002.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 002 [Study B7981092] RSI as adopted in June 2024.
Title: A Prospective Active Surveillance Study to Monitor the Real-World Safety of Ritlecitinib Among Adolescents with Alopecia areata

17.2.9. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 003.9

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 003.8 [***Protocol Amendment for study OP0006***] RSI as adopted in May 2024

17.2.10. Rozanolixizumab - RYSTIGGO (CAP) - EMEA/H/C/005824/MEA 001

Applicant: UCB Pharma

PRAC Rapporteur: Maria del Pilar Rayon

Scope: ***Draft PASS Protocol***/ Real-world observational secondary data study (MG0027).(Non-Imposed)
A Multi-National Cohort Study to evaluate the safety of rozanolixizumab in generalized myasthenia gravis patients

17.2.11. Ruxolitinib - OPZELURA (CAP) - EMEA/H/C/005843/MEA 001.2

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 001.1 [REVISED PROTOCOL for PASS INCB 88888-037] RSI as adopted in May 2024.
Title: To evaluate the safety of long-term ruxolitinib cream use with respect to incidence of non-melanoma skin cancers

17.2.12. Somapacitan - SOGROYA (CAP) - EMEA/H/C/005030/MEA 005.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: ***Revised protocol (v. 3.0) / Study No. NN8640-4787***
Title: A non-interventional, observational, register-based study to investigate long-term safety and clinical parameters of somapacitan treatment in paediatric patients with GHD in the setting of routine clinical practice.

As a follow-up of MEA 005.1, the MAH needs to provide the answers to a second Request for supplementary information. A revised study protocol is expected

17.3. Results of PASS imposed in the marketing authorisation(s)[48]

None

17.4. Results of PASS non-imposed in the marketing authorisation(s)[49]

17.4.1. COVID-19 Vaccine Janssen (Ad26.COV2.S) - JCOVDEN (CAP)[50] - EMEA/H/C/005737/II/0078/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Mari Thorn

Scope: A grouped application consisting of three Type II variations, as follows:
C.I.13: Submission of the final report from study COV3003 listed as a category 3 study in the RMP. This is a randomized, double-blind, phase 3 study to evaluate 6 dose levels of Ad26.COV2.S administered as a two-dose schedule in healthy adults. The RMP version 8.3 has also been submitted.

C.I.13: Submission of the final report from study COV3009 listed as a category 3 study in the RMP. This is a randomized, double-blind, placebo controlled phase 3 study to assess the efficacy and safety ofAd26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older.

C.I.13: Submission of the final report from study RSV2008 listed as a category 3 study in the RMP. This is a randomized, observer-blind, phase 1 study to evaluate innate and pro-inflammatory responses of an Ad26.RSV.preF-based vaccine, Ad26.COV2.S vaccine and

[48] In accordance with Article 107p-q of Directive 2001/83/EC
[49] 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
[50] European Commission decision for withdrawal of marketing authorisation for Jcovden (COVID-19 Vaccine Janssen (Ad26.COV2.S)) in the European Union (EU) is dated 26 July 2024. The withdrawal was at the request of the marketing authorisation holder, Janssen-Cilag International N.V., which notified the European Commission of its decision to permanently discontinue the marketing of the product for commercial reasons.

Ad26.ZEBOV vaccine in adults aged 18 to 59 years

17.4.2. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/WS2620/0092; Dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/WS2620/0047; Dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/WS2620/0056; Dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/WS2620/0118

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.6 of the SmPC in order to update information about the use of DTG-containing regimens in pregnancy and at conception based on final results from non-interventional Tsepamo study and the Eswatini Birth Outcomes Surveillance study. In addition, data from other cohort studies and pregnancy registries, including the APR, DOLOMITE-EPPICC (Study 208613) and DOLOMITE-NEAT-ID Network study (Study 208759) both listed as category 3 studies in the RMP; and the US Chart Review (Study 212976) as well as data from literature are included. DOLOMITE-EPPICC (Study 208613) is a s a non-interventional study to Assess "real-world" maternal and foetal outcomes following DTG use during pregnancy and to describe patterns of DTG utilization; DOLOMITE NEAT ID Network Study (208759) is a non-interventional, multi-site observational study to define the safety and effectiveness of Dolutegravir use in HIV positive pregnant women. The Package Leaflet is updated accordingly. The RMP version 19 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to sections 4.4 and 4.5 of the SmPC

17.4.3. Lasmiditan - RAYVOW (CAP) - EMEA/H/C/005332/II/0007

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Anna Mareková

Scope: Submission of the final report from study H8H-MC-B005, listed as a category 3 study in the RMP (MEA/003). This is a Real-World Observational Study to Assess Drug Utilisation Patterns in the US Among Migraine Patients Treated with Lasmiditan. The RMP version 2.1 is submitted alongside the final study report

17.4.4. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/II/0056

Applicant: Eisai GmbH

PRAC Rapporteur: Mari Thorn

Scope: Update of section 5.1 of the SmPC in order to update the safety and efficacy information for the current HCC indication based on final results from study E7080-M000-508 (STELLAR), listed as a category 3 PASS in the RMP; this is a multicentre non-interventional, observational Phase 4 study to evaluate the safety and tolerability of lenvatinib in patients with advanced or unresectable HCC. The RMP version 17.0 has also been submitted

17.4.5. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/II/0043

Applicant: Gruenenthal GmbH

PRAC Rapporteur: Eamon O'Murchu

Scope: Submission of the final report from the PASS study D3820R0008 listed as a category 3 study in the RMP. This is a US post-marketing, comparative, observational study to evaluate the cardiovascular safety of Naloxegol in patients with non-cancer pain in comparison to other treatments for opioid induced constipation. The RMP version 9.0 has also been submitted

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

17.4.7. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/II/0091/G, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

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

C.I.4: Update of the Annex II based on final results from study B3461001 (THAOS) listed as a category 3 study in the RMP. This is a global, multi-center, longitudinal, observational survey of patients with documented transthyretin gene mutations or wild-type transthyretin amyloidosis.

C.I.13: Submission of the final report from study B3461042 listed as a category 3 study in the RMP. This is a post-marketing safety surveillance study in Japanese patients with AATR-PN.

The RMP version 10.0 has also been submitted. In addition, the MAH took the opportunity to provide B3461028 Clinical Study Report (CSR) Errata

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

17.5.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 043

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: From R/55:
An Observational Registry of Abatacept in Patients with Juvenile Idiopathic Arthritis is ongoing. The primary objective is to describe the long-term safety of abatacept treatment

for JIA in routine clinical practice by quantifying the incidence rates of serious infections, autoimmune disorders, and malignancies. Recruitment updates are provided each February, and interim reports will be submitted in 2014, 2019, and 2024. The planned date for submission of final data is 2029.
The data in these studies do not change the safety profile of abatacept. The MAH will supply interim reports from the above mentioned studies according to the set schedules.
Third Interim Report / Study IM101240

17.5.2. Botulinum toxin type A - NUCEIVA (CAP) - EMEA/H/C/004587/MEA 002.5

Applicant: Evolus Pharma B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: ***Second Interim Report / Study EV-010***
Title: Non-Interventional Post-Authorisation Safety Study of NUCEIVA for the Treatment of Moderate-to-Severe Glabellar Lines

17.5.3. COVID-19 mRNA vaccine - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 065.5

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: From II/0028:
Study mRNA-1273-P910
Clinical course, outcomes and risk factors of myocarditis and pericarditis following administration of Moderna vaccines targeting SARS-CoV-2.
5th Interim Report & revised protocol & Responses to MEA 065.3

17.5.4. Ganaxolone - ZTALMY (CAP) - EMEA/H/C/005825/MEA 002

Applicant: Marinus Pharmaceuticals Emerald Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: From initial MAA (RMP)
Safety Review Study LLF001 (CANDID observational study):
Endpoint Enabling Study in Cyclin-dependent kinase-like 5 Deficiency Disorder.
ANNUAL UPDATE (Milestone reports after 50 and 100 participants have completed the 1st year vistit)

17.5.5. Ganaxolone - ZTALMY (CAP) - EMEA/H/C/005825/MEA 003

Applicant: Marinus Pharmaceuticals Emerald Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: From RMP:
Safety review CDD-IPR-CDD-01 CDKL5 Deficiency Disorder International Patient Registry. Six monthly updates (data lock points [DLPs] in line with those of the ganaxolone Periodic Safety Update Report [PSUR; 17 Mar & 17 Sept]
SIX MONTHS UPDATES / CDD-IPR-CDD-01 CDKL5 Patient Registry

17.5.6. Imiglucerase - CEREZYME (CAP) - EMEA/H/C/000157/MEA 040.12

Applicant: Sanofi B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: ***Tenth Interim report from the Gaucher Pregnancy and Lactation Sub-Registry***
Covering the period: 08 May 2021 to 03 May 2024

17.5.7. Siponimod - MAYZENT (CAP) - EMEA/H/C/004712/MEA 002.5

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: ***Third Annual Interim Report for PRIM / study no CBAF312A2411 + MAH's responses to MEA 002.4 [Second Annual Interim Report for PRIM]***
Study title: Evaluation of pregnancy and infant outcomes in Mayzent patients using PRegnancy outcomes Intensive Monitoring (PRIM) data – The Mayzent PRIM study

17.5.8. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 024.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: ***Second Interim Report / A3921347 study*** (RMP category 3 study)
Study A3921347 - 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

17.5.9. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 041.6

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: ***Fourth Interim Report / Study C4591036***
Clinical study to characterize the clinical course, risk factors, long-term sequelae, and quality oflife in children and young adults <21 years with acute post-vaccine myocarditis

17.6. Others

17.6.1. Capivasertib - TRUQAP (CAP) - EMEA/H/C/006017/MEA 001

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Hrabcik

Scope: ***Feasibility Assessment***
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)

17.6.2. SARS-CoV-2, variant XBB.1.16, spike protein, receptor binding domain fusion homodimer, Selvacovatein - BIMERVAX (CAP) - EMEA/H/C/006058/MEA 010.2

Applicant: Hipra Human Health S.L.

PRAC Rapporteur: Zane Neikena

Scope: ***Study Progress Report (Version 1.0) / VAC4EU***
Post-authorisation Safety Study of BIMERVAX® Vaccine in Europe

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.

18.1.1. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/S/0063 (without RMP)

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Annual reassessment of the marketing authorisation

18.1.2. Ebola vaccine (rDNA[51], replication-incompetent) - MVABEA (CAP) - EMEA/H/C/005343/S/0022 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

[51] Recombinant deoxyribonucleic acid

Scope: Annual reassessment of the marketing authorisation

18.1.3. Ebola vaccine (rDNA[52], replication-incompetent) - ZABDENO (CAP) - EMEA/H/C/005337/S/0020 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual reassessment of the marketing authorisation

18.2. Annual reassessments of the marketing authorisation

18.2.1. Etranacogene dezaparvovec - HEMGENIX (CAP) - EMEA/H/C/004827/R/0020 (without RMP)

Applicant: CSL Behring GmbH, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.2. Exagamglogene autotemcel - CASGEVY (CAP) - EMEA/H/C/005763/R/0006 (without RMP)

Applicant: Vertex Pharmaceuticals (Ireland) Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.3. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/R/0035 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.3. Conditional renewals of the marketing authorisation

18.3.1. Arsenic trioxide - ARSENIC TRIOXIDE MYLAN (CAP) - EMEA/H/C/005235/R/0012 (without RMP)

Applicant: Mylan Ireland Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.2. Azacitidine - AZACITIDINE BETAPHARM (CAP) - EMEA/H/C/005075/R/0020 (without RMP)

Applicant: betapharm Arzneimittel GmbH

[52] Recombinant deoxyribonucleic acid

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

18.3.3. Budesonide, Formoterol fumarate dihydrate - GORESP DIGIHALER (CAP) - EMEA/H/C/004882/R/0016 (without RMP)

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: 5-year renewal of the marketing authorisation

18.3.4. Cefiderocol - FETCROJA (CAP) - EMEA/H/C/004829/R/0022 (with RMP)

Applicant: Shionogi B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

18.3.5. Cholera vaccine, oral, live - VAXCHORA (CAP) - EMEA/H/C/003876/R/0024 (without RMP)

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

18.3.6. Cinacalcet - CINACALCET ACCORDPHARMA (CAP) - EMEA/H/C/005236/R/0013 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.7. Influenza vaccine (surface antigen, inactivated, adjuvanted) - FLUAD TETRA (CAP) - EMEA/H/C/004993/R/0055 (without RMP)

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

18.3.8. Tigecycline - TIGECYCLINE ACCORD (CAP) - EMEA/H/C/005114/R/0007 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

18.3.9. Treprostinil sodium - TREPULMIX (CAP) - EMEA/H/C/005207/R/0020 (without RMP)

Applicant: SciPharm Sarl

PRAC Rapporteur: Zane Neikena

Scope: 5-year renewal of the marketing authorisation

18.4. Renewals of the marketing authorisation

None

19. Annex II – List of participants

including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 30 September – 03 October 2024 PRAC meeting, which was held remotely. Participants marked with "a" attended the plenary session while those marked with "b" attended the ORGAM.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ulla Wändel Liminga [a,b]	Chair	Sweden	No interests declared	
Jan Neuhauser [a]	Member	Austria	No interests declared	
Sonja Hrabcik [a]	Alternate	Austria	No interests declared	
Jean-Michel Dogné [a,b]	Member	Belgium	No interests declared	
Jo Robays [a,b]	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva [a,b]	Member	Bulgaria	No interests declared	
Petar Mas [a,b]	Member	Croatia	No interests declared	
Barbara Bytyqi [a,b]	Alternate	Croatia	No interests declared	
Elena Kaisis [a,b]	Member	Cyprus	No interests declared	
Panagiotis Psaras [a,b]	Alternate	Cyprus	No interests declared	
Eva Jirsová [a]	Member	Czechia	No interests declared	
Jana Lukacisinova [a,b]	Alternate	Czechia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Marie Louise Schougaard Christiansen [a]	Member	Denmark	No interests declared	
Karin Erneholm [a,b]	Alternate	Denmark	No interests declared	
Maia Uusküla [a,b]	Member	Estonia	No interests declared	
Terhi Lehtinen [a,b]	Member	Finland	No interests declared	
Kimmo Jaakkola [a,b]	Alternate	Finland	No interests declared	
Tiphaine Vaillant [a,b]	Member	France	No interests declared	
Martin Huber [a,b]	Member	Germany	No interests declared	
Gabriele Maurer [a,b]	Alternate	Germany	No participation in discussion, final deliberations and voting on:	6.1.10. Nivolumab, relatlimab - OPDUALAG (CAP) - PSUSA/00011018/202403 15.3.15. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2717/0146; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2717/01151 15.3.18. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/X/0144
Sofia Trantza [a,b]	Member	Greece	No interests declared	
Georgia Gkegka [a,b]	Alternate	Greece	No interests declared	
Julia Pallos [a]	Member	Hungary	No participation in discussion, final deliberations	6.1.10. Nivolumab, relatlimab - OPDUALAG (CAP) - PSUSA/00011018/202403

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			and voting on:	14.1.1. Adagrasib – KRAZATI (CAP) 15.3.14. Fedratinib - INREBIC (CAP) - EMEA/H/C/005026/II/0020, Orphan 15.3.18. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/X/0144 15.3.15. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/WS2717/0146; Ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/WS2717/0115 16.1.2. Atazanavir, cobicistat - EVOTAZ (CAP) - PSUSA/00010404/202401 16.1.14. Deucravacitinib - SOTYKTU (CAP) - PSUSA/00011046/202403 16.1.40. Pomalidomide - IMNOVID (CAP) - PSUSA/00010127/202402 17.5.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 043
Melinda Palfi [a,b]	Alternate	Hungary	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Guðrún Stefánsdóttir [a,b]	Member	Iceland	No restrictions applicable to this meeting	
Guðrún Þengilsdóttir [b]	Alternate	Iceland	No interests declared	
Rhea Fitzgerald [a,b]	Member	Ireland	No interests declared	
Eamon O'Murchu [a,b]	Alternate	Ireland	No interests declared	
Amelia Cupelli [a,b]	Member	Italy	No interests declared	
Emilio Clementi [a,b]	Alternate	Italy	No interests declared	
Zane Neikena [a,b]	Member	Latvia	No interests declared	
Rugile Pilviniene [a]	Member	Lithuania	No interests declared	
Lina Seibokiene [a,b]	Alternate	Lithuania	No interests declared	
Nadine Petitpain [a,b]	Member	Luxembourg	No restrictions applicable to this meeting	
Anne-Cecile Vuillemin[b]	Alternate	Luxembourg	No interests declared	
John Joseph Borg [a]	Member	Malta	No interests declared	
Liana Martirosyan [a,b]	Member	Netherlands	No interests declared	
Bianca Mulder [a,b]	Alternate	Netherlands	No interests declared	
David Olsen [a,b]	Member	Norway	No participation in discussion, final deliberations and voting on:	11.1.1. Fluoroquinolones for systemic and inhalation use: ciprofloxacin (NAP); levofloxacin (NAP); lomefloxacin (NAP); moxifloxacin (NAP); norfloxacin (NAP); ofloxacin

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				(NAP); pefloxacin (NAP); prulifloxacin (NAP); rufloxacin (NAP) - CZ/H/PSUFU/A31/1452/202210 15.3.20. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/X/0041 16.3.14. Iloprost (NAP) - PSUSA/00009190/202401
Pernille Harg[b]	Alternate	Norway	No interests declared	
Katarzyna Ziolkowska [a,b]	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins [a,b]	Member	Portugal	No interests declared	
Carla Torre [a]	Alternate	Portugal	No interests declared	
Roxana Dondera [a,b]	Member	Romania	No interests declared	
Irina Sandu [a]	Alternate	Romania	No interests declared	
Anna Mareková [a,b]	Member	Slovakia	No interests declared	
Miroslava Gocova [a]	Alternate	Slovakia	No interests declared	
Polona Golmajer [b]	Member	Slovenia	No interests declared	
Marjetka Plementas [a,b]	Alternate	Slovenia	No interests declared	
Maria del Pilar Rayon [a,b]	Member	Spain	No interests declared	
Monica Martinez Redondo [a,b]	Alternate	Spain	No interests declared	
Mari Thorn [a,b]	Member	Sweden	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
Karin Bolin [b]	Alternate	Sweden	No interests declared	
Annalisa Capuano [a]	Member	Independent scientific expert	No interests declared	
Milou-Daniel Drici [a,b]	Member	Independent scientific expert	No interests declared	
Maria Teresa Herdeiro [a,b]	Member	Independent scientific expert	No interests declared	
Patricia McGettigan [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark [a,b]	Member	Independent scientific expert	No interests declared	
Roberto Frontini [a,b]	Member	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	11.1.2. Human plasma protein - OCTAPLASLG - SE/H/1866/01-02/II/99
Salvatore Antonio Giuseppe Messana [a,b]	Alternate	Healthcare Professionals' Representative	No interests declared	
Michal Rataj [a]	Alternate	Patients' Organisation Representative	No interests declared	
Els Beghein [a]	Expert	Belgium	No interests declared	
Laurence de Fays [a]	Expert	Belgium	No interests declared	
Fabrice Moore [a]	Expert	Belgium	No interests declared	
Flora Musuamba Tshinanu [a]	Expert	Belgium	No restrictions applicable to this meeting	
Gabriela Burianová [a]	Expert	Czech Republic	No interests declared	
Veronika Descikova [a]	Expert	Czech Republic	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jana Kopecka [a]	Expert	Czech Republic	No interests declared	
Lucie Skalova [a]	Expert	Czech Republic	No interests declared	
Karina Suciu-Subert [a]	Expert	Czech Republic	No interests declared	
Petra Vacková [a]	Expert	Czech Republic	No interests declared	
Jan Vosatka [a]	Expert	Czech Republic	No interests declared	
Alexander Braathen [a]	Expert	Denmark	No interests declared	
Nicklas Hasselblad Lundstrøm [a]	Expert	Denmark	No interests declared	
Frederikke Hillebrand Laustsen [a],[b]	Expert	Denmark	No restrictions applicable to this meeting	
Kira Rosenkilde Underbjerg [a]	Expert	Denmark	No interests declared	
Per Sindahl [a]	Expert	Denmark	No interests declared	
Benjamin Burrus [a]	Expert	France	No interests declared	
Nicolas Camhaji [a]	Expert	France	No restrictions applicable to this meeting	
Katia Chemala [a]	Expert	France	No interests declared	
Cécile Choquet [a]	Expert	France	No interests declared	
Camille De-Kervasdoue [a]	Expert	France	No interests declared	
Nathalie Dumarcet [a]	Expert	France	No interests declared	
Stéphanie Hueber [a]	Expert	France	No interests declared	
Marion Perrin [a]	Expert	France	No interests declared	
Muriel Uzzan [a]	Expert	France	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Philippe Vella [a]	Expert	France	No interests declared	
Dominique Gaston [a]	Expert	Germany	No interests declared	
Dennis Lex [a,b]	Expert	Germany	No interests declared	
Graine Kirwann [a]	Expert	Ireland	No restrictions applicable to this meeting	
Aine McKenna [a]	Expert	Ireland	No interests declared	
Melanie Murphy [a]	Expert	Ireland	No restrictions applicable to this meeting	
Risteard Prendergast [a]	Expert	Ireland	No interests declared	
Magdalena Wielowieyska [a]	Expert	Luxembourg	No restrictions applicable to this meeting	
Esther de Vries [a]	Expert	Netherlands	No interests declared	
Margje Monster-Simons [a]	Expert	Netherlands	No interests declared	
Dennis van Eijl [a]	Expert	Netherlands	No interests declared	
Sophia Venzke [a]	Expert	Netherlands	No interests declared	
Susanne Dertz [a]	Expert	Norway	No interests declared	
Nelson Otieno [a]	Expert	NRA	No interests declared	
Zerlealem Tsegaye Sleshi [a]	Expert	NRA	No interests declared	
Charlotte Backman [a,b]	Expert	Sweden	No interests declared	
Karin Bolin [a]	Expert	Sweden	No interests declared	
Rolf Gedeborg [a]	Expert	Sweden	No restrictions	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			applicable to this meeting	
Jolanta Gulbinovic [a]	Expert	Sweden	No interests declared	
Karin Mathold [a]	Expert	Sweden	No interests declared	
Anna Schölin [a]	Expert	Sweden	No interests declared	
Philip Coyne [a]	Expert	WHO	No restrictions applicable to this meeting	
Noha Iessa [a]	Expert	WHO	No interests declared	
Eun Mi Kim [a]	Expert	WHO	No interests declared	
Denise Mupfasoni [a]	Expert	WHO	No interests declared	
A representative from the European Commission attended the meeting				
Observer from FDA (USA) 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