08 April 2025
EMA/PRAC/111789/2025
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of the meeting on 10-13 February 2025

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

Health and safety information

In accordance with the Agency's health and safety policy, delegates were briefed on health, safety and emergency information and procedures prior to the start of the meeting.

Disclaimers

Some of the information contained in the minutes is considered commercially confidential or sensitive and therefore not disclosed. With regard to intended therapeutic indications or procedure scope listed against products, it must be noted that these may not reflect the full wording proposed by applicants and may also change during the course of the review. Additional details on some of these procedures will be published in the PRAC meeting highlights once the procedures are finalised.

Of note, the minutes are a working document primarily designed for PRAC members and the work the Committee undertakes.

Note on access to documents

Some documents mentioned in the minutes cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006, Rev. 1).

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1. Introduction

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

The Chair opened the meeting by welcoming all participants. The meeting was held in-person.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates[1] and experts and on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics. Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. No new or additional competing interests were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

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

The Chair welcomed the new member(s) and alternate(s) and thanked the departing members/alternates for their contributions to the Committee.

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

1.2. Agenda of the meeting on 10-13 February 2025

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

1.3. Minutes of the previous meeting on 13-16 January 2025

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

Post-meeting note: the PRAC minutes of the meeting held on 13-16 January 2025 were published on the EMA website on 12 March 2025 (EMA/PRAC/67596/2025).

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

2.1. Newly triggered procedures

None

[1] No alternates for COMP

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

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

Applicant(s): various

PRAC Rapporteur: Jana Lukacisinova; 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

A referral procedure under Article 31 is ongoing for finasteride- and dutasteride-containing products following concerns regarding suicidal ideation and suicide. For further background, see PRAC minutes October 2024.

Summary of recommendation(s)/conclusions

- PRAC adopted a list of outstanding issues (LoOI) to the MAHs with a revised timetable for the procedure (EMA/PRAC 414468/2024 Rev 1).
- PRAC discussed the results of a descriptive study on suicidality incidence rates conducted via DARWIN EU (EUPAS1000000423). Based on these, PRAC agreed that the conduct of a comparative study is not feasible.
- PRAC noted the third-party interventions.

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

None

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

3.5. Others

None

4. Signals assessment and prioritisation[3]

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

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

See also Annex I 14.1.

4.1.1. Clozapine (NAP)

Applicant(s): various

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of haematological malignant tumours

EPITT 20150 – New signal

Background

Clozapine is an atypical antipsychotic indicated for the treatment of resistant schizophrenic patients or schizophrenic patients intolerant to other antipsychotics, and in psychotic disorders occurring during the course of Parkinson's disease, in cases where standard treatment has failed.

During routine signal detection activities, a signal of haematological malignant tumours was identified by France, based on literature[4,5,6] and on 1,108 cases retrieved from EudraVigilance. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from literature and the EudraVigilance database, PRAC agreed that further evaluation on the signal haematological malignant tumours is warranted.

PRAC appointed Amelia Cupelli as Rapporteur for the signal.

Summary of recommendation(s)

[3] Each signal refers to a substance or therapeutic class. The route of marketing authorisation is indicated in brackets (CAP for Centrally Authorised Products; NAP for Nationally Authorised Products including products authorised via Mutual Recognition Procedures and Decentralised Procedure). Product names are listed for reference Centrally Authorised Products (CAP) only. PRAC recommendations will specify the products concerned in case of any regulatory action required

[4] Tiihonen J, Tanskanen A, Bell JS, Dawson JL, Kataja V, Taipale H. Long-term treatment with clozapine and other antipsychotic drugs and the risk of haematological malignancies in people with schizophrenia: a nationwide case-control and cohort study in Finland. Lancet Psychiatry. mai 2022;9(5):353-62

[5] Chrétien B, Lelong-Boulouard V, Chantepie S, Sassier M, Bertho M, Brazo P, et al. Haematologic malignancies associated with clozapine v. all other antipsychotic agents: a pharmacovigilance study in VigiBase®. Psychol Med. juill 2021;51(9):1459-66

[6] Hu Y, Gao L, Zhou L, Liu W, Wei C, Liu B, Sun Q, Tian W, Chu RYK, Song S, Cheng FWT, Chan JKN, Ng APP, Lo HKY, Lee KCK, Chang WC, Wong WCW, Chan EWY, Wong ICK, Chai Y, Lai FTT. Rare but elevated incidence of hematological malignancy after clozapine use in schizophrenia: A population cohort study. PLoS Med. 2024 Dec 5;21(12):e1004457. doi: 10.1371/journal.pmed.1004457. PMID:39636825; PMCID: PMC11620352

- In the next PSUR[7], the MAH(s) for clozapine-containing products should submit a literature review on the risk of haematological malignancy associated with duration of treatment with clozapine including the identified literature[8,9,10], discuss the carcinogenic potential of clozapine including any relevant non-clinical evidence and the possible documented underlying mechanism, provide cases coming from clinical trials and describe the haematological monitoring performed during the treatment using the SMQ 'haematological malignant tumours'. In addition, the MAH(s) should provide a discussion on the need to update the product information and/or the risk management plan, and for any safety communication, as warranted.
- PRAC will assess the cumulative review within the PSUR procedure PSUSA/00000836/202503.

4.1.2. Ciltacabtagene autoleucel – CARVYKTI (CAP); idecabtagene vicleucel – ABECMA (CAP); tisagenlecleucel - KYMRIAH (CAP)

Applicants: Bristol-Myers Squibb Pharma EEIG (Abecma), Janssen-Cilag International NV (Carvykti), Novartis Europharm Limited (Kymriah), ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of progressive multifocal leukoencephalopathy

EPITT 20153 – New signal

Background

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

During routine signal detection activities, a signal of progressive multifocal leukoencephalopathy (PML) was identified by EMA, based on 5 cases retrieved from EudraVigilance and literature. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

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

PRAC appointed Gabriele Maurer as Rapporteur for the signal.

Summary of recommendation(s)

- The MAH for Abecma (idecabtagene vicleucel), Carvykti (ciltacabtagene autoleucel) and Kymriah (tisagenlecleucel) should submit to EMA, within 60 days, a cumulative review of the signal of PML, including an analysis of all case reports of human polyomavirus

[7] Data lock point: 3 March 2025
[8] Tiihonen J, Tanskanen A, Bell JS, Dawson JL, Kataja V, Taipale H. Long-term treatment with clozapine and other antipsychotic drugs and the risk of haematological malignancies in people with schizophrenia: a nationwide case-control and cohort study in Finland. Lancet Psychiatry. mai 2022;9(5):353-62
[9] Chrétien B, Lelong-Boulouard V, Chantepie S, Sassier M, Bertho M, Brazo P, et al. Haematologic malignancies associated with clozapine v. all other antipsychotic agents: a pharmacovigilance study in VigiBase®. Psychol Med. juill 2021;51(9):1459-66
[10] Hu Y, Gao L, Zhou L, Liu W, Wei C, Liu B, Sun Q, Tian W, Chu RYK, Song S, Cheng FWT, Chan JKN, Ng APP, Lo HKY, Lee KCK, Chang WC, Wong WCW, Chan EWY, Wong ICK, Chai Y, Lai FTT. Rare but elevated incidence of hematological malignancy after clozapine use in schizophrenia: A population cohort study. PLoS Med. 2024 Dec 5;21(12):e1004457. doi: 10.1371/journal.pmed.1004457. PMID:39636825; PMCID: PMC11620352

infection, John Cunningham (JC) virus cerebrospinal fluid test positive, JC virus granule cell neuronopathy, JC polyomavirus test positive, encephalitis viral, demyelination and JC virus infection and related terms, and a proposal for amending the product information, the RMP and educational material, as warranted.

- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.3. Idecabtagene vicleucel – ABECMA (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP

PRAC Rapporteur: Mari Thorn

Scope: Signal of sarcoidosis

EPITT 20154 – New signal

Background

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

During routine signal detection activities, a signal of sarcoidosis was identified by Spain, based on 2 cases retrieved from the Spanish database (FEDRA) and the literature. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from the retrieved cases and the literature, PRAC agreed that further evaluation on the signal of sarcoidosis is warranted.

Summary of recommendation(s)

- In the next PSUR[11], the MAH for Abecma (idecabtagene vicleucel) should submit a cumulative review of the signal, including the MedDRA high level term (HLT) acute and chronic sarcoidosis and related terms, as well as a literature review, data from spontaneous reports and reports from studies. In addition, the MAH should discuss any need to amend the product information and/or the RMP, as warranted.
- The PRAC will assess the cumulative review within the PSUR procedure PSUSA/00010954/202503.

4.1.4. Regorafenib - STIVARGA (CAP)

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Signal of hyperammonaemia, hyperammonaemic encephalopathy

EPITT 20147 – New signal

Background

[11] Data lock point: 25 March 2025

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

During routine signal detection activities, a signal of hyperammonaemia and hyperammonaemic encephalopathy was identified by EMA, based on 83 cases retrieved from EudraVigilance and literature. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence in EudraVigilance and in the literature, PRAC agreed that there is currently sufficient evidence to amend the product information (PI) to add hyperammonaemic encephalopathy as a warning and undesirable effect.

Summary of recommendation(s)

- The MAH for Stivarga (regorafenib) should submit to EMA, by 7 March 2025, comments on the proposal for amending the product information[12] as well as to propose a frequency for hyperammonaemic encephalopathy considering incidence rates estimated for regorafenib based on pooled clinical trial data across various indications.
- A 30-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.2. Signals follow-up and prioritisation

4.2.1. Adagrasib - KRAZATI (CAP) - EMEA/H/C/006013/SDA/003

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of thrombocytopenia

EPITT 20112 – Follow-up to October 2024

Background

For background information, see PRAC minutes October 2024.

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

Discussion

Having considered the available evidence in EudraVigilance and the MAH's responses, PRAC agreed that the current evidence is insufficient to establish a causal relationship between adagrasib and thrombocytopenia to further warrant an update to the product information and/or risk management plan at present.

Summary of recommendation(s)

- In the next PSUR, the MAH for Krazati (adagrasib) should monitor thrombocytopenia cases emphasising cases without confounded by other treatment.

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

4.2.2. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/SDA/003

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of colitis

EPITT 20113 – Follow-up to October 2024

Background

For background information, see PRAC minutes October 2024.

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

Discussion

Having considered the available evidence in EudraVigilance, in the literature, and the cumulative review submitted by the MAH, PRAC agreed that the product information should be amended to add colitis as an undesirable effect with a frequency 'common'.

Summary of recommendation(s)

- The MAH for Poteligeo (mogamulizumab) should submit to EMA, within 60 days, a variation[13] to update the product information.

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. Atropine - (CAP MAA) - EMEA/H/C/006385, PUMA[14]

Scope (pre D-180 phase): Treatment of myopia in children aged 3 years and older

5.1.2. Deutetrabenazine - (CAP MAA) - EMEA/H/C/006371

Scope (pre D-180 phase): Treatment of tardive dyskinesia

[13] Update of SmPC section 4.8. The package leaflet is to be updated accordingly.
[14] Paediatric Use Marketing Authorisation

5.1.3. Deutivacaftor, tezacaftor, vanzacaftor – (CAP MAA) - EMEA/H/C/006382, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

Scope (pre D-180 phase): Indicated for the treatment of cystic fibrosis

5.1.4. Inavolisib - (CAP MAA) - EMEA/H/C/006353

Scope (pre D-180 phase): Treatment of adult patients with PIK3CA-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer

5.1.5. L-Acetylleucine - (CAP MAA) - EMEA/H/C/006327, Orphan

Applicant: Intrabio Ireland Limited

Scope (pre D-180 phase): Indicated in adults and children from birth for chronic treatment of Niemann-Pick Type C (NPC)

5.1.6. Resminostat - (CAP MAA) - EMEA/H/C/006259, Orphan

Applicant: 4Sc AG

Scope (pre D-180 phase): Treatment of patients with advanced stage mycosis fungoides (MF) and Sézary syndrome (SS)

5.1.7. Sepiapterin - (CAP MAA) - EMEA/H/C/006331, Orphan

Applicant: PTC Therapeutics International Limited

Scope (pre D-180 phase): Treatment of hyperphenylalaninemia (HPA) in adult and paediatric patients with phenylketonuria (PKU)

5.1.8. Teprotumumab - (CAP MAA) - EMEA/H/C/006396

Scope (pre D-180 phase): Treatment of moderate to severe Thyroid Eye Disease (TED)

5.1.9. Zanidatamab - (CAP MAA) - EMEA/H/C/006380, Orphan

Applicant: Jazz Pharmaceuticals Ireland Limited

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

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

See Annex I 15.2.

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

See Annex I 15.3.

6. Periodic safety update reports (PSURs)

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

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

See also Annex I 16.1.

6.1.1. Cladribine[15] - MAVENCLAD (CAP) - PSUSA/00010634/202407

Applicant: Merck Europe B.V.

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Mavenclad, a centrally authorised medicine containing cladribine 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 Mavenclad (cladribine) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the wording on breastfeeding to reflect that there are limited data to indicate excretion in human milk. Therefore, the current terms of the marketing authorisation(s) should be varied[16].
- In the next PSUR, the MAH should provide a cumulative review of autoimmune haemolytic anaemia cases and discuss the need to update the product information (PI), as warranted. In addition, the MAH should provide a comprehensive analysis of the off-label use, as well as continue to review the medication errors and analyse the efficacy of the updated educational materials. The MAH should also discuss and propose the update of the PI regarding the observed liver injury cases in the post marketing setting, and add 'use in breastfed infants of exposed mothers' as a safety concern in the PSUR and propose an update to the PI regarding 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.

6.1.2. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/202407

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

[15] Multiple sclerosis indication only
[16] Update of SmPC section 4.6. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Opdivo, a centrally authorised medicine containing nivolumab 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 Opdivo (nivolumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding patients with pre-existing autoimmune disease (AID), as well as to add optic neuritis as an undesirable effect with frequency 'rare' for nivolumab monotherapy and in combination with ipilimumab (with or without chemotherapy), and with frequency 'not known' for nivolumab in combination with chemotherapy. Therefore, the current terms of the marketing authorisation(s) should be varied[17].
- In the next PSUR, the MAH should provide a cumulative review on the use of nivolumab in patients with pre-existing AID from all available sources, including post-marketing, clinical trial and literature data, and discuss the need to keep the missing information patients with AID in the summary of safety concerns. In addition, the MAH should provide cumulative reviews of hearing impairment and of immune-mediated adverse events in neonates following *in utero* exposure to nivolumab, including data from all available sources and discuss the need to update the product information, as warranted. The MAH should also continue to monitor cases of morphoea and scleroderma including additional analyses of flare-up and *de-novo* case reports, cases cholangitis sclerosing and immune-mediated cholangitis along with a discussion on the need to update the product information, as warranted.

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

6.1.3. Opicapone - ONGENTYS (CAP); ONTILYV (CAP) - PSUSA/00010516/202406

Applicant(s): Bial - Portela & Cª, S.A. (Ongentys), Bial Portela & Companhia S.A. (Ontilyv)

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Ongentys and Ontily, centrally authorised medicines containing opicapone and issued a recommendation on their marketing authorisation(s).

Summary of recommendation(s) and conclusions

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Ongentys and Ontily (opicapone) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add confusional state as undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[18].
- In the next PSUR, the MAH should provide a cumulative review of cases of drug-related hepatic injury especially those with cholestatic signs, differentiating if previous hepatic issues are present, and continue to monitor cases of rhabdomyolysis. The MAH should also provide a cumulative review of cases of patients with moderate/severe hepatic impairment, including an assessing of if a specific pattern of adverse event is reported and whether specific recommendations for patients are needed.

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. Sacubitril, valsartan - ENTRESTO (CAP); NEPARVIS (CAP) - PSUSA/00010438/202407

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Entresto and Neparvis, centrally authorised medicines containing sacubitril/valsartan 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 Entresto and Neparvis (sacubitril/valsartan) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the wording regarding breastfeeding to reflect the limited data on the excretion to the milk, and to add myoclonus as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[19].

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

6.1.5. Tobramycin[20] - TOBI PODHALER (CAP) - PSUSA/00009315/202406

Applicant: Viatris Healthcare Limited

[18] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[19] Update of SmPC sections 4.6 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[20] Inhalation powder, capsules only

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tobi Podhaler, a centrally authorised medicine containing tobramycin 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 Tobi Podhaler (tobramycin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning regarding nephrotoxicity and to add acute kidney injury as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[21].

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

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

See Annex I 16.1.1.

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

See also Annex I 16.3.

6.3.1. Acenocoumarol (NAP) - PSUSA/00000027/202407

Applicant(s): various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure

Background

Acenocoumarol is an antithrombotic agent which belongs to the group of Vitamin K antagonists indicated for the treatment and prevention of thromboembolic events.

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

Summary of recommendation(s) and conclusions

[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.

- Based on the review of the data on safety and efficacy, the benefit-risk balance of acenocoumarol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add anticoagulant related nephropathy as warning and undesirable effect with a frequency 'not known', as well as to add an interaction between acenocoumarol and semaglutide resulting in international normalised ratio decreased. Therefore, the current terms of the marketing authorisation(s) should be varied[22].

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

6.3.2. Busulfan (NAP) - PSUSA/00000464/202407

Applicant(s): various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

Background

Busulfan is a cytotoxic agent indicated for the conditioning treatment prior to haemopoietic progenitor cell transplantation in patients when the combination of high-dose busulfan and cyclophosphamide is considered the best available option, for the palliative treatment of the chronic phase of chronic myeloid leukaemia, in producing prolonged remission in polycythaemia vera particularly in cases with marked thrombocytosis, and in selected cases of essential thrombocythaemia and myelofibrosis, as warranted.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing busulfan 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 busulfan-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add pulmonary hypertension as undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[23].
- In the next PSUR, the MAHs should provide a cumulative review of cases reporting idiopathic pneumonia syndrome and of cardiac tamponade in patients with thalassemia should be provided for busulfan solution for injection only, as well as discuss any amendments in the product information, as warranted.

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

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

6.3.3. Thiocolchicoside (NAP); paracetamol, thiocolchicoside (NAP) - PSUSA/00010464/202407

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Background

Thiocolchicoside is a myorelaxant indicated as an adjuvant for treatment of painful muscle contractures in acute spinal pathology in adults and adolescents from 16 years onwards, for sciatica and lumbar backache, cervical and brachial neuralgia (pain and stiffness in the neck, shoulder and upper limbs), stubborn neck pain, post-traumatic and postoperative pain, as warranted.

Paracetamol is an analgesic and antipyretic. Thiocolchicoside/paracetamol is a fixed-dose combination (FDC) indicated for the treatment of pain.

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of thiocolchicoside- and thiocolchicoside/paracetamol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add injection site reactions including pain, erythema, swelling around the injection site and embolia cutis medicamentosa (Nicolau syndrome) as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[24].
- In the next PSUR, the MAH(s) of thiocolchicoside-containing products in the injectable formulations should provide a cumulative review of cases of intrathecal injection. In addition, the MAHs for the FDC thiocolchicoside/paracetamol should discuss the need to update the product information as regards the disseminated intravascular coagulation in a context of paracetamol overdose.

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

6.3.4. Tiagabine (NAP) - PSUSA/00002942/202406

Applicant(s): various

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

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Background

Tiagabine is an anticonvulsant indicated in adults and children over than 12 years old for the treatment of partial seizures as adjunctive therapy for refractory partial seizures with or without secondarily generalised seizures where control is not achieved by optimal doses of at least one other antiepileptic drug.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing tiagabine 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 tiagabine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add loss of consciousness and confusional state as symptoms in a context of overdose. Therefore, the current terms of the marketing authorisation(s) should be varied[25].

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

6.4. Follow-up to PSUR/PSUSA procedures

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

See also Annex I 16.5.

6.5.1. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0025, Orphan

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC in order to propose a combined Adverse Drug Reaction table for Dravet Syndrome and Lennox-Gastaut syndrome following PSUSA procedure EMEA/H/C/PSUSA/00010907/202306. The package leaflet is updated accordingly

Background

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

[25] Update of SmPC section 4.9. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit a variation to update the product information in order to add warnings and undesirable effects on valvular heart disease and pulmonary arterial hypertension. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation. For further background, see PRAC minutes January 2024.

Summary of recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed to a combined Adverse Drug Reaction table for Dravet Syndrome and Lennox-Gastaut syndrome[26].

6.5.2. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0127

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Update section 4.4 of the SmPC to update the safety information following PSUSA/00010341/202312 procedure in order to assess the safety topics of tuberculosis and hepatitis C virus with secukinumab. The Package Leaflet is updated accordingly

Background

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

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit a cumulative review of cases of tuberculosis and hepatitis C virus infection as part of a post-authorisation measure (PAM-LEG). PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation. For further background, see PRAC minutes September 2024.

Summary of recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed that the product information should be updated to amend the warning on tuberculosis[27].

6.6. Expedited summary safety reviews[28]

None

[26] Update of SmPC section 4.8.
[27] Update of SmPC section 4.4. The package leaflet is updated accordingly.
[28] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

7. Post-authorisation safety studies (PASS)

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

See Annex I 17.1.

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

See Annex I 17.2.

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

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[32]

See also Annex I 17.4.

7.4.1. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0130

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report from study CC-5013-MCL-005 listed as a category 3 study in the RMP. This is a non-interventional, post-authorization safety study of patients with relapsed or refractory mantle cell lymphoma to further investigate and characterize the association of lenalidomide with tumor flare reaction and high tumor burden. The RMP version 42.0 has also been submitted

Background

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

As stated in the RMP of Revlimid (lenalidomide), the MAH conducted a non-imposed non-interventional PASS (CC-5013-MCL-005) to characterize the association of lenalidomide with tumor flare reaction (TFR) and high tumor burden. The Rapporteur assessed the MAH's final study report.

Summary of advice

- Based on the available data and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be considered acceptable provided that the MAH submits satisfactory responses to a request for supplementary information (RSI).
- PRAC considered that the study can be removed from the RMP since it is completed, and

[29] In accordance with Article 107n of Directive 2001/83/EC
[30] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004
[31] In accordance with Article 107p-q of Directive 2001/83/EC
[32] 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

therefore the important identified risk TFR (in mantle cell lymphoma and follicular lymphoma indications) can be removed from the RMP but will remain as a safety concern in the PSUR. In addition, Annex IID and the educational material should be updated accordingly, while no further updates in the product information are warranted at this stage.

- A 60-day assessment timetable was recommended for the assessment.

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

See Annex I 17.5.

7.6. Others

None

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1.

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2.

8.3. Renewals of the marketing authorisation

See Annex I 18.3.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Levonorgestrel (NAP) - DE/H/xxxx/WS/1803

Applicant: Jenapharm GmbH & Co. KG (subsidiary of Bayer) (Mirena, Jaydess, Kyleena)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a worksharing variation procedure (DE/H/xxxx/WS/1803) to update the product information in order to emphasize the need for ultrasound examination after levonorgestrel-intrauterine system (LNG-IUS) insertion to assure correct location of

the IUS and to prevent (partial) perforation, following the conclusion of the PSUSA procedure on levonorgestrel (PSUSA/00010828/202305) concluded in January 2024, at request of Germany

Background

Levonorgestrel is a second-generation progestin (synthetic progesterone) indicated as long-acting reversible contraceptives.

For background information see PRAC minutes January 2024.

In the context of the evaluation of a worksharing variation procedure on updating the product information of LNG-IUS on the use of ultrasound examination, Germany requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC agreed that the product information should be updated to reflect the use of ultrasound examination in the section related to warnings and the method of administration. In addition, PRAC considered that the agreed wording is also applicable to the other LNG-IUS products and therefore should be considered by the relevant MAHs to ensure that the product information of their medicinal products is kept up to date with the current scientific knowledge.

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The Chair welcomed Magdalena Wielowieyska that was appointed as the new alternate for Luxembourg replacing Anne-Cecile Vuillemin who has taken over the role of member.

12.1.2. Vote by proxy

Annalisa Capuano gave a proxy to Milou-Daniel Drici to vote on behalf of her for the entire duration of the meeting.

Hedvig Nordeng gave a proxy to Annete Stark to vote on behalf of her for the entire duration of the meeting.

Georgia Gkegka gave a proxy to Panagiotis Psaras to vote on behalf of her for the entire duration of the meeting.

Gudrun Steffansdottir gave a proxy to David Olsen to vote on behalf of her for the entire duration of the meeting.

Anna Marekova gave a proxy to Eva Jirsova to vote on behalf of her for the entire duration of the meeting.

12.1.3. Committee Meeting Dates for 2027-2028

PRAC noted the information regarding the Committee meeting dates for the 2027-2028 period.

12.1.4. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q4 2024

In line with the adopted PRAC best practice guidance (BPG) on Committee efficiency (see PRAC minutes May 2016 and PRAC minutes June 2018) and the adopted implementation plan for the BPG including goals to measure compliance with the recommendations (see PRAC minutes June 2016 and PRAC minutes June 2018), PRAC was informed on the quantitative measures collected for Q4 2024 of PRAC meetings during the organisational, regulatory and methodological matters (ORGAM) meeting on 27 February 2025. For previous update, see PRAC minutes December 2024[33].

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. PRAC strategic review and learning meeting (SRLM) under the Polish presidency of the European Union (EU) Council – Warsaw, Poland, 1 - 2 April 2025 - agenda

PRAC lead: Adam Przybylkowski

PRAC was informed on the plans for the agenda for the 'PRAC strategic review and learning meeting (SRLM)', to be held on 1-2 April 2025 in Warsaw, Poland, under the Polish presidency of the Council of the European Union (EU). The committee was informed that this is a joined PRAC-CMDh meeting and was also briefed on the potential topics and requested to propose any new ones. The agenda will be finalised and the invitations will be sent by end of February 2025.

Post meeting note: The agenda was finalised and among the topics to be discussed are the PSUSA NAPs workload in the future, pharmacovigilance and safety in the paediatric population and breastfeeding approach, rare diseases, signal management and GVP updates, scientific/regulatory/administrative support to PRAC members, national patient reporting systems and management of adverse events.

12.5. Cooperation with International Regulators

None

[33] Held 25 - 28 November 2024

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. EU Pharmacovigilance system - quarterly workload measures and performance indicators – Q4 2024 and predictions

At the organisational, regulatory and methodological matters (ORGAM) meeting on 27 February 2025, the EMA Secretariat presented to PRAC an overview of the quarterly figures on the EMA pharmacovigilance system-related workload and performance indicators. In addition, PRAC was informed that the exercise to review the workload measures and pharmacovigilance indicators was finalised and that the next update with the revised indicators will be done next year. For the previous update and further information, see PRAC minutes November 2024[34].

12.8.2. PRAC workload statistics – Q4 2024

At the organisational, regulatory and methodological matters (ORGAM) meeting on 27 February 2025, the EMA secretariat informed PRAC about the quarterly and cumulative figures to estimate the evolution of the PRAC workload for Q4 2024, by reflecting on the number of procedures and agenda items covered at each PRAC plenary meeting. For previous update, see PRAC minutes November 2024[35].

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

[34] Held 28-31 October 2024
[35] Held 28-31 October 2024

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

None

12.10.3. PRAC workload in 2025 based on new PSUR frequencies predicted by the EURD Tool

PRAC lead: Ulla Wändel Liminga

The EMA Secretariat presented the PRAC workload provisioned for 2025 based on new PSUR frequencies predicted by the EURD Tool. PRAC discussed ways on how to manage the increased workload and agreed to further explore the possibilities before communicating to the relevant stakeholders.

12.10.4. PSURs repository

None

12.10.5. 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 February 2025, reflecting the PRAC's comments impacting on the data lock point (DLP) and PSUR submission frequencies of the substances/combinations. PRAC endorsed the newly allocated Rapporteurs for upcoming PSUSAs in accordance with the principles previously endorsed by PRAC (see PRAC minutes April 2013).

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

12.11. Signal management

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

PRAC lead: Martin Huber

PRAC was updated on the ongoing activities of the SMART working group – work stream Methods meeting held on 5 December 2024. Among the topics discussed were an update from the Pregnancy Focus Group and specifically on the pregnancy algorithm for identifying adverse events and some use cases, the feasibility of signal detection for the pharmacokinetic drug-drug interaction during pregnancy in spontaneous reporting systems,

and a brief update on the Health Data Lab. PRAC noted the information. For the previous update, see PRAC minutes December 2024[36].

12.11.2. Signals and safety analytics project – update on activities

PRAC lead: Martin Huber

An update on the ongoing signals and safety analytics (SSA) project intending to replace the current tools for signal detection and validation (i.e. t eRMR, line listing, ICSR form and EVDAs catalogue of reports) was presented to PRAC. For background information, see PRAC minutes February 2024. PRAC members were invited to provide their views on the proposal for the future handling of eRMR comments by 28 February 2025.

Post-meeting note: PRAC endorsed the proposals in writing on 10 March 2025.

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. Guideline on masking of personal data in Individual Case Safety Reports (ICSRs) submitted to EudraVigilance

Following the European Data Protection Supervisor (EDPS) recommendations triggered by the EDPS audit to EudraVigilance database, the EMA Secretariat presented to PRAC, at the organisational, regulatory and methodological matters (ORGAM) meeting on 27 February 2025, the developed guideline on masking of personal data for the ICSRs submitted to EudraVigilance. The steps done so far including the parties consulted have been presented, while this guideline is planned to be added as Addendum II of GVP VI. PRAC was asked to provide comments by 17 March 2025.

[36] Held 25 - 28 November 2024

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. Concept paper on clinical evaluation of therapeutic radiopharmaceuticals in oncology (EMA/CHMP/451705/2024)

At the organisational, regulatory and methodological matters (ORGAM) meeting on 27 February 2025 the EMA Secretariat presented the concept paper on clinical evaluation of therapeutic radiopharmaceuticals (tRPs) in oncology (EMA/CHMP/451705/2024) which has the objective to identify aspects that are specific for tRPs that need to be addressed in the future guideline and to complement the more general guideline on the clinical evaluation of anticancer medicinal products (EMA/CHMP/205/95 Rev.6). The work of the drafting group was presented along with the steps done so far, as the paper was released for public consultation in October 2024. Among others, the concept paper plans to collect post-approval data with long term follow-up to identify late toxicity and possible tRP-specific risk mitigation strategies. PRAC members were invited to send their comments in writing.

12.21.2. Good Pharmacovigilance Practice (GVP) Guideline on product or population specific considerations III: pregnancy and breastfeeding

PRAC lead: Ulla Wändel Liminga

The EMA Secretariat presented an outline on the work done so far regarding the update of GVP P.III which was released for public consultation in 2020. For further background, see PRAC minutes October 2019[37] and PRAC minutes December 2022[38]. PRAC was informed on the updates proposed by the drafting group and PRAC members were invited to provide any comments on the final draft text by the middle of March 2025.

12.21.3. Good Pharmacovigilance Practices (GVP) module XVI – Addendum on pregnancy - update

PRAC lead: Ulla Wändel Liminga

The topic was postponed to an upcoming PRAC meeting.

12.21.4. HES court case - key points from the General Court's judgment

The EMA Secretariat presented to PRAC the key points from the General Court's judgement regarding the HES court case (Case T-416/22) as well as learnings for the regulation of risks related to the off-label use. In its judgment of 15 May 2024, the General Court sided with EMA and the Commission and ruled that the suspension of HES products was lawful, confirming that the risks related to the off-label use of a medicinal product may inform the assessment of the risk-benefit balance and may serve as the basis for (post-authorisation) regulatory action. PRAC noted the information.

12.21.5. IRIS training - demo

The EMA Secretariat provided a demo on the IRIS functionalities as well as the impact of the transition to IRIS for PRAC, including format of monthly agendas. PRAC noted the information.

[37] Held 30 September – 03 October 2019
[38] Held 28 November - 01 December 2022

12.21.6. Revision of the procedural advice on CHMP/CAT/PRAC Rapporteur/Co-Rapporteur appointment principle

The EMA Secretariat presented the revised procedural advice on CHMP/CAT/PRAC (Co-) Rapporteur appointment principle and highlighted the changes affecting PRAC. PRAC noted the revision, and members were invited to provide any comments. The procedural advice is foreseen to be published on the external EMA website after its adoption.

Post-meeting note: the Procedural advice on CHMP/CAT/PRAC rapporteur/corapporteur appointment principles, objective criteria and methodology in accordance with Article 62(1) of Regulation (EC) No 726/2004 was published on the EMA website on 27 February 2025.

12.21.7. US-FDA-EMA collaboration on gene therapies for (ultra) rare diseases (CoGenT) pilot

At the organisational, regulatory and methodological matters (ORGAM) meeting on 27 February 2025, the EMA Secretariat presented the pilot project with the US-FDA to enhance collaboration on gene therapies for (ultra) rare diseases. The aim of the pilot is to exchange information and enhance participation as observers in each other's meetings. PRAC noted the information.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[39]

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[40].

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Vortioxetine – BRINTELLIX (CAP); NAP

Applicant(s): H. Lundbeck A/S, various

PRAC Rapporteur: Jo Robays

Scope: Signal of hallucinations, not related to serotoninergic syndrome

EPITT 20152 – New signal

[39] 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

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

14.2. New signals detected from other sources

None

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

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

15.1.1. Denosumab - (CAP MAA) - EMEA/H/C/006434

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

15.1.2. Denosumab - (CAP MAA) - EMEA/H/C/006435

Scope (pre D-180 phase): Prevention of skeletal related events with advanced malignancies

15.1.3. Denosumab - (CAP MAA) - EMEA/H/C/006199

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

15.1.4. Denosumab - (CAP MAA) - EMEA/H/C/006376

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

15.1.5. Denosumab - (CAP MAA) - EMEA/H/C/006152

Scope (pre D-180 phase): For the treatment of osteoporosis and bone loss

15.1.6. Denosumab - (CAP MAA) - EMEA/H/C/006377

Scope (pre D-180 phase): For the treatment of osteoporosis and bone loss

15.1.7. Octreotide - (CAP MAA) - EMEA/H/C/006322, Orphan

Applicant: Camurus AB

Scope (pre D-180 phase): Treatment of acromegaly

15.1.8. Teriparatide - (CAP MAA) - EMEA/H/C/005687

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

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. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/WS2819/0053; Semaglutide - WEGOVY (CAP) - EMEA/H/C/005422/WS2819/0029

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: To align the RMPs to the version approved for Rybelsus on 3 October 2024

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

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

15.3.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/II/0026

Applicant: AstraZeneca AB

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Extension of indication to include CALQUENCE as monotherapy for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy based on final results from study ACE-LY-004 (D8225C00002); this is an open-label, phase 2 study of ACP-196 in subjects with Mantle Cell Lymphoma. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial and formatting changes to the PI

15.3.2. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0052, Orphan

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.2 of the SmPC in order to update the posology recommendations by removing the current recommendation of a maximum of four implants per year, based on a literature review and analysis of safety data. The Package Leaflet is updated accordingly. The RMP version 9.8 has also been submitted. In addition, the MAH took the opportunity to introduce a minor editorial change to the Product Information

15.3.3. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/II/0044

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information based on the final results from study 18-513 (ANNEXA-I), listed as a specific obligation in the Annex II; this is a phase 4 randomised controlled trial to investigate the efficacy and safety of andexanet alfa versus usual care in patients with acute intracranial haemorrhage taking apixaban, rivaroxaban or edoxaban. Consequently, the MAH proposes a switch from conditional marketing authorisation to full marketing authorisation. The Annex II and Package Leaflet are updated accordingly. The updated RMP version 4.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to bring it in line with the latest QRD template version 10.3

15.3.4. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/II/0046/G

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: A grouped application consisting of:
C.I.4: Update of sections 4.2, 4.4, 4.6 and 4.8 of the SmPC in order to add the immune-mediated adverse reactions sclerosing cholangitis, arthritis, polymyalgia rheumatica, and Sjogren's syndrome based on post-marketing data and literature. The Package Leaflet is updated accordingly. The RMP version 7.3 has also been submitted.

C.I.4: Update of section 4.8 of the SmPC in order to update the immunogenicity information based on results from studies EMR100070-003, B9991003 and 100/B9991001. Study EMR100070-003 is a Phase 2, single-arm, open label, multicenter study to investigate the clinical activity and safety of avelumab in patients with mMCC. T. Study B9991003 is a Phase 3 multinational, multicenter, randomized (1:1), open-label, parallel 2 - arm study of avelumab in combination with axitinib versus sunitinib monotherapy in the 1L treatment of participants with aRCC. Study 100/B9991001 is a Phase 3, multicenter, multinational, randomized, open-label, parallel-arm efficacy and safety study of avelumab plus best supportive care (BSC) versus BSC alone as a maintenance treatment in adult participants with locally advanced or metastatic UC whose disease did not progress after completion of 1L platinum-containing chemotherapy

15.3.5. Bempedoic acid - NILEMDO (CAP) - EMEA/H/C/004958/WS2798/0045; Bempedoic acid, ezetimibe - NUSTENDI (CAP) - EMEA/H/C/004959/WS2798/0050

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.2, 4.4, and 5.2 of the SmPC in order to amend information concerning renal impairment based on the final results from Study 1002-071 listed as a category 3 study in the RMP; this is a phase 1, open-label, single-dose study to evaluate the pharmacokinetics of bempedoic acid in healthy subjects with normal renal function and subjects with end-stage renal disease receiving haemodialysis; the Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted

15.3.6. Chikungunya virus, strain delta5nsP3, live attenuated - IXCHIQ (CAP) - EMEA/H/C/005797/II/0001

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include active immunisation for the prevention of disease caused by chikungunya virus (CHIKV) in adolescents 12 years and older for IXCHIQ, based on interim 6 months results from study VLA1553-321; this is a randomized, double-blinded, multicentre study to evaluate the immunogenicity and safety of the adult dose of VLA1553 6 months following vaccination in adolescents from 12 years to less than 18 years of age after a single immunization. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI

15.3.7. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/II/0036, Orphan

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: Update of sections 4.8, and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs), and update clinical efficacy and safety information based on second interim analysis from study 68284528MMY3002 (CARTITUDE-4); this is a phase 3 randomized study comparing ciltacabtagene autoleucel, a chimeric antigen receptor T cell (CAR-T) therapy directed against BCMA, versus Pomalidomide, Bortezomib and Dexamethasone (PVd) or Daratumumab, Pomalidomide and Dexamethasone (DPd) in subjects with relapsed and lenalidomide-refractory multiple myeloma; The RMP version 5.3 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

15.3.8. Covid-19 Vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/II/0096/G

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Grouped quality variations; RMP version 6.1 has also been submitted

15.3.9. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0077, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include daratumumab for the treatment of adult patients with smouldering multiple myeloma (SMM) at high risk of developing multiple myeloma based on results from studies 54767414SMM3001 (AQUILA) and 54767414SMM2001 (CENTAURUS). SMM3001 (AQUILA) is a Phase 3 Randomized, Multicenter Study of Subcutaneous Daratumumab Versus Active Monitoring in Subjects with High-risk Smoldering Multiple Myelom. SMM2001 (CENTAURUS) is a Randomized Phase 2 Trial to

Evaluate Three Daratumumab Dose Schedules in Smoldering Multiple Myeloma.
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 11.2 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI in accordance with the latest EMA excipients guideline

15.3.10. Ebola vaccine (rDNA[41], replication-incompetent) - MVABEA (CAP) - EMEA/H/C/005343/II/0021

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy based on final results from study VAC52150EBL3010 listed as a category 3 study in the RMP as well as study VAC52150EBL3008 and two post-authorization vaccination campaigns. Study VAC52150EBL3010 is a phase 3 open-label randomized clinical trial to evaluate the safety, reactogenicity and immunogenicity of a 2-dose Ebola vaccine regimen of Ad26.ZEBOV followed by MVA-BN-Filo in healthy pregnant women. The Package Leaflet is updated accordingly. The RMP version 3.3 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI

15.3.11. Ebola vaccine (rDNA[42], replication-incompetent) - ZABDENO (CAP) - EMEA/H/C/005337/II/0019

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy based on final results from study VAC52150EBL3010 listed as a category 3 study in the RMP as well as study VAC52150EBL3008 and two post-authorisation vaccination campaigns. Study VAC52150EBL3010 is a phase 3 open-label randomized clinical trial to evaluate the safety, reactogenicity and immunogenicity of a 2-dose Ebola vaccine regimen of Ad26.ZEBOV followed by MVA-BN-Filo in healthy pregnant women. The Package Leaflet is updated accordingly. The RMP version 3.3 has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the Product Information

15.3.12. Glofitamab - COLUMVI (CAP) - EMEA/H/C/005751/II/0010, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Submission of the updated 2-year follow-up report from study NP30179 listed as a Specific Obligation in the Annex II of the Product Information. This is a multicenter, open-label Phase I/II study to evaluate the safety, efficacy, tolerability, and pharmacokinetics of escalating doses of glofitamab in patients with relapsed/refractory B-cell Non-Hodgkin's Lymphoma (NHL). The Annex II and the RMP version 4.0 are updated accordingly. Consequently, the MAH proposes a switch from conditional marketing authorisation to full

[41] Ribosomal deoxyribonucleic acid
[42] Ribosomal deoxyribonucleic acid

marketing authorisation

15.3.13. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/X/0043/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Extension application to:
- introduce a new pharmaceutical form (concentrate for solution for infusion), a new strength (200 mg) and a new route of administration (intravenous use)
- add a new strength of 200 mg for solution for injection (in pre-filled syringe / pre-filled pen) for subcutaneous use
This application is grouped with a type II variation (C.I.6.a) to include the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy, a biologic treatment, or a Janus kinase (JAK) inhibitor for Tremfya, based on results of a Phase 2b/3 clinical development programme (CNTO1959UCO3001) consisting of 3 separate studies, an Induction dose finding Study 1 Phase 2b, an Induction Study 2 Phase 3 and a Phase 3 Maintenance Study. These studies were randomized, double-blind, placebo-controlled, parallel-group, multicenter studies that evaluated the efficacy and safety of guselkumab in participants with moderately to severely active UC. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC of the already approved form 100 mg solution for injection are updated. The Package Leaflet and Labelling are updated in accordance. Version 10.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce editorial changes to the PI

15.3.14. Inebilizumab - UPLIZNA (CAP) - EMEA/H/C/005818/II/0012

Applicant: Horizon Therapeutics Ireland DAC

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of adult patients with Immunoglobulin G4-Related Disease (IgG4-RD) for UPLIZNA, based on primary analysis results from study MITIGATE (VIB0551.P3.S2) for all subjects from the completed 52-week randomised-controlled period. This is a pivotal phase 3 multicentre, randomised, double-blind, placebo-controlled, parallel-cohort study to evaluate the efficacy and safety of inebilizumab in adult subjects with IgG4-RD. As a consequence, sections 4.1, 4.2, 4.4 ,4.5, 4.6, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and Package Leaflet are updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI and to bring it in line with the latest QRD template version 10.4. As part of the application, the MAH is requesting a 1-year extension of the market protection

15.3.15. Quadrivalent influenza vaccine (recombinant, prepared in cell culture) (rDNA[43]) - SUPEMTEK TETRA (CAP) - EMEA/H/C/005159/II/0021/G

Applicant: Sanofi Winthrop Industrie

[43] Ribosomal deoxyribonucleic acid

PRAC Rapporteur: Zoubida Amimour

Scope: Grouped application comprising two type II variations as follows:
C.I.6.a – Extension of indication to include the treatment of children 9 years of age and older for Supemtek, based on final results from study VAP00027; this is a Phase III, non-randomized, open-label, uncontrolled study to demonstrate the non-inferior HAI immune response of RIV4 for the 4 strains in participants aged 9 to 17 years vs participants aged 18 to 49 years; As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted.
C.I.4 - Update of sections 4.8 and 5.1 of the SmPC in order to update paediatric information based on final results from study VAP00026; this is a Phase III, randomized, modified double-blind, active-controlled 2-arm to demonstrate the non-inferior HAI immune response of RIV4 vs licensed IIV4 for the 4 strains based on the egg-derived antigen in all participants. Version 2.0 of the RMP has also been submitted

15.3.16. Liraglutide - SAXENDA (CAP) - EMEA/H/C/003780/II/0042

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include the use of SAXENDA for weight management in children from the age of 6 years to less than 12 years based on results from study NN8022-4392; this is a 56-week, double-blind, randomised, placebo-controlled study investigating safety and efficacy of liraglutide on weight management in children with obesity aged 6 to <12 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 34.0 of the RMP has also been submitted

15.3.17. Maralixibat - LIVMARLI (CAP) - EMEA/H/C/005857/X/0015, Orphan

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new pharmaceutical form (tablet) associated with new strengths 10 mg, 15 mg, 20 mg and 30 mg.
The RMP (version 5.0) is updated in accordance

15.3.18. Odevixibat - KAYFANDA (CAP) - EMEA/H/C/006462/II/0001/G

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application consisting of:
C.I.4: Update of sections 4.4, 4.8, and 5.1 of the SmPC based on results from Study A4250-015 listed as a category 3 study in the RMP; this is a Phase 3, multicentre, open-label extension study to evaluate the long-term safety and efficacy of odevixibat in patients with ALGS. The Package Leaflet is updated accordingly. The RMP version 6.2 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.

C.I.13: Submission of the 72 week report from study A4250-008. This is a Phase 3, multicentre, open-label extension study to investigate the long-term efficacy and safety of odevixibat in patients with Progressive Familial Intrahepatic Cholestasis Types 1 and 2 (PEDFIC 2)

15.3.19. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/X/0127

Applicant: Upjohn EESV

PRAC Rapporteur: Liana Martirosyan

Scope: Extension application to introduce a new pharmaceutical form (orodispersible tablet)

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. Ritlecitinib - LITFULO (CAP) - EMEA/H/C/006025/II/0007

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of section 4.8 of the SmPC in order to update of the long-term efficacy and safety information based on interim results from study B7981032 listed as a category 3 study in the RMP; this is a Phase 3 Open-Label, Multi-Center, Long-Term Study Investigating the Safety and Efficacy of PF-06651600 in Adult and Adolescent Participants With Alopecia Areata. The RMP version 2 has also been submitted

15.3.22. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/X/0031

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new pharmaceutical form (film-coated tablets) associated with new strengths (40 mg, 80 mg, 120 mg and 160 mg).
The RMP (version 7.1) is updated in accordance

15.3.23. Sorafenib - NEXAVAR (CAP) - EMEA/H/C/000690/II/0059, Orphan

Applicant: Bayer AG

PRAC Rapporteur: Mari Thorn

Scope: Update of section 5.3 of the SmPC in order to update preclinical safety data on

carcinogenicity studies based on final results from studies T4079666 - Carcinogenicity Study in CD-1 Mice (2 Years Administration by Diet) and T8076320 - Carcinogenicity Study in Wistar Rats (2 Years Administration in the Diet with Dose Adjustment). In addition, the MAH took the opportunity to introduce editorial changes to the PI and to update the list of local representatives in the Package Leaflet

15.3.24. Spesolimab - SPEVIGO (CAP) - EMEA/H/C/005874/X/0011

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Zoubida Amimour

Scope: Extension application to add a new strength of 300 mg (150 mg/ml) for solution for injection in a pre-filled syringe.
The RMP (version 3.0) is updated in accordance.
In addition, the applicant has updated SmPC (Annex I) and Package Leaflet (Annex IIIB) for both 450 mg concentrate for solution for infusion and 150 mg and 300 mg solution for injection in line with the new excipient guideline

15.3.25. Tasimelteon - HETLIOZ (CAP) - EMEA/H/C/003870/X/0039, Orphan

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (4 mg/ml oral solution). The new formulation is indicated for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in paediatric patients 3 to 15 years of age. The RMP (version 5.0) is updated in accordance

15.3.26. Tirzepatide - MOUNJARO (CAP) - EMEA/H/C/005620/II/0038

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of symptomatic chronic heart failure with preserved ejection fraction (HFpEF) in adults with obesity for MOUNJARO, based on results from the Phase 3 trial I8F-MC-GPID (SUMMIT). SUMMIT was a randomized, multicenter, international, placebo-controlled, double-blind, parallel-arm study in participants with HFpEF and obesity. The study was designed to evaluate the effect of tirzepatide compared with placebo on both clinical and symptomatic or functional outcomes. As a consequence, sections 4.1, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted

15.3.27. Tislelizumab - TEVIMBRA (CAP) - EMEA/H/C/005919/II/0017

Applicant: Beigene Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include, in combination with gemcitabine and cisplatin, the first-line treatment of adult patients with recurrent or metastatic nasopharyngeal carcinoma (NPC) for TEVIMBRA based on final results from study BGB-A317-309 (study 309). Study

309 was a Phase 3 randomised, double-blind, placebo-controlled, Asia-only study that compared the efficacy and safety of tislelizumab combined with gemcitabine plus cisplatin (GC) versus placebo combined with GC as 1L treatment for recurrent or metastatic NPC. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.6 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce editorial and administrative changes to the PI as well as to update the PI in line with the Excipients Guideline

15.3.28. Trabectedin - YONDELIS (CAP) - EMEA/H/C/000773/II/0070

Applicant: Pharma Mar, S.A.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.4 and 4.6 of the SmPC in order to update the contraceptive precautions when receiving Yondelis, in line with EMA recommendations. The Package Leaflet is updated accordingly. The RMP version 11.1 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4

15.3.29. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/II/0048

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include treatment of adult patients with unresectable or metastatic HER2-low or HER2-ultralow breast cancer (BC) who have received at least one endocrine therapy in the metastatic setting for ENHERTU, based on results from study D9670C00001 (DESTINY-Breast06); this is a phase 3, randomized, multicentre, open-label study of trastuzumab deruxtecan (DS-8201a) compared with investigator's choice chemotherapy in, hormone receptor-positive, HER2-low and HER2-ultralow BC patients whose disease has progressed on endocrine therapy in the metastatic setting. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI, to update the list of local representatives in the Package Leaflet and to update the PI according to the Excipients Guideline

15.3.30. Ustekinumab - PYZCHIVA (CAP) - EMEA/H/C/006183/X/0006

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new strength (45 mg solution for injection in a vial) for partial use in paediatric patients

15.3.31. Valoctocogene roxaparvovec - ROCTAVIAN (CAP) - EMEA/H/C/005830/II/0014, Orphan

Applicant: BioMarin International Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Update of the Annex II in order to propose changes to the current marketing authorisation obligations for ROCTAVIAN. The RMP version 1.3 has also been submitted

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

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

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

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

16.1.1. Anifrolumab - SAPHNELO (CAP) - PSUSA/00010980/202407

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.2. Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/202407

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.3. Atazanavir - REYATAZ (CAP) - PSUSA/00000258/202406

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.1.4. Avapritinib - AYVAKYT (CAP) - PSUSA/00010878/202407

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.5. Beclometasone, formoterol, glycopyrronium bromide - RIARIFY (CAP); TRIMBOW (CAP); TRYDONIS (CAP) - PSUSA/00010617/202407

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.6. Birch bark extract[44] - FILSUVEZ (CAP) - PSUSA/00010446/202407

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

16.1.7. Brexpiprazole - RXULTI (CAP) - PSUSA/00010698/202407

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Miroslava Gocova

Scope: Evaluation of a PSUSA procedure

16.1.8. Brexucabtagene autoleucel - TECARTUS (CAP) - PSUSA/00010903/202407

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.9. Budesonide[45] - JORVEZA (CAP) - PSUSA/00010664/202407

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

16.1.10. Canakinumab - ILARIS (CAP) - PSUSA/00000526/202406

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.11. Casirivimab, imdevimab - RONAPREVE (CAP) - PSUSA/00010963/202407

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

[44] Centrally authorised product(s) only
[45] For centrally authorised product(s) indicated for eosinophilic esophagitis only

Scope: Evaluation of a PSUSA procedure

16.1.12. Cenegermin - OXERVATE (CAP) - PSUSA/00010624/202407

Applicant: Dompe' Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.13. Danicopan - VOYDEYA (CAP) - PSUSA/00011056/202407

Applicant: Alexion Europe

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.14. Darolutamide - NUBEQA (CAP) - PSUSA/00010843/202407

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.15. Decitabine, cedazuridine - INAQOVI (CAP) - PSUSA/00000118/202407

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.1.16. Eptacog beta (activated) - CEVENFACTA (CAP) - PSUSA/00011006/202407

Applicant: Laboratoire Francais du Fractionnement et des Biotechnologies

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.17. Faricimab - VABYSMO (CAP) - PSUSA/00011016/202407

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

16.1.18. Finerenone - KERENDIA (CAP) - PSUSA/00010978/202407

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.19. Gefapixant - LYFNUA (CAP) - PSUSA/00000132/202407

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.20. Glucagon[46] - BAQSIMI (CAP); OGLUO (CAP) - PSUSA/00010826/202407

Applicant(s): Amphastar France Pharmaceuticals (BAQSIMI), Tetris Pharma B.V. (Ogluo)

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.1.21. Glucarpidase - VORAXAZE (CAP) - PSUSA/00010968/202407

Applicant: SERB S.A.S.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.22. Guselkumab - TREMFYA (CAP) - PSUSA/00010652/202407

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.23. Ibandronic acid - BONDRONAT (CAP); BONVIVA (CAP) - PSUSA/00001702/202406

Applicant(s): Atnahs Pharma Netherlands B.V. (Bondronat, Bonviva)

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.24. Icatibant - FIRAZYR (CAP) - PSUSA/00001714/202407

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.25. Icosapent ethyl - VAZKEPA (CAP) - PSUSA/00010922/202407

Applicant: Amarin Pharmaceuticals Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

[46] For centrally authorised product(s) only

16.1.26. Imipenem, cilastatin, relebactam - RECARBRIO (CAP) - PSUSA/00010830/202407

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.27. Inotersen - TEGSEDI (CAP) - PSUSA/00010697/202407

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

16.1.28. Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/202407

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.29. Mirabegron - BETMIGA (CAP) - PSUSA/00010031/202406

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

16.1.30. Odevixibat - BYLVAY (CAP) - PSUSA/00010949/202407

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.31. Paliperidone - BYANNLI (CAP); INVEGA (CAP); TREVICTA (CAP); XEPLION (CAP) - PSUSA/00002266/202406

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.1.32. Palivizumab - SYNAGIS (CAP) - PSUSA/00002267/202406

Applicant: AstraZeneca AB

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.1.33. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted, prepared in cell cultures) - INCELLIPAN (CAP); zoonotic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted, prepared in cell cultures) - CELLDEMIC (CAP) - PSUSA/00011057/202407

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.34. Pirtobrutinib - JAYPIRCA (CAP) - PSUSA/00000155/202407

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.35. Remimazolam - BYFAVO (CAP) - PSUSA/00010924/202407

Applicant: Paion Pharma GmbH

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.1.36. Smallpox and monkeypox vaccine (Live Modified Vaccinia Virus Ankara) - IMVANEX (CAP) - PSUSA/00010119/202407

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.37. Spheroids of human autologous matrix-associated chondrocytes - SPHEROX (CAP) - PSUSA/00010630/202407

Applicant: Co.Don GmbH, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.38. Tafasitamab - MINJUVI (CAP) - PSUSA/00010951/202407

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.39. Tebentafusp - KIMMTRAK (CAP) - PSUSA/00010991/202407

Applicant: Immunocore Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.40. Tocofersolan - VEDROP (CAP) - PSUSA/00002981/202407

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

16.1.41. Voclosporin - LUPKYNIS (CAP) - PSUSA/00011020/202407

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.42. Voretigene neparvovec - LUXTURNA (CAP) - PSUSA/00010742/202407

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

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

16.2.1. Cabazitaxel - CABAZITAXEL ACCORD (CAP); JEVTANA (CAP); NAP - PSUSA/00000476/202406

Applicant(s): Accord Healthcare S.L.U. (Cabazitaxel Accord), Sanofi Winthrop Industrie (Jevtana), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

16.3.1. Benzalkonium chloride, ethyl alcohol (NAP); benzalkonium chloride, isopropyl alcohol (NAP) - PSUSA/00000342/202407

Applicant(s): various

PRAC Lead: Guðrún Stefánsdóttir

Scope: Evaluation of a PSUSA procedure

16.3.2. Brivudine (NAP) - PSUSA/00000434/202407

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.3.3. Clebopride (NAP) - PSUSA/00000789/202406

Applicant(s): various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

16.3.4. Dexchlorpheniramine (NAP) - PSUSA/00000989/202406

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.3.5. Glibenclamide, metformin hydrochloride (NAP) - PSUSA/00002002/202406

Applicant(s): various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

16.3.6. Human fibrinogen (NAP) - PSUSA/00001624/202406

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.3.7. Human plasma proteins with no less than 95% albumin (NAP) - PSUSA/00010605/202407

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.3.8. Manidipine (NAP) - PSUSA/00001932/202406

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.3.9. Nilutamide (NAP) - PSUSA/00002163/202407

Applicant(s): various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.3.10. Nimesulide[47] (NAP) - PSUSA/00009236/202406

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.3.11. Phentermine, topiramate (NAP) - PSUSA/00010956/202407

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.3.12. Propranolol[48] (NAP) - PSUSA/00010251/202406

Applicant(s): various

PRAC Lead: Guðrún Stefánsdóttir

Scope: Evaluation of a PSUSA procedure

16.3.13. Rabbit anti-human T-lymphocyte immunoglobulin (NAP) - PSUSA/00010252/202406

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

16.3.14. Rabbit anti-human thymocyte immunoglobulin (NAP) - PSUSA/00010184/202406

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

16.3.15. Tianeptine (NAP) - PSUSA/00002943/202406

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.4. Follow-up to PSUR/PSUSA procedures

None

[47] Systemic formulation(s) only
[48] All except centrally authorised product(s) only

16.5. Variation procedure(s) resulting from PSUSA evaluation

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

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

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

16.6. Expedited summary safety reviews[49]

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)[50]

17.1.1. Exagamglogene autotemcel – CASGEVY (CAP) - EMEA/H/C/PSA/S/0113.2

Applicant: Vertex Pharmaceuticals (Ireland), ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Substantial amendment to a protocol for a long-term registry-based study of patients with transfusion-dependent β-thalassemia (TDT) or sickle cell disease (SCD) treated with exagamglogene autotemcel (exa-cel) [MAH's response to PSA/S/0113.1]

17.1.2. Voretigene neparvovec – LUXTURNA (CAP) - EMEA/H/C/PSA/S/0114.1

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Substantial amendment to a post-authorization observational study to collect long-term safety information (i.e., for 5 years after treatment) associated with voretigene neparvovec (vector and/or transgene), its subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products [MAH's response

[49] 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
[50] In accordance with Article 107n of Directive 2001/83/EC

to PSA/S/0114]

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[51]

17.2.1. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 006.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Petar Mas

Scope: From II-0010
Revised Protocol for PASS B7451120
Title: A Prospective Active Surveillance Study to Monitor Growth, Development, and Maturation Among Adolescents with Atopic Dermatitis Exposed to Abrocitinib" (as listed in PART III of the EU Risk Management Plan (Version 4.4)

17.2.2. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 003.4

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: PASS Study No. PS0036 (non-imposed/non-interventional)
Bimekizumab pregnancy exposure and outcome registry. An OTIS Autoimmune Diseases in Pregnancy Study.
The objective of this study is to assess maternal, foetal and infant outcomes among people who become pregnant while exposed to bimekizumab relative to the outcomes in 2 matched comparator populations.
Revised Protocol (Version 3, Amendment #2) / Study No. PS0036

17.2.3. Cannabidiol - EPIDYOLEX (CAP) - EMEA/H/C/004675/MEA 012

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: From initial MAA
Proposal for change in data collection for PASS GWEP21042
A Prospective, Observational Cohort Study to Assess Long-Term Safety in Patients Prescribed Epidyolex with a Focus on Drug-induced Liver Injury (DILI).

17.2.4. Covid-19 Vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 004.8

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: ***Updated Protocol / Study 2019nCoV-402*** Protocol version 5.0
UK Post-Authorisation Safety Study Using the Clinical Practice Research Datalink (CPRD): A surveillance study to characterise the safety profile of Nuvaxovid in adults aged 18 years and older in the real-world setting using the UK CPRD

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

17.2.5. Covid-19 Vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 006.5

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: ***Updated Protocol / Study 2019nCoV-404*** Protocol version 5.0
US Post-authorisation safety study to evaluate the pooled of risk of selected AESI within specified time periods after vaccination with Nuvaxovid using a claim and/or EHR database

17.2.6. Crovalimab - PIASKY (CAP) - EMEA/H/C/006061/MEA 002

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: From initial MAA
Protocol for PASS MO45473 (Cat. 3/non-imposed/RMP)
Crovalimab safety study to characterise safety events and special conditions including pregnancy and infant outcomes in the IPIG registry

17.2.7. Delgocitinib - ANZUPGO (CAP) - EMEA/H/C/006109/MEA 003

Applicant: LEO Pharma A/S

PRAC Rapporteur: Liana Martirosyan

Scope: From initial MAA
PASS Protocol (Cat. 3/NI/NI)
Delgocitinib cream 20 mg/g in moderate to severe chronic hand eczema and risk of non-melanoma skin cancer: a nationwide registry based long-term post-authorization safety study

17.2.8. Eptinezumab - VYEPTI (CAP) - EMEA/H/C/005287/MEA 004.6

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Martirosyan

Scope: **Revised Protocol for PASS No 19756N**
Observational, historical cohort study of patients initiating eptinezumab in routine clinical practice and is investigating the long-term cardiovascular safety and real-world use of Eptinezumab

17.2.9. Etrasimod - VELSIPITY (CAP) - EMEA/H/C/006007/MEA 001.1

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Bolin

Scope: From Initial MAA:
PASS Revised Protocol / Study C5041046
Title: An Active Surveillance, Post-Authorization Safety Study to Characterize the Safety of Etrasimod in Patients with Ulcerative Colitis Using Real-World Data in the European Union

(C5041046)

17.2.10. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 018.1

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: From initial MAA
Amended Protocol for PASS GLPG0634-CL-408
Evalutation of the effectiveness of the additional risk minimization measures for filgotinib (Jyseleca) use in patients with moderate to severe active rheumatoid arthritis within European registries

17.2.11. Lebrikizumab - EBGLYSS (CAP) - EMEA/H/C/005894/MEA 001.1

Applicant: Almirall, S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: From Initial MAA:
Revised Protocol for PASS J2T-MC-B003 (non-imposed)
Title: Observational Database Study of Pregnancy and Infant Outcomes among Women Exposed to Lebrikizumab During Pregnancy

17.2.12. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 001.11

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: From initial MAA
Revised Protocol for PASS Study No. OP0005 (NINI)
European non-interventional post-authorisation safety study (PASS) related to the adherence to the cardiovascular risk minimization measures for romosozumab, by the EU-ADR Alliance

17.2.13. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 002.12

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: From Initial MAA:
Revised Protocol for PASS Study No. OP0004:
European non-interventional post-authorisation safety study (PASS) related to serious cardiovascular adverse events of myocardial infarction and stroke for romosozumab by the EU-ADR Alliance to evaluate potential differences in terms of serious cardiovascular adverse events between romosozumab and currently available therapies used in comparable patients in real-world conditions

17.2.14. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 003.11

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: From Initial MAA:
Revised Protocol for PASS Study No. OP0006
European non-interventional post-authorisation safety study (PASS) related to serious infections risk for romosozumab by the EU-ADR Alliance to evaluate potential differences in terms of serious infection between romosozumab and currently available therapies used in comparable patients in real-world conditions

17.2.15. Single-stranded 5' capped mRNA encoding the Respiratory syncytial virus glycoprotein F stabilized in the prefusion conformation - MRESVIA (CAP) - EMEA/H/C/006278/MEA 003.1

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

Scope: ***Updated Study Protocol / mRNA-1345-P902 and mRNA-1345-P903***(RMP (v. 0.4))
mRNA-1345-P902: Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1345 Vaccine for respiratory syncytial virus (RSV) in the United States.

mRNA-1345-P903: Post-Authorization Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1345 Vaccine for respiratory syncytial virus (RSV) in Europe

17.3. Results of PASS imposed in the marketing authorisation(s)[52]

None

17.4. Results of PASS non-imposed in the marketing authorisation(s)[53]

17.4.1. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/II/0219

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Karin Bolin

Scope: Submission of the final report from study P10-262 listed as a category 3 study in the RMP. This is a long-term, multi-center, longitudinal, post-marketing observational registry to assess long-term safety and effectiveness of Humira (adalimumab) in children with moderately to severely active polyarticular or polyarticular-course juvenile idiopathic arthritis (JIA). The RMP version 16.1 has also been submitted

17.4.2. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/II/0054

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

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

Scope: Submission of the final report from study D3250R00042 listed as a category 3 study in the RMP. This is a noninterventional, descriptive post authorisation safety study of the incidence of malignancy in severe asthma patients receiving benralizumab and other therapies. The RMP version 7.1 has also been submitted

17.4.3. Human C1-esterase inhibitor - CINRYZE (CAP) - EMEA/H/C/001207/II/0104

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.6, 5.1 and 5.3 of the SmPC based on final results from the Icatibant Outcome Survey (IOS), listed as an imposed PASS in the Annex II. This is a prospective, observational disease registry. The Package Leaflet is updated accordingly. The RMP version 11.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to bring the product information in line with the latest QRD template version 10.4 and to update Annex II of the PI

17.4.4. Icatibant - FIRAZYR (CAP) - EMEA/H/C/000899/II/0061

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Mari Thorn

Scope: Update of section 4.6 based on final results from the Icatibant Outcome Survey (IOS) registry listed as a category 3 study in the RMP; this is a prospective, observational disease registry. The RMP version 8 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI and to bring the PI in line with the latest QRD template version 10.4

17.4.5. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0149

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final clinical study report (CSR) for the PASS study CA209234 listed as a category 3 study in the RMP. This is an observational, multicenter, prospective study in patients treated with nivolumab for melanoma and lung cancer in order assess the safety experience, survival, adverse event management, and outcomes of adverse events associated with nivolumab (monotherapy or with ipilimumab) in routine oncology care facilities. The RMP version 42.0 has also been submitted

17.4.6. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2802/0070; Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/WS2802/0067

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the final report for study CLCZ696B2014 listed as a category 3 study in the RMP; this is a non-interventional post-authorization multi-database safety study to characterize the risk of angioedema and other specific safety events of interest in

association with use of Entresto (sacubitril/valsartan) in adult patients with heart failure. The RMP version 9.0 for Entresto and Neparvis has also been submitted

17.4.7. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2803/0071; Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/WS2803/0068

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the final report for study CLCZ696B2015 listed as a category 3 study in the RMP for Entresto and Neparvis; this is a non-interventional post-authorization multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of sacubitril/valsartan. The RMP version 9.0 for Entresto and Neparvis has also been submitted

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 043.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH Response to MEA 043 Study No. IM101240 as adopted in October 2024: Responses to the questions raised during assessment of the third interim report for Study IM101240, An Observational Registry of Abatacept in Patients with Juvenile Idiopathic Arthritis (JIA).

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. The data in these studies do not change the safety profile of abatacept

17.5.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/ANX 002.7

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Karin Erneholm

Scope: From initial MAA
Fourth Annual Interim Report for PASS KT-EU-471-0117
Title: Long-term, non-interventional study of recipients of Yescarta for treatment of relapsed or refractory Diffuse Large B-cell Lymphoma and Primary Mediastinal B-cell Lymphoma (EU PAS Register no.: EUPAS32539)

17.5.3. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/MEA 003.5

Applicant: Merck Europe B.V.

PRAC Rapporteur: Carla Torre

Scope: From initial MAA
PASS study protocol (Study MS700568-0004: Pregnancy outcomes in women exposed to oral cladribine: a multi-country cohort database study - CLEAR)
FIRST INTERIM REPORT

17.5.4. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/MEA 007.6

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: PASS No TG4005 (non-imposed/non-interventional)
Pregnancy surveillance program of women and infants exposed to Tegsedi during pregnancy.
Fourth Interim Report

17.5.5. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/MEA 009.10

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: [MAH Response to MEA 009.8 as adopted in October 2024]

PASS Study EVM-18888
Title: Linaclotide Safety Study for the Assessment of Diarrhoea Complications and Associated Risk Factors in Selected European Populations with Irritable Bowel Syndrome with Constipation (IBS-C)

17.5.6. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/MEA 004.3

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: ***INTERIM STUDY REPORT*** / PASS Study BA39730:
Long-term surveillance of ocrelizumab-treated patients with Multiple Sclerosis (MANUSCRIPT study; Category 3, non-interventional, multi-source, multi-country, longitudinal cohort study to assess and characterise the long-term safety data, including malignancies, from the use of ocrelizumab in patients with MS)

17.5.7. Rimegepant - VYDURA (CAP) - EMEA/H/C/005725/MEA 003.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: ***First Annual Progress Report, Updated Protocol & SAP*** / Study C4951017 (CV PASS)
(Formerly Biohaven Protocol Number BHV3000-408)
Post-Authorisation Safety Study of Rimegepant in Patients with Migraine and History of Cardiovascular Disease in European Countries

17.5.8. Turoctocog alfa pegol - ESPEROCT (CAP) - EMEA/H/C/004883/ANX 001.4

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: From Initial MAA:
Post-authorisation safety study (PASS):
In order to investigate the potential effects of PEG accumulation in the choroid plexus of the brain and other tissues/organs, the MAH should conduct and submit the results of a post-authorisation safety study according to an agreed protocol.

Study ID: NN7088-4029 A multinational, prospective, open labelled, non-controlled, non-interventional post-authorisation study of turoctocog alfa pegol (N8-GP) during long-term routine prophylaxis and treatment of bleeding episodes in patients with haemophilia A.

PASS Fourth Progress Report, Study ID: NN7088-4029

MAH also includes the interim results of the study with the data cut-off date 23-Apr-2023

17.5.9. Vamorolone - AGAMREE (CAP) - EMEA/H/C/005679/MEA 001.1

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 001 [***Feasibility Interim Study Results / No. SNT-IV-VAM-10***] RSI as adopted in August 2024.
Feasibility Report for a Registry-Based Post-authorisation Safety Study (PASS) to Evaluate the Safety of Vamorolone (AGAMREE) in Patients with Duchenne Muscular Dystrophy (DMD)

17.6. Others

None

17.7. New Scientific Advice

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

17.8. Ongoing Scientific Advice

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

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

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

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

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

18.1. Annual reassessments of the marketing authorisation

18.1.1. Cholic acid - ORPHACOL (CAP) - EMEA/H/C/001250/S/0056 (without RMP)

Applicant: Theravia

PRAC Rapporteur: Maria Poulianiti

Scope: Annual reassessment of the marketing authorisation

18.1.2. Eladocagene exuparvovec - UPSTAZA (CAP) - EMEA/H/C/005352/S/0025 (without RMP)

Applicant: PTC Therapeutics International Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Annual reassessment of the marketing authorisation

18.1.3. Fosdenopterin - NULIBRY (CAP) - EMEA/H/C/005378/S/0012 (without RMP)

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

18.1.4. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/S/0041 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

18.1.5. Tocofersolan - VEDROP (CAP) - EMEA/H/C/000920/S/0050 (without RMP)

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

18.2. Conditional renewals of the marketing authorisation

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Conditional renewal of the marketing authorisation

18.2.2. Mosunetuzumab - LUNSUMIO (CAP) - EMEA/H/C/005680/R/0014 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.2.3. Pemigatinib - PEMAZYRE (CAP) - EMEA/H/C/005266/R/0019 (without RMP)

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.4. Selumetinib - KOSELUGO (CAP) - EMEA/H/C/005244/R/0019 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

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

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Apixaban - APIXABAN ACCORD (CAP) - EMEA/H/C/005358/R/0012 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

18.3.2. Bevacizumab - AYBINTIO (CAP) - EMEA/H/C/005106/R/0022 (without RMP)

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Karin Erneholm

Scope: 5-year renewal of the marketing authorisation

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

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.4. Phenylephrine, Ketorolac - OMIDRIA (CAP) - EMEA/H/C/003702/R/0030 (without RMP)

Applicant: Rayner Surgical (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

19. Annex II – List of participants

Including any restrictions with respect to involvement of members/alternates/experts following evaluation of declared interests for the 10-13 February 2025 PRAC meeting, which was held in-person. Participants marked with "a" attended the plenary session while those marked with "b" attended the ORGAM.

An asterisk (*) after the role, in the second column, signals that the member/alternate attended remotely. Additional experts participated in (part of) the meeting, either in person or remotely.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of 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	
Jean-Michel Dogné [a]	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]	Alternate*	Croatia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Panagiotis Psaras [a,b]	Alternate	Cyprus	No interests declared	
Eva Jirsová [a,b]	Member	Czechia	No interests declared	
Jana Lukacisinova [a]	Alternate	Czechia	No interests declared	
Marie Louise Schougaard Christiansen [a,b]	Member	Denmark	No interests declared	
Karin Erneholm [a,b]	Alternate	Denmark	No interests declared	
Maia Uusküla [a]	Member	Estonia	No interests declared	
Terhi Lehtinen [a,b]	Member	Finland	No interests declared	
Kimmo Jaakkola [a,b]	Alternate	Finland	No interests declared	
Tiphaine Vaillant [a,b]	Member	France	No interests declared	
Zoubida Amimour [a,b]	Alternate	France	No participation in discussion, final deliberations and voting on:	4.1.2. Ciltacabtagene autoleucel – CARVYKTI (CAP); idecabtagene vicleucel – ABECMA (CAP); tisagenlecleucel - KYMRIAH (CAP) 4.1.3. Idecabtagene vicleucel – ABECMA (CAP) 4.2.1. Adagrasib - KRAZATI (CAP) - EMEA/H/C/006013/SDA/003 6.1.2. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/202407 7.4.1. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/00071

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				7/II/0130 16.1.3. Atazanavir - REYATAZ (CAP) - PSUSA/00000258 /202406 17.4.5. Nivolumab - OPDIVO (CAP) - EMEA/H/C/00398 5/II/0149 17.5.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/00070 1/MEA 043.1
Martin Huber [a]	Member	Germany	No interests declared	
Gabriele Maurer [a]	Alternate	Germany	No interests declared	
Georgia Gkegka [a]	Member*	Greece	No interests declared	
Maria Poulianiti [a],[b]	Alternate*	Greece	No participation in discussion, final deliberations and voting on:	3.2.1. Dutasteride (NAP); dutasteride, tamsulosin (NAP); finasteride (NAP); finasteride, tadalafil (NAP); finasteride, tamsulosin (NAP) – EMEA/H/A-31/1539 16.3.7. Human plasma proteins with no less than 95% albumin (NAP) - PSUSA/00010605 /202407
Julia Pallos [a],[b]	Member	Hungary	No participation in discussion, final	4.1.2. Ciltacabtagene autoleucel – CARVYKTI (CAP); idecabtagene vicleucel – ABECMA (CAP);

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			deliberations and voting on:	tisagenlecleucel - KYMRIAH (CAP) 4.1.3. Idecabtagene vicleucel – ABECMA (CAP) 4.2.1. Adagrasib - KRAZATI (CAP) - EMEA/H/C/006013/SDA/003 6.1.2. Nivolumab - OPDIVO (CAP) - PSUSA/00010379/202407 7.4.1. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0130 16.1.3. Atazanavir - REYATAZ (CAP) - PSUSA/00000258/202406 17.4.5. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0149 17.5.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 043.1
Melinda Palfi [a]	Alternate*	Hungary	No interests declared	
Guðrún Stefánsdóttir [b]	Member*	Iceland	No restrictions applicable to this meeting	
Guðrún Þengilsdóttir [b]	Alternate*	Iceland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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]	Alternate*	Italy	No interests declared	
Zane Neikena [a,b]	Member	Latvia	No interests declared	
Diana Litenboka [a,b]	Alternate*	Latvia	No interests declared	
Rugile Pilviniene [a,b]	Member*	Lithuania	No interests declared	
Lina Seibokiene [a]	Alternate	Lithuania		
Anne-Cecile Vuillemin [b]	Member*	Luxembourg	No interests declared	
Magdalena Wielowieyska [a,b]	Alternate	Luxembourg	No participation in discussion, final deliberations and voting on:	16.1.24. Icatibant - FIRAZYR (CAP) - PSUSA/00001714 /202407 16.3.7. Human plasma proteins with no less than 95% albumin (NAP) - PSUSA/00010605 /202407 17.4.3. Human C1-esterase inhibitor - CINRYZE (CAP) - EMEA/H/C/00120 7/II/0104 17.4.4. Icatibant - FIRAZYR (CAP) - EMEA/H/C/00089 9/II/0061
Liana Martirosyan [a]	Member (Vice-Chair)	Netherlands	No interests declared	
Bianca Mulder [a,b]	Alternate	Netherlands	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
David Olsen [a],[b]	Member	Norway	No participation in discussion, final deliberations and voting on:	4.1.4. Regorafenib - STIVARGA (CAP) 11.1.1. Levonorgestrel (NAP) - DE/H/xxxx/WS /1803 15.3.20. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/X/0041 15.3.23. Sorafenib - NEXAVAR (CAP) - EMEA/H/C/000690/II /0059 16.1.14. Darolutamide - NUBEQA (CAP) - PSUSA/00010843 /202407 16.1.18. Finerenone - KERENDIA (CAP) - PSUSA/00010978 /202407 16.3.4. Dexchlorpheniramine (NAP) - PSUSA/00000989 /202406
Pernille Harg [a],[b]	Alternate	Norway	No interests declared	
Adam Przybylkowski [a]	Member	Poland	No interests declared	
Katarzyna Ziolkowska[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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Roxana Dondera [a,b]	Member*	Romania	No interests declared	
Irina Sandu [a,b]	Alternate	Romania	No interests declared	
Anna Mareková [a]	Member*	Slovakia	No interests declared	
Miroslava Gocova [a,b]	Alternate*	Slovakia	No interests declared	
Polona Golmajer [a]	Member	Slovenia	No interests declared	
Marjetka Plementas[b]	Alternate*	Slovenia	No interests declared	
Maria del Pilar Rayon [a]	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	
Karin Bolin [a,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]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark [a]	Member	Independent scientific expert	No interests declared	
Roberto Frontini [a]	Member	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	16.3.6. Human fibrinogen (NAP) - PSUSA/00001624/202406 16.3.7. Human plasma proteins with no less than 95% albumin (NAP) -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				PSUSA/00010605 /202407
Salvatore Antonio Giuseppe Messana [a]	Alternate	Healthcare Professionals' Representative	No interests declared	
Marko Korenjak [a]	Member*	Patients' Organisation Representative	No interests declared	
Michal Rataj [a]	Alternate	Patients' Organisation Representative	No interests declared	
Gabriela Burianová [a]	Expert	Czech Republic	No interests declared	
Jan Vosatka [a]	Expert	Czech Republic	No interests declared	
Emma Stadsbjerg [a]	Expert	Denmark	No restrictions applicable to this meeting	
Wilma Fischer-Barth [a]	Expert	Germany	No interests declared	
Dennis Lex [a],[b]	Expert	Germany	No interests declared	
Susanne Liebig [a]	Expert	Germany	No restrictions applicable to this meeting	
Anne-Charlotte Lübow [a]	Expert	Germany	No restrictions applicable to this meeting	
Nina Pannwitz [a]	Expert	Germany	No interests declared	
Laura Zein [a]	Expert	Germany	No interests declared	
Toth Szilvia [a]	Expert	Hungary	No restrictions applicable to this meeting	
Marcel Kwa [a]	Expert	Netherlands	No interests declared	
Serena Marchetti [b]	Expert	Netherlands	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Anne Slomp [a]	Expert	Netherlands	No restrictions applicable to this meeting	
Dennis van Eijl [a]	Expert	Netherlands	No interests declared	
Frederika Adriana Vermeij-van Nimwegen [a]	Expert	Netherlands	No restrictions applicable to this meeting	
Emma Redondo [a]	Expert	Spain	No interests declared	
Charlotte Backman [a],[b]	Expert	Sweden	No interests declared	
Rolf Gedeborg [a]	Expert	Sweden	No restrictions applicable to this meeting	
Jolanta Gulbinovic [a]	Expert	Sweden	No interests declared	
Jenny Jönsson [a]	Expert	Sweden	No restrictions applicable to this meeting	
Sissela Liljeqvist [a]	Expert	Sweden	No restrictions applicable to this meeting	
Observers from Health Canada (Canada) and MLHW (Japan) attended the meeting.				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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