27 March 2026
EMA/PRAC/59896/2026
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 09 – 12 February 2026

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 Chairperson opened the 09-12 February 2026 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 and experts and on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics. Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. No new or additional competing interests were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

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

The Chair 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 09-12 February 2026

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

1.3. Minutes of the previous meeting on 12-15 January 2026

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

Post-meeting note: the PRAC minutes of the meeting held on 12-15 January 2026 were published on the EMA website on 11 March 2026 (EMA/PRAC/46601/2026).

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

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

3.1. Newly triggered procedures

None

3.2. Ongoing Procedures

None

3.3. Procedures for finalisation

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

Applicants: various

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

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

Background

A referral procedure under Article 31 of Directive 2001/83/EC for levamisole-containing medicines is to be concluded. A final assessment of the data submitted was produced by the Rapporteurs according to the agreed timetable.

Discussion

PRAC reviewed the available data in relation to the risk of leukoencephalopathy and central nervous system (CNS) demyelination associated with the use of levamisole-containing medicinal products. This included the responses submitted by the MAHs in writing, data from clinical trials, spontaneous reporting and literature, non-clinical data, as well as the views expressed by a group of independent experts.

Based on the data assessed, PRAC confirmed a causal association between levamisole and leukoencephalopathy, a serious, long-lasting, debilitating, and potentially life-threatening neurologic disease. Moreover, PRAC could not identify risk factors for levamisole-induced leukoencephalopathy and noted that the risk was unpredictable, occurring even after a single dose. In addition, PRAC could not identify any risk minimisation measures that would effectively reduce the risk of leukoencephalopathy and concluded that the risks of leukoencephalopathy outweigh the benefit of levamisole in the treatment of intestinal helminth infections, which are in most cases of mild nature.

Furthermore, PRAC could not identify conditions which, if fulfilled, would demonstrate a positive benefit-risk balance for levamisole-containing medicinal products in a defined patient population.

As a consequence, PRAC considered that the benefit-risk balance of levamisole-containing products is not favourable.

Summary of recommendation(s)/conclusions

- PRAC adopted, by consensus the revocation of the marketing authorisations for levamisole-containing medicines and adopted a recommendation to be considered by CMDh for a position.
- PRAC agreed the distribution of a direct healthcare professional communication (DHPC) together with a communication plan.

For further details, see Levamisole-containing medicinal products - referral | European Medicines Agency (EMA).

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

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

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

See also Annex I 14.1.

4.1.1. Chikungunya vaccine (live) - IXCHIQ (CAP)

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Signal of new aspect of the known risk of aseptic meningitis

EPITT 20250 – New signal

Lead Member State(s): DE

Background

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

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

A signal of new aspect of the known risk of aseptic meningitis was identified by Belgium, based on 1 case retrieved from EudraVigilance. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from the EudraVigilance database, PRAC agreed that further evaluation on the signal of new aspect of the known risk of aseptic meningitis is warranted.

Summary of recommendation(s)

- The MAH for Ixchiq (Chikungunya vaccine (live)) should submit to EMA, by 23 February 2026, responses to the list of questions related to potential quality issues of the identified batch, current exposure numbers stratified by age groups and geographical region, and any further information related to the index case. In addition, the MAH should discuss the need to update the product information and/or the RMP, including any need for additional risk minimisation measures and a proposal for a direct healthcare professional communication (DHPC).
- An accelerated timetable was recommended for the assessment of this review leading to a further PRAC recommendation in March 2026.

4.2. Signals follow-up and prioritisation

4.2.1. Risankizumab – SKYRIZI (CAP) - EMEA/H/C/004759/SDA/011

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of pemphigoid

EPITT 20192 – Follow-up to September 2025

Background

For background information, see PRAC minutes September 2025.

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

Discussion

Having considered the available evidence in EudraVigilance, the literature and the responses of the MAH, PRAC concluded that the current evidence is insufficient to establish a causal relationship between risankizumab and pemphigoid diseases to further warrant an update to the product information and/or risk management plan at present.

Summary of recommendation(s)

- The MAH for Skyrizi (risankizumab) should continue to monitor pemphigoid events as part of routine pharmacovigilance.

4.3. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

5.1.1. Alpelisib - (CAP MAA) - EMEA/H/C/006539, Orphan

Scope (pre D-180 phase): Treatment of adult and paediatric patients aged 2 years and older with severe or life-threatening manifestations of PIK3CA-related overgrowth spectrum (PROS)

5.1.2. Diazoxide choline - (CAP MAA) - EMEA/H/C/006576, Orphan

Scope (pre D-180 phase): Treatment of adult and paediatric patients with Prader-Willi syndrome (PWS)

5.1.3. Lerodalcibep - (CAP MAA) - EMEA/H/C/006694, PUMA

Scope (pre D-180 phase): Is indicated in adults with primary hypercholesterolaemia (heterozygous familial (HeFH) and non-familial) or mixed dyslipidaemia as an adjunct to diet

5.1.4. Nerandomilast - (CAP MAA) - EMEA/H/C/006405

Scope (pre D-180 phase): Treatment of adult patients with Idiopathic Pulmonary Fibrosis (IPF) and adult patients with Progressive Pulmonary Fibrosis (PPF)

5.1.5. Onasemnogene abeparvovec - (CAP MAA) - EMEA/H/C/006498, Orphan

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

5.1.6. Sasanlimab - (CAP MAA) - EMEA/H/C/006641

Scope (pre D-180 phase): Treatment of bladder cancer for adults

5.1.7. Tarlatamab - (CAP MAA) - EMEA/H/C/006451, Orphan

Scope (pre D-180 phase): Treatment of extensive-stage small cell lung 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. Brexucabtagene autoleucel – TECARTUS (CAP) – EMA/PSUR/0000305034

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010903/202507)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tecartus, a centrally authorised medicine containing brexucabtagene autoleucel 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 Tecartus (brexucabtagene autoleucel) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding secondary malignancy of myeloid origin. Therefore, the current terms of the marketing authorisation(s) should be varied[3].
- In the next PSUR, the MAH should present any new cases of immune effector cell associated enterocolitis, including a causality assessment. In addition, the MAH should provide a review of new safety information on the topic of immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome and discuss the need for updating the product information, as warranted. The MAH should also continue to monitor the topic of progressive multifocal leukoencephalopathy (PML) and discuss any new cases in detail in future PSURs.

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

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

6.1.2. Bulevirtide – HEPCLUDEX (CAP) – EMA/PSUR/0000305044

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010873/202507)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Hepcludex, a centrally authorised medicine containing bulevirtide 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 Hepcludex (bulevirtide) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should further monitor the use of bulevirtide in paediatric patients.

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. Lecanemab – LEQEMBI (CAP) – EMA/PSUR/0000305053

Applicant: Eisai GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00011132/202507)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Leqembi, a centrally authorised medicine containing lecanemab 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 Leqembi (lecanemab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to revise the package leaflet so that the warning on amyloid-related imaging abnormalities (ARIA) is aligned with the information in the SmPC and the patient card, including the statement that ARIA symptoms may lead to serious or even fatal outcomes. Therefore, the current terms of the marketing authorisation(s) should be varied[4].
- In the next PSUR, the MAH should provide a cumulative review with a thorough case-by-case assessment of all fatal cases with a focus on (but not limited to) ARIA-haemorrhage (ARIA-H) and ARIA-oedema (ARIA-E) cases, as well as intracerebral haemorrhage >1 cm. The MAH should closely monitor off-label and misuse cases and discuss any (additional) risk minimisation measures that would be deemed necessary to further mitigate these risks, as

[4] Update of the package leaflet. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

warranted. In addition, the MAH should provide a cumulative review and assessment of cases of acute kidney injury or related renal events, including a discussion on potential mechanistic explanations, and reassess the signal using all new data and analyses, providing a justification on whether the signal remains open or can be closed. The MAH should also provide a summary of case narratives for all cases originating from non - marketed European countries in the future PSUR submissions.

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. Rotavirus vaccine, live – ROTARIX (CAP) – EMA/PSUR/0000305060

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00002665/202507)

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Rotarix (rotavirus vaccine, live) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add anaphylactic reaction as a warning and as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[5].
- In the next PSUR, the MAH should provide a cumulative review and discuss the observed changes in medication error trends over time, including a thorough assessment of the pattern of associated adverse reactions, potential causes, and their geographical distribution.
- As part of a post-authorisation measure, the MAH should provide a cumulative review of cases of all serious cases of rotavirus gastroenteritis in children without immune deficiency (DLP 11 July 2025), including data from literature, post-marketing setting and clinical trials, along with a discussion on possible biological plausibility. In addition, the MAH should also provide a cumulative review of cases of vomiting, focusing on serious cases without a co-administered vaccine(s) nor an established alternative aetiologies/diagnosis, along with a causality assessment. The MAH should discuss the need for update of the product information and/or risk management plan, 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.

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

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

See Annex I 16.2.

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

See also Annex I 16.3.

6.3.1. Albendazole (NAP) – EMA/PSUR/0000305020

Applicants: various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00000073/202507)

Background

Albendazole is a benzimidazole carbamate with anthelmintic and antiprotozoal activity indicated for the treatment of intestinal (including cutaneous larva migrans) and tissue parasites.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing albendazole 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 albendazole-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add hepatitis as a warning and as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[6].
- In the next PSUR, all MAHs should further monitor cases of neurological disorders, including encephalopathy, as well as of blood and lymphatic disorders, with special focus on cases on hypereosinophilia.

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. Metronidazole / miconazole (NAP); chlorquinaldol / metronidazole (NAP) – EMA/PSUR/0000305029

Applicants: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00002042/202507)

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

Background

Metronidazole is an antibiotic, miconazole is an antifungal agent and chlorquinaldol is an antibacterial agent. The combination of metronidazole with chlorquinaldol or with miconazole is indicated for the treatment of vaginal infections.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing metronidazole/miconazole and chlorquinaldol/metronidazole 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 metronidazole/miconazole- and chlorquinaldol/metronidazole-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) for chlorquinaldol/metronidazole-containing products should be maintained.
- The product information for metronidazole/miconazole-containing products should be updated to include a warning on the drug-drug interaction between miconazole and warfarin or other vitamin K antagonists. Therefore, the current terms of the marketing authorisation(s) should be varied[7].
- In the next PSUR, the MAH Gedeon Richter should provide an assessment of the use of metronidazole/miconazole during breastfeeding based on all available data, including a proposal 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.

6.3.3. Ropinirole (NAP) – EMA/PSUR/0000305037

Applicants: various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00002661/202507)

Background

Ropinirole is a dopamine agonist indicated for treatment of Parkinson's Disease (PD) as monotherapy, or in combination with levodopa when the effect of levodopa wears off or becomes inconsistent and when fluctuations in the therapeutic effect occur. Ropinirole is also indicated for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome (RLS).

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

Summary of recommendation(s) and conclusions

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of ropinirole-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add aggressive behaviours (already listed in section 4.8 as associated with psychotic reactions as well as compulsive symptoms) in the warning on impulse control disorders and to add aggression in the list of possible impulse control disorders manifestations. Therefore, the current terms of the marketing authorisation(s) should be varied[8].
- In the next PSUR, all MAHs should continue to closely monitor pregnancy cases, as well as cases of cardiac rhythm disorders (effects on cardiac repolarisation) and of haematopoiesis disorders. In addition, all MAHs should provide cumulative reviews of cases of dystonias and detail any new case of dropped head syndrome, based on the data from literature, clinical trials and post-marketing setting, along with a causality assessment, and discuss the need for update of the product information, as warranted. Finally, all MAHs should continue to monitor cases of sexual dysfunction and erectile dysfunction reported in literature, clinical trials and post-marketing setting, along with a causality assessment and discuss the need for update of 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.

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Ustekinumab – STELARA (CAP) – EMA/PAM/0000274988

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Responses to the LEG 058 RSI adopted on 27 March 2025 - From PSUSA/00003085/202312: An updated cumulative review (clinical trial, registry, postmarketing, literature and other sources) of severe depression/suicidal ideation, using an appropriate SMQ (Depression and suicide/self injury) for all relevant data streams.

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 further data on severe depression/suicidal ideation topic. The responses were assessed by the Rapporteur for further PRAC advice.

Summary of advice/conclusion(s)

- Based on the available data and the Rapporteur's assessment, PRAC considered that further characterisation of the risk of suicidality for ustekinumab through additional pharmacovigilance or other observational study is not warranted in light of the current knowledge, and that

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

severe depression and suicidality should continue to be monitored through routine pharmacovigilance. At the next regulatory opportunity the MAH should remove 'serious depression including suicidality' from the list of important potential risks in the RMP.

6.5. Variation procedure(s) resulting from PSUSA evaluation

See Annex I 16.5.

6.6. Expedited summary safety reviews[9]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[10]

See also Annex I 17.1.

7.1.1. Beremagene geperpavec – VYJUVEK (CAP) – EMA/PASS/0000287685

Applicant: Krystal Biotech Netherlands B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: PASS protocol [107n]: A prospective, non-interventional, multi-country study to confirm the long-term safety profile, including in paediatric patients less than 6 months of age, of B-VEC for the treatment of DEB wounds in a real-life clinical setting.

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.

The MAH has submitted to EMA an updated PASS protocol version 2.0 dated 26 November 2025 with the aim to confirm the long-term safety profile of beremagene geperpavec, including in paediatric patients less than 6 months of age, for the treatment of dystrophic epidermolysis bullosa (DEB) wounds in a real-life clinical setting. This is a non-interventional PASS conducted pursuant to an obligation imposed by an EU competent authority, and listed as Category 1 study in the RMP.

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 2.0 in accordance with Article 107n of Directive 2001/83/EC, PRAC objected to the draft protocol for the above listed medicinal product(s), as the Committee considered that the design of the study did not fulfil the study at this stage.
- PRAC therefore recommended updates of the primary outcome and primary objective of the study. PRAC also requested further clarification on the pre-defined ranges for body surface area (BSA) for patients <3 years old treated with beremagene geperpavec, as well as on the

[9] 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

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

analysis for patients <3 years old and how the first administration of beremagene geperpavec is captured for these patients. PRAC also requested the MAH to amend the risk minimisation measures effectiveness questionnaire in order to allow input from healthcare professionals, in addition to patients/caregivers. Regarding the questionnaires planned for use in the study, the MAH should explain their strategies to ensure sufficient response of patients/caregivers to these questionnaires, in terms of response rate and the number of completed questionnaires. Moreover, the MAH should collect information on prior inclusion in a clinical trial or early access/compassionate use programs as a baseline variable. Finally, the MAH should provide instructions to the prescribers in relation to the selection of the wound for follow-up and if another wound is selected instead, the reasons for this decision should be documented.

- The MAH should submit a revised PASS protocol within 60 days to EMA. A 60 days-assessment timetable will be followed.

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[11]

See Annex 17.2.

7.3. Results of PASS imposed in the marketing authorisation(s)[12]

7.3.1. Eliglustat – CERDELGA (CAP) – EMA/PASS/0000287682

Applicant: Sanofi B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: PASS results [107q]: A prospective multicenter observational post-authorization safety sub-registry study (PASS) to characterize the long-term safety profile of commercial use of eliglustat (Cerdelga) in adult patients with Gaucher disease.

Background

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

In order to fulfil the obligation to submit the results of an imposed non-interventional PASS in accordance with Article 107p of Directive 2001/83/EC, the Marketing Authorisation Holder/consortium Sanofi submitted to EMA on 21 July 2025 a PASS final study report for eliglustat.

PRAC discussed the final study results in addition to the MAH's responses to the request for supplementary information (RSI).

Summary of recommendation(s) and conclusions

- Based on the review of the final report of the non-interventional PASS entitled 'A prospective multicenter observational post-authorization safety sub-registry study (PASS) to characterize the long-term safety profile of commercial use of eliglustat (Cerdelga®) in adult patients with Gaucher disease', PRAC considered that the benefit-risk balance of Cerdelga (eliglustat) remains unchanged. As a consequence, PRAC recommended that the terms of the marketing

[11] 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
[12] In accordance with Article 107p-q of Directive 2001/83/EC

authorisation(s) for Cerdelga (eliglustat) should be varied to remove the PASS as an obligation from the 'conditions or restrictions with regard to the safe and effective use of the medicinal product' and to remove the product from the additional monitoring list. In addition, PRAC considered that the following safety concerns should be removed from the RMP: 'use in patients with a history of or current cardiac ischemia or heart failure, clinically significant arrhythmias or conduction findings', 'use during pregnancy and lactation', 'safety in long-term treatment use', 'use in patients who are CYP2D6 ultra-rapid metabolizers (URMs)' as missing information and 'cardiac conduction disorders and arrythmias' as important potential risk.

7.4. Results of PASS non-imposed in the marketing authorisation(s)[13]

See also Annex I 17.5.

7.4.1. Fenfluramine – FINTEPLA (CAP) – EMA/VR/0000296039

Applicant: UCB Pharma

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report for study EP0220 listed as a category 3 study in the RMP. This is a non-interventional study to assess the effectiveness of risk minimization measures in approved indications for fenfluramine hydrochloride. The RMP version 5.1 has been 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.

As stated in the RMP of Fintepla (fenfluramine), the MAH conducted a non-imposed non-interventional PASS study EP0220 to assess the effectiveness of risk minimisation measures (RMMs) of Fintepla (fenfluramine) in the approved indications. The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI).

Summary of advice

- Based on the available data, the MAH's responses to the RSI and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be considered acceptable provided that the MAH submits satisfactory responses to a RSI.
- PRAC considered that the proposed measures to improve healthcare professionals' (HCPs) adherence to the recommendations in the educational materials, as well as to enhance the safety of fenfluramine use, are not fully adequate or effective in achieving the intended improvement in adherence. In the light of the ongoing drug utilisation study, which will also provide data on the extent and frequency of echocardiographic monitoring, these results should be discussed by the MAH together with all other available data (including EP0220) in terms of effectiveness of the existing educational materials. Consideration should then be given to whether the educational material would need further revision, especially in terms of streamlining, up to date graphical representation of information and readability. In this

[13] 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

respect, user-testing of materials (see GVP Module XVI) should be performed. PRAC considered that the other proposed measures to inform both HCPs and patients/caregivers about identified risks and measures to minimise them can already be implemented on a voluntary basis. In addition, PRAC emphasized the importance of ensuring that HCPs and patients/caregivers have access to, and are familiar with, the existing educational materials in order to comply with the recommendations they contain. Therefore, a QR code leading directly to the relevant educational material or to the website where the educational material can be found should be included in the package leaflet, together with the corresponding internet address. Additionally, the SmPC should include a reference to the existing educational materials (including the one for patients) in alignment with GVP Module XV. The proposed poster and reminder letter were not supported at PRAC level.

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

See Annex I 17.6.

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 the Member States, CHMP or the EMA

None

11. Scientific advice procedures

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

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The Chair thanked Martin Huber for his contribution as a member representing Germany.

12.1.2. Nominated proxy

Panagiotis Psaras (Cyprus) granted a proxy to Ana Sofia Diniz Martins (Portugal), Annalisa Capuano granted a proxy to Maria Teresa Herdeiro, Maia Uusküla (Estonia) granted a proxy to Zane Neikena (Latvia), Georgia Gkegka (Greece) granted a proxy to Marjetka Plementas (Slovenia), and Hedvig Marie Egeland Nordeng granted a proxy to Anette Kristine Stark, all covering the entire meeting.

12.1.3. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q4 2025

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 2025 of PRAC meetings. For previous update, see PRAC minutes November 2025[14].

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Scientific Advice Working Party (SAWP) - SAWP composition – new appointment of PRAC representative(s)

PRAC appointed Marie Louise Schougaard Christiansen and Patricia McGettigan as new

[14] Held on 27-30 October 2025

representatives of PRAC to the SAWP. The full SAWP composition will subsequently be proposed to and adopted by the CHMP.

12.4. Cooperation within the EU regulatory network

None

12.5. Cooperation with International Regulators

12.5.1. International Conference on Harmonisation (ICH) E2D(R1) - Guideline

Anja Van Haren presented to PRAC the main updates and late-stage comments related to the final ICH E2D (R1) which has been endorsed by ICH Management Committee on 15 September 2025 and by CHMP on 18 September 2025, with an effective date for coming into force in the EU of 18th of March 2026. PRAC was also informed on the transition period details and the implementation strategy for the E2D (R1) as well as about the training material available on the ICH website. PRAC members were requested to provide their comments in writing by 20 February 2026.

Post-meeting note: PRAC endorsed the proposed Implementation Strategy Document for the ICH E2D(R1) Guideline on 20 February 2026 (EU implementation strategy of ICH E2D(R1) Guideline - Post-approval safety data: Definitions and standards for management and reporting of individual case safety reports).

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 - annual workload measures and performance indicators – 2025

The EMA Secretariat presented to PRAC an overview of the annually figures on the EMA pharmacovigilance system-related workload and performance indicators. For the previous update and further information, see PRAC minutes February 2025.

12.8.2. PRAC workload statistics – Q4 2025

The EMA secretariat informed PRAC about the quarterly and cumulative figures to estimate the evolution of the PRAC workload for Q4 2025, by reflecting on the number of procedures and agenda items covered at each PRAC plenary meeting. For previous update, see PRAC minutes November 2025[15].

[15] Held on 27-30 October 2025

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

None

12.10.3. PSURs repository

None

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

In line with the criteria for plenary presentation of updates to the EURD List adopted by PRAC in December 2021, PRAC endorsed the draft revised EURD list, version February 2026, reflecting the PRAC's comments impacting on the data lock point (DLP) and PSUR submission frequencies of the substances/combinations. PRAC endorsed the newly allocated Rapporteurs for upcoming PSUSAs in accordance with the principles previously endorsed by PRAC (see PRAC minutes April 2013).

Post-meeting note: following the PRAC meeting of February 2026, the updated EURD list was adopted by CHMP and CMDh at their February 2026 meetings and published on the EMA website, see: Home> Human Regulatory>Post-authorisation>Pharmacovigilance>Periodic safety update reports>> List of Union reference dates and frequency of submission of periodic safety update reports (PSURs)

12.10.5. Good Pharmacovigilance Practice (GVP) Module VIII - update

PRAC lead: Maria del Pilar Rayon, Patricia McGettigan

The EMA Secretariat presented to PRAC for endorsement the proposal for the revision of the GVP Module VIII - Post-authorisation safety studies. The revision includes several updates in accordance with the Implementation Regulation (EU) 2025/1466 amending Implementing

Regulation (EU) No 520/2012, as well as updates referencing ICH M14. The PRAC members were invited to send their comments in writing by 20 March 2026.

12.11. Signal management

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

PRAC lead: Martin Huber

The EMA Secretariat presented to PRAC an update on the activities of the SMART Method group as well as the proposed workplan with the areas of prioritisation (real world evidence integration, Artificial Intelligence in pharmacovigilance and collaborations to enhance further the knowledge) for the period 2026-2029. In addition, PRAC was informed on the other topics discussed in the group related to the activities of the health data lab (HDL) and other activities. PRAC noted the information and endorsed the proposed research areas for prioritisation.

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. Changes to EudraVigilance

The EMA Secretariat presented to PRAC the proposed changes to EudraVigilance related to a new field (Vaccine dosage sequence), including an overview of the next steps. PRAC agreed with the proposed changes.

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. DARWIN EU® study on the utilisation of commonly used benzodiazepines during pregnancy and the incidence of pregnancy losses - PRAC Sponsor's critical appraisal of feasibility assessment

PRAC discussed the PRAC Sponsor's appraisal of the DARWIN EU® Study 'Utilisation of commonly used benzodiazepines during pregnancy and the incidence of pregnancy losses' (EUPAS1000000536).

The study was requested to investigate the risk of miscarriage following exposure to benzodiazepines based on some epidemiological studies indicating that there may be an increased risk of miscarriage after exposure to benzodiazepines during pregnancy compared with unexposed women.

The DARWIN EU® study was a retrospective, descriptive cohort of pregnancies (2010–2023). The cohort included women aged 12-55 at pregnancy start in three data sources (one for Spain and two for Norway). The variables were collected for benzodiazepine and alternative treatments regarding exposures treatments, indications, pregnancy loss, and other demographic and clinical covariates.

The overall prevalence of benzodiazepine exposure during pregnancy was ~0.9% in Norway and ~4.9% in Spain. The exposure at early pregnancy was highest in week 1 of pregnancy and declined thereafter. Overall pregnancy loss incidence ranged across the three data sources from 125 to 248 per 1,000 pregnancy-years.

PRAC discussed and agreed with the PRAC Sponsor's appraisal. PRAC considered one of the limitations of the descriptive estimates is heterogeneity and representativeness of the data, as reflected in the large differences in prevalence of exposure and outcome between the data of the two countries. PRAC considered that these data sources, as they are portrayed in the report, are not suitable for a causal inference study because important confounders cannot be adequately adjusted due to them not being captured (e.g. lifestyle) or containing excessive missing data (e.g. indication), and the identification of several significant biases. This compromises the feasibility of conducting a study aimed at causal inference.

In conclusion, the DARWIN EU® study report was a descriptive analysis of exposure and outcome, and may be considered as a first step to explore the feasibility of a causal inference study. Given the large proportion of missing key covariates, it does not confirm whether a future comparative study would provide sufficient regulatory value.

12.21.2. Scientific Explorer – update - integration of European public assessment reports for initial marketing authorisations (EPARs)

The EMA Secretariat presented to PRAC the Scientific Explorer which is built to enable fast, easy precise searching of regulatory documents, including on topics of interest extracted by artificial intelligence. In March 2026, the tool's search functionality will be extended to support EMA and national competent authorities (NCAs) in finding information related to initial marketing authorisation applications of human medicines, including public assessment reports. PRAC was provided with a short live training including examples and access instructions. PRAC noted the information.

13. Any other business

None

13.1. Newly triggered procedures

None

13.2. Procedures for finalisation

None

14. Annex I – Signals assessment and prioritisation[16]

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[17].

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

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

Applicant: Celltrion Healthcare Hungary Kft., Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Signal of acquired haemophilia

EPITT 19385 – New signal

Lead Member State: SE

14.2. Signals follow-up and prioritisation

None

14.3. Variation procedure(s) resulting from signal evaluation

None

[16] 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

[17] 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

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. Clesrovimab - (CAP MAA) - EMEA/H/C/006497

Scope (initial application in the decision making phase): Prevention of infections with respiratory syncytial virus (RSV) and lower respiratory tract disease (LRTD)

15.1.2. Colchicine - (CAP MAA) - EMEA/H/C/006653

Scope (pre D-180 phase): Indicated to reduce the risk of myocardial infarction (MI), stroke, coronary revascularization, and cardiovascular death in patients with atherosclerotic disease or with multiple risk factors for cardiovascular disease.

15.1.3. Palbociclib - (CAP MAA) - EMEA/H/C/006624

Scope (pre D-180 phase): Treatment of breast cancer factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer:
- in combination with an aromatase inhibitor;
- in combination with fulvestrant in women who have received prior endocrine therapy .

15.1.4. Plozasiran - (CAP MAA) - EMEA/H/C/006579, Orphan

Scope (pre D-180 phase): Treatment of familial chylomicronaemia syndrome (FCS).

15.1.5. Ranibizumab - (CAP MAA) - EMEA/H/C/006634

Scope (pre D-180 phase): Treatment of adults with neovascular (wet) age-related macular degeneration (AMD), visual impairment and other retinopathies

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. Durvalumab – IMFINZI (CAP); Olaparib – LYNPARZA (CAP) – EMA/VR/0000296305

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: To extend the due date for the phase III PAES study D9311C00001 (DUO-E) from December 2026 to November 2028 in the RMP and Annex II of the SmPC. In addition, the MAH has taken this opportunity to correct an error identified for the DUO-E study involving a raw data mapping issue that affected the COVID-19 study disruption data and impacts the COVID-19 tables in the CSR. As there is no change in the interpretation or the overall conclusion this has exceptionally been included as part of this type IB.

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

15.3.1. Asciminib – SCEMBLIX (CAP) – EMA/X/0000256688

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: Extension application to introduce a new strength (100 mg film-coated tablets) grouped with a type II variation (C.I.6.a) to add a new indication (treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) harbouring the T315I mutation), based on final results from study CABL001X2101 and study CABL001A2004. Study CABL001X2101 is a Phase I, multicenter, open-label, dose escalation FIH study to define the MTD/RDEs, to characterize safety and tolerability, and to assess the PK profile and preliminary evidence of efficacy of asciminib given as single agent or in combination with either nilotinib or imatinib or dasatinib in patients with Ph+ CML or Ph+ ALL.

Study CABL001A2004 assessed the real-world effectiveness of asciminib and treatment patterns in patients with Chronic Myeloid Leukemia with T315I mutation. As a consequence, sections 1, 2, 3, 4, 5, 6 and 8 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 3.0 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection.

15.3.2. Atezolizumab – TECENTRIQ (CAP) – EMA/VR/0000315105

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: A grouped application consisting of:

C.I.4: Update of section 4.4 of the SmPC to enhance the text to explicitly advise healthcare professionals to monitor for signs of Immune-mediated myocarditis/myositis/myasthenia gravis overlap syndrome based on postmarketing data. The Package Leaflet is updated accordingly. The RMP version 33.0 has also been submitted.

C.I.4: Update of section 4.8 of the SmPC to add hypoalbuminemia, hypophosphatemia, hypocalcaemia, and gamma-glutamyltransferase increased as adverse drug reactions for atezolizumab based on postmarketing data. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement editorial changes to the SmPC.

15.3.3. Atogepant – AQUIPTA (CAP) – EMA/VR/0000310717

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: A grouped application comprised of 1 Type II Variation and 3 Type I Variations, as follows:

Type II (C.I.6): Extension of indication to include acute treatment of migraine with or without aura in adults, based on interim results from study M24-305; this is a 24-week, global, Phase 3, multicenter, randomized, double blind, placebo-controlled, multiple-migraine attack study with an open label period to evaluate the safety and efficacy of atogepant in adult participants for the acute treatment of migraine (ECLIPSE). 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 2.2 of the RMP has also been submitted.

15.3.4. Avelumab – BAVENCIO (CAP) – EMA/VR/0000314741

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: A grouped application comprised of 2 Type II Variations, as follows:

C.I.4: Update of section 4.4 of the SmPC in order to update the warning on 'immune mediated adverse reactions', particularly regarding myositis, myocarditis, and myasthenia gravis (Triple-M syndrome), based on a safety review. The Package Leaflet is updated accordingly.

C.I.4: Update of section 4.8 of the SmPC in order to update the frequency of 'sarcoidosis' in the list of adverse drug reactions (ADRs) for avelumab monotherapy from 'uncommon' to 'rare', and to add it to the list of ADRs for avelumab in combination with axitinib with frequency 'not known', based on a safety review. The Package Leaflet is updated accordingly.

The RMP version 9.3 has been submitted. In addition, the MAH took the opportunity to introduce alignment changes to the PI.

15.3.5. Axicabtagene ciloleucel – YESCARTA (CAP); Brexucabtagene autoleucel – TECARTUS (CAP) – EMA/VR/0000308229

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Update of sections 4.2, 4.4, 4.5. 4.7 and 6.4 of the SmPC in order to modify the pre- and post-infusion monitoring recommendations and requirements related to the risk of CRS (cytokine release syndrome) and ICANS (immune effector cell-associated neurotoxicity syndrome) based on data from clinical trials, post-marketing experience and literature. The Package Leaflet is updated accordingly. The RMP version 7.1 has also been submitted. In addition, Annex II has been udated accordingly. Furthermore, the MAH took the opportunity to

update the list of local representatives in the Package Leaflet, to bring the PI in line with the latest QRD template version 10.4 and to implement editorial changes to the PI.

15.3.6. Baricitinib – OLUMIANT (CAP) – EMA/X/0000257923

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new pharmaceutical form (oral suspension) associated with a new strength (2 mg/ml).

15.3.7. Baricitinib – OLUMIANT (CAP) – EMA/VR/0000288098

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of adolescent patients (12 to less than 18 years) with severe alopecia areata for OLUMIANT, based on results from study I4V-MC-JAIO; this is a Phase 3, double-blind, randomised, placebo-controlled trial to evaluate the efficacy, safety, and pharmacokinetics of baricitinib in children from 6 years to less than 18 years of age with alopecia areata. 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 26.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI and to update the list of local representatives in the Package Leaflet.

15.3.8. Benralizumab – FASENRA (CAP) – EMA/VR/0000288520

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include treatment of adults and adolescents with hypereosinophilic syndrome (HES) for FASENRA, based on interim results from study D3254C00001 (NATRON); this is a multicentre, randomised, double-blind, parallel-group, placebo-controlled, 24-week phase III study with an open-label extension to evaluate the efficacy and safety of benralizumab in patients with HES; 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 8 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce editorial and administrative updates to the PI and to update the list of local representatives in the Package Leaflet. Furthermore, section 6.5 of the SmPC was updated.

15.3.9. Berotralstat – ORLADEYO (CAP) – EMA/X/0000268892

Applicant: Biocryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Extension application to introduce a new pharmaceutical form associated with new strengths (78 mg, 96 mg,108 and 132 film - coated granules). The new presentations are indicated to include treatment for paediatric patients aged 2 to less than 12 years. The extension application is grouped with a type II clinical variation (C.I.4). 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 and Labelling are updated in accordance. Version 2.1 of the RMP has also been submitted.

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

Applicant: Hipra Human Health S.L.

PRAC Rapporteur: Zane Neikena

Scope: Update of section 4.5 of the SmPC in order to add coadministration information with seasonal influenza vaccines based on final results from study HIPRA-HH-11. HIPRA-HH-11 was a Phase II randomized, double-blind, multi-centre trial to evaluate the safety and immunogenicity of BIMERVAX when coadministered with seasonal surface antigen, inactivated adjuvanted influenza vaccine (SIIV) in adults older than 65 years of age fully vaccinated against COVID-19. The Package Leaflet is updated accordingly. The RMP version 3.0 is also submitted. In addition, the MAH took the opportunity to introduce minor changes to the PI.

15.3.11. Darunavir / Cobicistat – REZOLSTA (CAP) – EMA/X/0000268372

Applicant: Janssen Cilag International

PRAC Rapporteur: Amelia Cupelli

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (600 mg darunavir/90 mg cobicistat dispersible tablet). The new presentation is indicated to include treatment for paediatric patients aged ≥ 3 years and older weighing at least 15 kg and less than 25 kg. The extension application is grouped with a type II clinical variation (C.I.4) to update sections 4.2, 4.4, 4.8, 5.1 and 5.2 in order to add efficacy and PK data in children based on final results from study GS-US-215-0128; this is a Phase 2/3, Multicentre, Open-label, Multicohort Study Evaluating Pharmacokinetics (PK), Safety, and Efficacy of Cobicistat-boosted Atazanavir (ATV/co) or Cobicistat-boosted Darunavir (DRV/co) and Emtricitabine/Tenofovir Alafenamide (F/TAF) in HIV-1 Infected, Virologically Suppressed Paediatric Participants. The Package Leaflet and Labelling are updated in accordance. Version 7.2 of the RMP has also been submitted.

15.3.12. Difelikefalin – KAPRUVIA (CAP) – EMA/VR/0000316094

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: A grouped application consisting of safety data from three studies of the oral difelikefalin formulation to support the safety of the intravenous difelikefalin formulation:

C.I.13: Submission of the final report from study CR845-310301 listed as a category 3 study in the RMP. This is a multicenter, randomized, double-blind, placebo-controlled 12-week study to evaluate the safety and efficacy of oral difelikefalin in advanced chronic kidney disease subjects with moderate-to-severe pruritus with an up to 52-week long-term extension. The RMP version 3.0 has also been submitted.

C.I.13: Submission of the final report from study CR845-310302 listed as a category 3 study in the RMP. This is a multicenter, randomized, double-blind, placebo-controlled 12-week study to evaluate the safety and efficacy of oral difelikefalin in advanced chronic kidney disease subjects with moderate-to-severe pruritus with an up to 52-week long-term extension

C.I.13: Submission of the final report from study CR845-310501 listed as a category 3 study in the RMP. This is a two-part, multicenter, randomized, double-blind study to evaluate the efficacy and safety of oral difelikefalin as adjunct therapy to a topical corticosteroid for moderate-to-severe pruritus in adult subjects with atopic dermatitis.

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

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

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

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

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

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

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

15.3.14. Enfortumab vedotin – PADCEV (CAP) – EMA/VR/0000312495

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include PADCEV, in combination with pembrolizumab, for use as neoadjuvant treatment and continued as adjuvant treatment following radical cystectomy, is indicated for the treatment of adult patients with muscle-invasive bladder cancer (MIBC) who are ineligible for cisplatin-containing chemotherapy, based on interim results from study EV-303/KN-905; this is a randomized phase 3 study evaluating cystectomy with perioperative pembrolizumab and cystectomy with perioperative enfortumab, vedotin and pembrolizumab versus cystectomy alone in participants who are cisplatin-ineligible or decline cisplatin with muscle-invasive bladder cancer. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, and to bring the PI in line with the latest QRD template version 10.4.

15.3.15. Enzalutamide – XTANDI (CAP) – EMA/VR/0000313098

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect the updated safety and efficacy data based on final results from 9785-CL-0335 (EMBARK) study; this is a phase 3, randomized, double-blind, placebo-controlled efficacy and safety study of enzalutamide plus androgen deprivation therapy (ADT) versus placebo plus ADT in patients with metastatic hormone sensitive prostate cancer (mHSPC); the Package Leaflet is updated accordingly. The RMP version 20.0 has also been submitted.

15.3.16. Epcoritamab – TEPKINLY (CAP) – EMA/VR/0000311043

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Extension of indication to include in combination with rituximab and lenalidomide treatment of patients with relapsed/refractory follicular lymphoma (FL) for Tepkinly, based on interim results from study M20-638; this is a Phase 3, open-label study to evaluate safety and efficacy of epcoritamab in combination with rituximab and lenalidomide (R2) compared to R2 in subjects with relapsed or refractory follicular lymphoma (EPCORE FL-1). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.2.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.17. Ferric maltol – FERACCRU (CAP) – EMA/VR/0000268118

Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of paediatric population (adolescents aged 12 years and above) for FERACCRU, based on results from phase 1 study ST10-01-103, phase 3 study ST10-01-305 and a supportive phase 1 study ST10-01-104. 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 9.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to implement editorial changes to the PI. Furthermore, the PI is brought in line with the latest QRD template version 10.4.

15.3.18. Influenza vaccine (live, nasal) – FLUENZ (CAP) – EMA/VR/0000302352

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to introduce self-administration instructions based on postmarketing data and literature. The Package Leaflet and Labelling updated accordingly. The RMP version 13.1 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.

15.3.19. Lazertinib – LAZCLUZE (CAP) – EMA/VR/0000315717

Applicant: Janssen Cilag International

PRAC Rapporteur: Petar Mas

Scope: Update of section 4.8 of the SmPC in order to add information regarding elevations in alkaline phosphatase and bilirubin with lazertinib monotherapy within the 'hepatotoxicity' subsection, based on a cumulative safety review. The RMP version 2.1 has also been submitted.

15.3.20. Lomitapide – LOJUXTA (CAP) – EMA/X/0000258068

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to add a new strength of 2 mg hard capsules. This application is grouped with

- type II variation (C.I.6.a): an Extension of Indication to include treatment of paediatric patients aged 5 years and older with homozygous familial hypercholesterolaemia (HoFH) for LOJUXTA, based on final results from the pivotal paediatric study APH-19; this is a phase 3,

single-arm, open-label, international, multi-centre study to evaluate the efficacy and safety of lomitapide in paediatric patients with homozygous familial hypercholesterolaemia (HOFH) on stable lipid-lowering therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Annex II and Package Leaflet are updated accordingly. The RMP version 7.1 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.

- 3 x type IB variations (C.I.7.b): to delete the 30 mg, 40 mg and 60 mg strengths from the Lojuxta marketing authorisation (EU/1/13/851/004 - 006).

15.3.21. Lorlatinib – LORVIQUA (CAP) – EMA/VR/0000292366

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Update of sections 4.2, 5.1 and 5.2 of the SmPC in order to update dosing recommendations in patients with moderate and severe hepatic impairment based on final results from study B7461040 listed as a category 3 study in the RMP; this is a Phase 1, Open-Label, Single-Dose, Parallel-Group Study to Evaluate the Plasma Pharmacokinetics and Safety of Lorlatinib in Participants with Moderate and Severe Hepatic Impairment Relative to Participants with Normal Hepatic Function. The Package Leaflet is updated accordingly. The RMP version 5.4 has also been submitted.

15.3.22. Mitapivat – PYRUKYND (CAP) – EMA/VR/0000315433

Applicant: Agios Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from study AG348-C-011 listed as a category 3 study in the RMP. This is a Phase 3, Multicenter, Open-label, Long-term, Extension Study of Mitapivat in Adults with PK Deficiency Previously Treated in Studies AG348-C-006 or AG348-C-007. The RMP version 2.1 has also been submitted.

15.3.23. Nivolumab / Relatlimab – OPDUALAG (CAP) – EMA/VR/0000314728

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on Myocarditis-Myositis-Myasthenia Gravis Overlap Syndrome, and add Myocarditis-Myositis-Myasthenia Gravis Overlap Syndrome to the list of adverse drug reactions (ADRs) with frequency Uncommon based on postmarketing data and literature; the Package Leaflet is updated accordingly. The RMP version 5.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.24. Nivolumab – OPDIVO (CAP) – EMA/X/0000304427

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Extension application to add a new strength of 300 mg solution for injection.

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

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

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

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of section 5.3 of the SmPC in order to update preclinical information based on results from study RTA-P-21070: this is a 104-week once daily oral gavage toxicity and toxicokinetic study with RTA 408 in rats. The RMP version 2.0 has also been submitted.

15.3.27. Pembrolizumab – KEYTRUDA (CAP) – EMA/VR/0000312515

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include in combination with enfortumab vedotin, as neoadjuvant treatment and then continued after radical cystectomy as adjuvant treatment of adults with muscle invasive bladder cancer (MIBC) who are ineligible for cisplatin containing

chemotherapy for KEYTRUDA, based on interim results from study KEYNOTE-905, an open label, randomised, interventional phase 3 study. As consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 51.1 of the RMP has also been submitted.

15.3.28. Ponatinib – ICLUSIG (CAP) – EMA/X/0000296489

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (5 mg hard capsule) grouped with an Extension of Indication to include treatment of paediatric patients aged 6 years and older with chronic phase chronic myeloid leukaemia (CP-CML) who are resistant or intolerant to at least one tyrosine kinase inhibitor for ICLUSIG, based on interim results from study INCB 84344-102 and a final results from early-terminated study Ponatinib-1501; the first is an ongoing open-label, single-arm, Phase 1/2 study evaluating the safety and efficacy of ponatinib MONOTHERAPY for the treatment of R/R leukemias, lymphomas, or solid tumors in pediatric participants. The second is a Phase 1/2, single-arm, open-label, multicenter study designed to evaluate the safety, tolerability, PK, and efficacy of ponatinib when administered IN COMBINATION WITH multiagent CHEMOTHERAPY in pediatric patients with Ph+ ALL, Ph+ MPAL, or Ph-like ALL who had a relapse, were resistant or intolerant to at least 1 prior BCR-ABL1 TKI therapy, or had the T315I mutation. As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.8, 5.1, 5.2, 6.1 and 6.5 of the SmPC are updated. Package Leaflet is updated accordingly. The RMP version 23.4 has also been submitted.

15.3.29. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – MRESVIA (CAP) – EMA/VR/0000312911

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by Respiratory Syncytial Virus (RSV) in all adults 18 years of age and older for mRESVIA, based on results from Study mRNA-1345-P101, Study mRNA-1345-P301, Study mRNA-1345-P303 Part A, and Study mRNA-1345-P302 Part A and Part B. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.0 of the RMP has also been submitted.

15.3.30. Roflumilast – DAXAS (CAP) – EMA/VR/0000315545

Applicant: AstraZeneca AB

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Submission of the final report from study ROF-MD-07. This is a 52-Week, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study to Evaluate the Effect of Roflumilast

500 µg on Exacerbation Rate in Patients With Chronic Obstructive Pulmonary Disease (COPD) Treated With a Fixed-Dose Combination of Long-Acting Beta Agonist and Inhaled Corticosteroid (LABA/ICS). The RMP version 24 has also been submitted.

15.3.31. Sacituzumab govitecan – TRODELVY (CAP) – EMA/VR/0000312649

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication for treatment of adult patients with PD-L1-negative metastatic triple- negative breast cancer or PD-L1-positive metastatic triple-negative breast cancer previously treated with an anti-PD-(L)1 agent in the curative setting for Trodelvy, based on results from study GS-US-592-6238 (ASCENT-03), which is a phase 3 study of sacituzumab govitecan (IMMU-132) versus treatment of physician's choice (TPC) in Patients With Previously Untreated, Locally Advanced, Inoperable or Metastatic Triple-Negative Breast Cancer Whose Tumors Do Not Express PD-L1 or in Patients Previously Treated With Anti-PD-(L)1 Agents in the Early Setting Whose Tumors Do Express PD-L1. As a consequence, sections 4.1, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted

15.3.32. Setmelanotide – IMCIVREE (CAP) – EMA/VR/0000288021

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Miroslava Gocova

Scope: Extension of indication to include reduction in hunger (or hyperphagia) and BMI (Body Mass Index)/BMI z-score, improvement of metabolic parameters, and increase in energy expenditure in adults and children 4 years of age and above, following rapid and severe weight gain associated with hypothalamic injury and/or impairment for IMCIVREE, based on results from study RM-493-040 as well as supportive study RM-493-030. RM-493-040 is a phase 3, double blind, randomized, placebo-controlled trial to evaluate the efficacy and safety of setmelanotide in patients with acquired hypothalamic obesity, while RM-493-030 is a phase 2, open-label 20-week study to evaluate the safety and efficacy of setmelanotide in subjects with hypothalamic obesity. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are being updated. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorial and administrative changes to the PI.

15.3.33. Smallpox and monkeypox vaccine (live modified vaccinia virus Ankara) – IMVANEX (CAP) – EMA/VR/0000316261

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Dirk Mentzer

Scope: A grouped application as follows:

Type II (C.I.4): Update of sections 4.8 and 5.1 in order to update clinical information based on the final clinical study report of study DMID 22-0020 stage 2, listed as a Specific Obligation in the Annex II. This is a Phase 2 randomized open label multisite trial to inform Public Health strategies involving the use of MVA-BN vaccine for Mpox. The Annex II and Package Leaflet are updated in accordance. The RMP version 11.1 has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the PI.

Type IA (A.6): To change the ATC Code from 'other viral vaccines, ATC code: J07BX' to 'smallpox and monkeypox vaccines, ATC code: J07BX01'

15.3.34. Sotatercept – WINREVAIR (CAP) – EMA/VR/0000315667

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Update of sections 4.4, 4.8, and 5.1 of the SmPC in order to update efficacy and safety information based on the final results from the study MK-7962-005 (HYPERION). MK-7962-005 (HYPERION) is a Phase 3, randomized, double-blind, placebo-controlled study designed to evaluate the effect of sotatercept in participants who had received the diagnosis less than 1 year earlier, had an intermediate or high risk of death, and were receiving double or triple background therapy. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.35. Tirzepatide – MOUNJARO (CAP) – EMA/VR/0000310637

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to reduce the risk of major adverse cardiovascular events (cardiovascular death, myocardial infarction, or stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease for MOUNJARO, based on final results from study I8F-MC-GPGN (SURPASS-CVOT). SURPASS-CVOT was a Phase 3, event-driven, multicentre, international, randomized, double-blind, active-comparator, parallel-group study to assess the effect of tirzepatide versus dulaglutide on major adverse cardiovascular events in participants with type 2 diabetes. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial and formatting changes to the PI.

15.3.36. Upadacitinib – RINVOQ (CAP) – EMA/X/0000304823

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength and change of pharmacokinetics (1 mg/ml oral solution) grouped with an extension of indication (C.I.6.a) to include the treatment of active polyarticular course juvenile idiopathic arthritis (pcJIA) in patients 2 years of age and older based on clinical data and results from clinical phase 1 study (study M15-340). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC have been updated. The Package Leaflet has been updated accordingly. Version 17 of the RMP has also been submitted. In addition, the MAH took the opportunity to update Annex II.

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

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

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

15.3.38. Ustekinumab – OTULFI (CAP) – EMA/VR/0000296289

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Quality

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. Aclidinium – BRETARIS GENUAIR (CAP); EKLIRA GENUAIR (CAP) – EMA/PSUR/0000305035

Applicant: Covis Pharma Europe B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00009005/202507)

16.1.2. Afamelanotide – SCENESSE (CAP) – EMA/PSUR/0000305040

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010314/202506)

16.1.3. Alectinib – ALECENSA (CAP) – EMA/PSUR/0000305041

Applicant: Roche Registration GmbH

PRAC Rapporteur: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00010581/202507)

16.1.4. Anifrolumab – SAPHNELO (CAP) – EMA/PSUR/0000305059

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010980/202507)

16.1.5. Avapritinib – AYVAKYT (CAP) – EMA/PSUR/0000305025

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010878/202507)

16.1.6. Beclometasone / Formoterol / Glycopyrronium bromide – TRIMBOW (CAP); TRYDONIS (CAP) – EMA/PSUR/0000305048

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010617/202507)

16.1.7. Belatacept – NULOJIX (CAP) – EMA/PSUR/0000305012

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00000311/202506)

16.1.8. Budesonide – JORVEZA (CAP) – EMA/PSUR/0000305032

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure (PSUSA/00010664/202507)

16.1.9. C1 esterase inhibitor (human) – CINRYZE (CAP) – EMA/PSUR/0000305079

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010104/202506)

16.1.10. Cefepime / Enmetazobactam – EXBLIFEP (CAP) – EMA/PSUR/0000305019

Applicant: Advanz Pharma Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000305/202506)

16.1.11. Cenegermin – OXERVATE (CAP) – EMA/PSUR/0000305014

Applicant: Dompe Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010624/202507)

16.1.12. Darolutamide – NUBEQA (CAP) – EMA/PSUR/0000305057

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010843/202507)

16.1.13. Decitabine / Cedazuridine – INAQOVI (CAP) – EMA/PSUR/0000305018

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000118/202507)

16.1.14. Eptacog beta (activated) – CEVENFACTA (CAP) – EMA/PSUR/0000305028

Applicant: Laboratoire Francais Du Fractionnement Et Des Biotechnologies

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011006/202507)

16.1.15. Finerenone – KERENDIA (CAP) – EMA/PSUR/0000305023

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010978/202507)

16.1.16. Garadacimab – ANDEMBRY (CAP) – EMA/PSUR/0000305046

Applicant: CSL Behring GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011109/202507)

16.1.17. Gefapixant – LYFNUA (CAP) – EMA/PSUR/0000305009

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000132/202507)

16.1.18. Glucagon – BAQSIMI (CAP); OGLUO (CAP) – EMA/PSUR/0000305033

Applicants: Amphastar France Pharmaceuticals, Strongbridge Dublin Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00010826/202507)

16.1.19. Glucarpidase – VORAXAZE (CAP) – EMA/PSUR/0000305021

Applicant: Serb

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010968/202507)

16.1.20. Guselkumab – TREMFYA (CAP) – EMA/PSUR/0000305076

Applicant: Janssen Cilag International

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010652/202507)

16.1.21. Inotersen – TEGSEDI (CAP) – EMA/PSUR/0000305036

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00010697/202507)

16.1.22. Lomitapide – LOJUXTA (CAP) – EMA/PSUR/0000305062

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010112/202507)

16.1.23. Netarsudil – RHOKIINSA (CAP) – EMA/PSUR/0000305050

Applicant: Santen Oy

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00107812/202506)

16.1.24. Odevixibat – BYLVAY (CAP); KAYFANDA (CAP) – EMA/PSUR/0000305038

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010949/202507)

16.1.25. 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) – EMA/PSUR/0000305049

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00011057/202507)

16.1.26. Phenylephrine / Ketorolac – OMIDRIA (SRD) (CAP) – EMA/PSUR/0000305058

Applicant: Rayner Surgical (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010419/202507)

16.1.27. Pirtobrutinib – JAYPIRCA (CAP) – EMA/PSUR/0000305011

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000155/202507)

16.1.28. Remimazolam – BYFAVO (CAP) – EMA/PSUR/0000305045

Applicant: Paion Pharma GmbH

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00010924/202507)

16.1.29. Smallpox and monkeypox vaccine (live modified vaccinia virus Ankara) – IMVANEX (CAP) – EMA/PSUR/0000305075

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010119/202507)

16.1.30. Sofosbuvir / Velpatasvir – EPCLUSA (CAP) – EMA/PSUR/0000305055

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010524/202506)

16.1.31. Tafasitamab – MINJUVI (CAP) – EMA/PSUR/0000305027

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010951/202507)

16.1.32. Teprotumumab – TEPEZZA (CAP) – EMA/PSUR/0000305056

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011148/202507)

16.1.33. Tocofersolan – VEDROP (CAP) – EMA/PSUR/0000305051

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00002981/202507)

16.1.34. Voretigene neparvovec – LUXTURNA (CAP) – EMA/PSUR/0000305077

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010742/202507)

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

16.2.1. Dasatinib – SPRYCEL (CAP); NAP – EMA/PSUR/0000305016

Applicants: Bristol-Myers Squibb Pharma EEIG, various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000935/202506)

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

16.3.1. Alfacalcidol (NAP) – EMA/PSUR/0000305008

Applicants: various

PRAC Lead: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000080/202506)

16.3.2. Amlodipine/irbesartan (NAP) – EMA/PSUR/0000305030

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00010876/202506)

16.3.3. Ascorbic acid / paracetamol / phenylephrine hydrochloride (NAP) – EMA/PSUR/0000305010

Applicants: various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00000255/202506)

16.3.4. Benzylpenicillin (NAP); benzathine benzylpenicillin (NAP); benzathine benzylpenicillin / lidocaine (NAP); procaine benzylpenicillin (NAP); benzathine benzylpenicillin / procaine benzylpenicillin (NAP) – EMA/PSUR/0000305013

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00000383/202506)

16.3.5. Bethanechol (NAP) – EMA/PSUR/0000305015

Applicants: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000402/202506)

16.3.6. Calcifediol (NAP) – EMA/PSUR/0000305017

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000491/202506)

16.3.7. Clonazepam (NAP) – EMA/PSUR/0000305022

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00000812/202506)

16.3.8. Diphtheria / tetanus / pertussis (acellular (NAP); component) and poliomyelitis (inactivated) vaccine (adsorbed) (NAP); diphtheria / tetanus / pertussis (acellular (NAP); component) and poliomyelitis (inactivated) vaccine (adsorbed (NAP); reduced antigen(s) content) (NAP) – EMA/PSUR/0000305024

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00001126/202507)

16.3.9. Ethinylestradiol / etonogestrel (NAP) – EMA/PSUR/0000305026

Applicants: various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001307/202507)

16.3.10. Ganciclovir (NAP) – EMA/PSUR/0000305047

Applicants: various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00001516/202506)

16.3.11. Itopride (NAP) – EMA/PSUR/0000305039

Applicants: various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00010606/202506)

16.3.12. Magnesium sulfate (NAP) – EMA/PSUR/0000305052

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00009225/202506)

16.3.13. Misoprostol (gastrointestinal indication) (NAP) – EMA/PSUR/0000305043

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010291/202506)

16.3.14. Mitoxantrone (NAP) – EMA/PSUR/0000305042

Applicants: various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00002076/202506)

16.3.15. Nitrous oxide (NAP); nitrous oxide / oxygen (NAP) – EMA/PSUR/0000305054

Applicants: various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00010572/202506)

16.3.16. Rifabutin (NAP) – EMA/PSUR/0000305031

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00002639/202507)

16.4. Follow-up to PSUR/PSUSA procedures

None

16.5. Variation procedure(s) resulting from PSUSA evaluation

16.5.1. Natalizumab (NAP) – EMA/VR/0000315289

Applicants: various

PRAC Rapporteur: Dirk Mentzer

Scope: Update of sections 4.2, 4.4 of the SmPC, and Annex II in order to align with the revised content of the additional risk minimisation materials in the RMP following the PRAC recommendation in EU PSUR 23 for the Tysabri (EMEA/H/C/PSUSA/00002127/202408). The Package Leaflet is updated accordingly. The RMP version 34.1 has been submitted; the due date for the provision of the final CSR for category 3 PASS study 101MS412 is also being revised.

16.6. Expedited summary safety reviews[18]

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)[19]

17.1.1. Ketoconazole – KETOCONAZOLE ESTEVE (CAP) – EMA/PASS/0000287667

Applicant: Esteve Pharmaceuticals S.A.

PRAC Rapporteur: Petar Mas

Scope: PASS amendment [107o]: Prospective, Multi-Country, Observational Registry to collect clinical information on patients with endogenous CS exposed to Ketoconazole ESTEVE (using the existing European Registry on CS (ERCUSYN)), to assess drug utilization pattern and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of Ketoconazole ESTEVE.

[18] 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

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

17.1.2. Odevixibat – KAYFANDA (CAP) – EMA/PASS/0000262884

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: PASS protocol [107n]: Prospective non-interventional study evaluating the long-term safety of odevixibat in patients with Alagille Syndrome (ALGS)

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[20]

17.2.1. Birch bark extract – FILSUVEZ (CAP) – EMA/PAM/0000316631

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Zane Neikena

Scope: Submission of an amended protocol for the non-imposed (category 3) Post-Authorisation Safety Study (PASS) Foster, "A long-term non-interventional study to assess the incidence of skin malignancies in patients with dystrophic and junctional epidermolysis bullosa receiving treatment with Filsuvez "

17.2.2. Concizumab – ALHEMO (CAP) – EMA/PAM/0000280062

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of the category 3 PASS NN7415-7533 protocol: A registry-based observational cohort study to characterise the safety profile of concizumab in people with haemophilia in the real-world setting.

17.2.3. Dimethyl fumarate – SKILARENCE (CAP) – EMA/PAM/0000316578

Applicant: Almirall S.A.

PRAC Rapporteur: Karin Bolin

Scope: Submission of amended protocol for the non-imposed (category 3) Post Authorisation Safety Study (PASS) M-41008-40, “An Observational Post-Authorisation Safety Study of Skilarence in European Psoriasis Registers”; Protocol, version 3.0, dated 25 November 2025; former EMA/PAM/0000280214

[20] 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

17.2.4. Efanesoctocog alfa – ALTUVOCT (CAP) – EMA/PAM/0000269605

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Amelia Cupelli

Scope: Response to PRAC Rapporteur's Request for Supplementary Information of EMEA/H/C/005968/MEA/002.

Updated protocol of the Observational Registry Study in Previously Untreated Patients (PUPs) with Hemophilia A (ATHN), a non-imposed non-interventional post-authorization safety study (NI-PASS)

17.2.5. Galcanezumab – EMGALITY (CAP) – EMA/PAM/0000309244

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: New PASS protocol addendum for ongoing non-interventional PASS I5Q-MC-B001: A Cohort Study to Assess Drug Utilisation and Long-Term Safety of Galcanezumab in US Patients in the Course of Routine Clinical Care (category 3 study in the RMP).

17.2.6. Inavolisib – ITOVEBI (CAP) – EMA/PAM/0000301716

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: PASS Protocol GO46271: Evaluating safety in insulin-requiring diabetic receiving inavolisib plus endrocrine therapy-based regiments in the real world.

17.2.7. Marstacimab – HYMPAVZI (CAP) – EMA/PAM/0000273932

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of responses to questions following the submission of the PASS protocol for the category 3 post-authorisation study B7841016, a Post-Authorisation Safety Study to Evaluate the Safety of Marstacimab Among Patients with Severe Haemophilia A or B using Real-World Data in European Haemophilia Register

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

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

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

17.3. Results of PASS imposed in the marketing authorisation(s)[21]

None

17.4. Results of PASS non-imposed in the marketing authorisation(s)[22]

17.4.1. Levofloxacin – QUINSAIR (CAP) – EMA/VR/0000310972

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the amended final report for study CLI-LEVFLAA1-01. This is a post-marketing, observational safety study of Quinsair (levofloxacin hemihydrate) in patients with cystic fibrosis.

Action: For adoption

17.4.2. Linaclotide – CONSTELLA (CAP) – EMA/VR/0000281586

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study EVM-18888 (P21-481) listed as a category 3 study in the RMP. The study, titled "Linaclotide Safety Study for the Assessment of Diarrhoea Complications and Associated Risk Factors in Selected European Populations with IBS-C," is an observational safety study. It assesses the risk of severe complications of diarrhoea (SCD) during treatment with linaclotide, as well as other risk factors among patients with IBS-C in the UK, Sweden, and Spain. The RMP version 11.2 has also been submitted.

Action: For adoption

17.4.3. Ofatumumab – KESIMPTA (CAP) – EMA/VR/0000315689

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Update of section 4.6 'pregnancy' of the SmPC based on the final reports from Kesimpta Pregnancy Registry and the PRegnancy outcomes Intensive Monitoring (PRIM) study.

[21] In accordance with Article 107p-q of Directive 2001/83/EC
[22] 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

Action: For adoption

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

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

Action: For adoption

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

17.5.1. Axicabtagene ciloleucel – YESCARTA (CAP) – EMA/PAM/0000316955

Applicant: Kite Pharma EU B.V. ATMP

PRAC Rapporteur: Karin Erneholm

Scope: Fifth annual safety Report for the non-interventional post authorisation safety study (PASS) for Yescarta: Study KT-EU-471-0117

17.5.2. Drospirenone / Estetrol – DROVELIS (CAP) – EMA/PAM/0000281181

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Second interim study report with cut-off date of 21 April 2025 of PASS study titled "International Active Surveillance Study: Native Estrogen Estetrol (E4) Safety Study (INAS-NEES)"

17.5.3. Drospirenone / Estetrol – LYDISILKA (CAP) – EMA/PAM/0000281178

Applicant: Estetra

PRAC Rapporteur: Martin Huber

Scope: Second interim study report with cut-off date of 21 April 2025 of PASS study titled "International Active Surveillance Study: Native Estrogen Estetrol (E4) Safety Study (INAS-NEES)"

17.5.4. Exagamglogene autotemcel – CASGEVY (CAP) – EMA/PAM/0000316999

Applicant: Vertex Pharmaceuticals (Ireland) Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: PASS Study (VX22-290-101) Annual Progress Report for Casgevy (exagamglogene autotemcel) covering the reporting period January to October 2025.

17.5.5. Galcanezumab – EMGALITY (CAP) – EMA/PAM/0000314992

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Study Progress Reports for non-interventional studies I5Q-MC-B001, I5Q-MC-B002 and I5Q-MC-B003

17.5.6. Inotersen – TEGSEDI (CAP) – EMA/PAM/0000314977

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: TEG 005 = Pregnancy Surveillance Programme - covering the period from 17 Oct 2019 to 16 Oct 2025. Interim report.

17.5.7. Interferon beta-1a – AVONEX (CAP) – EMA/PAM/0000315762

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the Study Report for joint PASS INFORM - Interferon-Beta Exposure in the 2nd and 3rd Trimester of Pregnancy - a Register-Based Drug Utilisation Study in Finland and Sweden.

17.5.8. Interferon beta-1b – BETAFERON (CAP) – EMA/PAM/0000309054

Applicant: Bayer AG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the Study Report for joint PASS INFORM - Interferon-Beta Exposure in the 2nd and 3rd Trimester of Pregnancy - a Register-Based Drug Utilisation Study in Finland and Sweden.

17.5.9. Interferon beta-1a – REBIF (CAP) – EMA/PAM/0000315764

Applicant: Merck Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the Study Report for joint PASS INFORM - Interferon-Beta Exposure in the 2nd and 3rd Trimester of Pregnancy - a Register-Based Drug Utilisation Study in Finland and Sweden.

17.5.10. Ivosidenib – TIBSOVO (CAP) – EMA/PAM/0000316636

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Responses to PRAC List of Requests issued for the Post-Authorisation Measure (MEA 003.1) MEA/01297/1

PASS - IMPACTA - EUPAS1000000190

Patients survey study to assess the effectiveness of the additional risk minimisation measures.

Cross-sectional study to assess the effectiveness of the patients' alert card to inform on risk of differentiation syndrome in AML patients treated with TIBSOVO (Ivosidenib).

17.5.11. Peginterferon beta-1a – PLEGRIDY (CAP) – EMA/PAM/0000315767

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the Study Report for joint PASS INFORM - Interferon-Beta Exposure in the 2nd and 3rd Trimester of Pregnancy - a Register-Based Drug Utilisation Study in Finland and Sweden.

17.5.12. Rimegepant – VYDURA (CAP) – EMA/PAM/0000314939

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: The second progress report (MEA003) for the study entitled Post-Authorisation Safety Study of Rimegepant in Patients with Migraine and History of Cardiovascular Disease in European Countries.

17.5.13. Somapacitan – SOGROYA (CAP) – EMA/PAM/0000314915

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Fifth study progress report with the data cut-off date of 31 Aug 2025 for PASS NN8640-4515: a multi-national, multi-centre, prospective, single-arm, observational, non-interventional post-authorisation safety study to investigate long-term safety of Sogroya® (somapacitan) in adults with growth hormone deficiency (AGHD) under routine clinical practice.

17.5.14. Somapacitan – SOGROYA (CAP) – EMA/PAM/0000316564

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: 1st interim report for PASS NN8640-4787 (REAL 10): a non-interventional, observational, register-based study to investigate long-term safety and clinical parameters of

somapacitan treatment in paediatric patients with GHD in the setting of routine clinical practice.

17.5.15. Turoctocog alfa pegol – ESPEROCT (CAP) – EMA/PAM/0000314924

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Dirk Mentzer

Scope: 5th PASS progress report for Study 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.

17.5.16. Ustekinumab – STELARA (CAP) – EMA/PAM/0000316549

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Third interim study report - An observational post authorization safety study to describe the safety of ustekinumab and other treatments of ulcerative colitis in a cohort of patients with ulcerative colitis using the independent French Nationwide Claims Database (SNDS; PCSIMM002659); former MEA 0048

17.6. New Scientific Advice

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

17.7. Ongoing Scientific Advice

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

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

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

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

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

18.1. Annual reassessments of the marketing authorisation

18.1.1. Cholic acid – ORPHACOL (CAP) – EMA/S/0000310692

Applicant: Theravia

PRAC Rapporteur: Maria Poulianiti

Scope: Annual reassessment of the marketing authorisation

18.1.2. Fosdenopterin – NULIBRY (CAP) – EMA/S/0000312759

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

18.1.3. Idebenone – RAXONE (CAP) – EMA/S/0000310527

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

18.1.4. Mecasermin – INCRELEX (CAP) – EMA/S/0000293938

Applicant: Esteve Pharmaceuticals S.A.

PRAC Rapporteur: Terhi Lehtinen

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

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

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Veronika Macurova

Scope: Conditional renewal of the marketing authorisation

18.2.2. Mosunetuzumab – LUNSUMIO (CAP) – EMA/R/0000314743

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.2.3. Selumetinib – KOSELUGO (CAP) – EMA/R/0000316378

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.2.4. Zanidatamab – ZIIHERA (CAP) – EMA/R/0000316461

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Abiraterone acetate – ABIRATERONE MYLAN (CAP) – EMA/R/0000312706

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

18.3.2. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence – STRIMVELIS (CAP) – EMA/R/0000290462

Applicant: Fondazione Telethon Ets

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

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

Applicant: UCB Pharma

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

18.3.4. Icatibant – ICATIBANT ACCORD (CAP) – EMA/R/0000300686

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.5. Ranibizumab – BYOOVIZ (CAP) – EMA/R/0000312514

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Karin Bolin

Scope: 5-year renewal of the marketing authorisation

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

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Miroslava Gocova

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 09-12 February 2026 PRAC meeting, which was held in-person.

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 DoI	Topics for which restriction apply
Ulla Wändel Liminga	Chair	Sweden	No interests declared	
Jan Neuhauser	Member*	Austria	No interests declared	
Sonja Radowan	Alternate*	Austria	No interests declared	
Jean-Michel Dogné	Member	Belgium	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Jo Robays	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva	Member	Bulgaria	No interests declared	
Stanislav Stoilov	Alternate	Bulgaria	No interests declared	
Petar Mas	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi	Alternate*	Croatia	No interests declared	
Panagiotis Psaras	Member*	Cyprus	No interests declared	
Elena Kaisis	Alternate*	Cyprus	No interests declared	
Eva Jirsová	Member*	Czechia	No interests declared	
Veronika Macurova	Alternate	Czechia	No interests declared	
Marie Louise Schougaard Christiansen	Member	Denmark	No interests declared	
Karin Erneholm	Alternate	Denmark	No interests declared	
Maia Uusküla	Member*	Estonia	No interests declared	
Krõõt Aab	Alternate*	Estonia	No interests declared	
Terhi Lehtinen	Member	Finland	No interests declared	
Kimmo Jaakkola	Alternate*	Finland	No interests declared	
Tiphaine Vaillant	Member	France	No interests declared	
Zoubida Amimour	Alternate*	France	No participation in discussion, final deliberations and voting on:	15.3.23. EMA/VR/0000314728 15.3.24. EMA/X/0000304427 16.1.7. EMA/PSUR/0000305012 16.2.1. EMA/PSUR/0000305016

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Martin Huber	Member	Germany	No interests declared	
Dirk Mentzer	Alternate	Germany	No interests declared	
Georgia Gkegka	Member*	Greece	No interests declared	
Maria Poulianiti	Alternate*	Greece	No restrictions applicable to this meeting	
Julia Pallos	Member	Hungary	No participation in discussion, final deliberations and voting on:	15.3.23. EMA/VR/00003 14728 15.3.24. EMA/X/000030 4427 16.1.7. EMA/PSUR/000 0305012 16.2.1. EMA/PSUR/000 0305016
Melinda Palfi	Alternate*	Hungary	No interests declared	
Guðrún Stefánsdóttir	Member*	Iceland	No participation in discussion, final deliberations and voting on:	5.1.7. EMEA/H/C/006 451 6.1.3. EMA/PSUR/000 0305056
Rhea Fitzgerald	Member	Ireland	No interests declared	
Eamon O Murchu	Alternate	Ireland	No interests declared	
Amelia Cupelli	Member	Italy	No interests declared	
Zane Neikena	Member	Latvia	No interests declared	
Diana Litenboka	Alternate*	Latvia	No interests declared	
Lina Seibokiene	Alternate	Lithuania	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Anne-Cecile Vuillemin	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No restrictions applicable to this meeting	
Liana Martirosyan	Member	Netherlands	No interests declared	
Bianca Mulder	Alternate	Netherlands	No interests declared	
David Olsen	Member	Norway	No participation in discussion, final deliberations and voting on:	16.1.12. EMA/PSUR/0000305057 16.1.15. EMA/PSUR/0000305023 17.5.8. EMA/PAM/0000309054
Pernille Harg	Alternate	Norway	No interests declared	
Adam Przybylkowski	Member*	Poland	No restrictions applicable to this meeting	
Katarzyna Ziolkowska	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins	Member	Portugal	No interests declared	
Carla Torre	Alternate	Portugal	No restrictions applicable to this meeting	
Roxana Dondera	Member	Romania	No interests declared	
Roxana Stefania Udrescu	Alternate	Romania	No interests declared	
Miroslava Gocova	Member	Slovakia	No interests declared	
Jana Pecherova	Alternate	Slovakia	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Marjetka Plementas	Alternate	Slovenia	No interests declared	
Maria del Pilar Rayon	Member	Spain	No interests declared	
Maria Martinez Gonzalez	Alternate	Spain	No interests declared	
Mari Thorn	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin	Alternate	Sweden	No restrictions applicable to this meeting	
Annalisa Capuano	Member*	Independent scientific expert	No restrictions applicable to this meeting	
Milou-Daniel Drici	Member	Independent scientific expert	No restrictions applicable to this meeting	
Maria Teresa Herdeiro	Member	Independent scientific expert	No restrictions applicable to this meeting	
Patricia McGettigan	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark	Member	Independent scientific expert	No restrictions applicable to this meeting	
Roberto Frontini	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Martin Votava	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Yiannoula Koulla	Member*	Patients' Organisation Representative	No interests declared	
Michal Rataj	Alternate	Patients' Organisation Representative	No interests declared	
Christelle Bizimungu	Expert	Belgium	No interests declared	
Martine Sabbe	Expert	Belgium	No interests declared	
Chloé Wyndham-Thomas	Expert	Belgium	No restrictions applicable to this meeting	
Dominik Dautović	Expert	Croatia	No interests declared	
Behija Hudina	Expert	Croatia	No restrictions applicable to this meeting	
Nina Lalić	Expert	Croatia	No restrictions applicable to this meeting	
Jana Kopecka	Expert	Czech Republic	No interests declared	
Michaela Skorepova	Expert	Czech Republic	No interests declared	
Kristina Bech Jensen	Expert	Denmark	No interests declared	
Cecilie Louise Pedersen	Expert	Denmark	No participation in discussion, final deliberations and voting on:	15.3.33. EMA/VR/00003 16261 16.1.29. EMA/PSUR/000 0305075 17.2.2. EMA/PAM/0000 280062 17.5.13. EMA/PAM/0000 314915 17.5.14. EMA/PAM/0000 316564

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				17.5.15. EMA/PAM/0000 314924
Karima Adamo	Expert	France	No interests declared	
Thomas Berbain	Expert	France	No interests declared	
Jean-Daniel Lelièvre	Expert	France	No restrictions against giving the SAG report for Levamisole	
Marion Perrin	Expert	France	No interests declared	
Dennis Lex	Expert	Germany	No interests declared	
Christopher Schulze	Expert	Germany	No interests declared	
Laura Zein	Expert	Germany	No interests declared	
Kevin Keohane	Expert	Ireland	No interests declared	
Sharon Essink	Expert	Netherlands	No restrictions applicable to this meeting	
Lisa Heltzel	Expert	Netherlands	No restrictions applicable to this meeting	
Sophia Venzke	Expert	Netherlands	No interests declared	
Ruxandra-Ana Moldoveanu	Expert	Romania	No interests declared	
Irina Sandu	Expert	Romania	No interests declared	
Iulia-Maria Stanescu	Expert	Romania	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Bernice Aronsson	Expert	Sweden	No interests declared	
Helena Back	Expert	Sweden	No interests declared	
Charlotte Backman	Expert	Sweden	No interests declared	
Jenny Jönsson	Expert	Sweden	No participation in discussion, final deliberations and voting on:	15.2.1. EMA/VR/00002 96305 15.3.2. EMA/VR/00003 15105 15.3.27. EMA/VR/00003 12515
Karin Nylén	Expert	Sweden	No interests declared	
A representative from the European Commission attended the meeting				
Observers from Health Canada (Canada) attended the meeting.				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

None

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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

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

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