14 November 2025
EMA/PRAC/352486/2025
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes for PRAC meeting on 29 September – 02 October 2025

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

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

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

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

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

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

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

1.2. Agenda of the meeting on 29 September-02 October 2025

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

1.3. Minutes of the previous meeting on 01-04 September 2025

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

Post-meeting note: the PRAC minutes of the meeting held on 01-04 September 2025 were published on the EMA website on 24 October 2025 (EMA/PRAC/326133/2025).

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[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

4.1.1. Tirzepatide – MOUNJARO (CAP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Signal of drug interaction with warfarin and other coumarin derivatives leading to

[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

international normalised ratio decreased

EPITT 20198 – New signal

Lead Member State(s): NL

Background

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

During routine signal detection activities, a signal of drug interaction with warfarin and other coumarin derivatives leading to international normalised ratio decreased was identified by Spain, based on 4 cases retrieved from EudraVigilance and the literature. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from case reports in EudraVigilance and in the literature, PRAC agreed that further evaluation on the signal of drug interaction with warfarin and other coumarin derivatives leading to international normalised ratio decreased is warranted.

Summary of recommendation(s)

- The MAH for Mounjaro (tirzepatide) should submit to EMA, within 90 days, a cumulative review of cases of drug-drug interaction with warfarin and other coumarin derivatives leading to international normalised ratio (INR) decreased, including an analysis from all sources, i.e. preclinical studies, clinical studies, non-interventional studies, spontaneous reports and scientific literature. The MAH should discuss the need to amend the product information and/or the risk management plan (RMP), as warranted.
- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.2. Pancreatin (NAP)

Applicant: various

PRAC Rapporteur: Martin Huber

Scope: Signal of infection due to viral transmission

EPITT 20205 – New signal

Lead Member State(s): DE

Background

Pancreatin is a pancreatic enzyme preparation derived from porcine pancreatic glands, indicated for pancreatic enzyme replacement treatment (PERT) in pancreatic exocrine insufficiency due to cystic fibrosis or other conditions (e.g. chronic pancreatitis, pancreatectomy or pancreatic cancer), in infants, children, adolescents and adults.

During routine signal detection activities, a signal of infection due to viral transmission was identified by EMA, based on literature and cases retrieved from EudraVigilance. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from the literature including case reports of chronic hepatitis E virus (HEV) infection under PERT and information from manufactures of porcine pancreatin products on virus depletion, PRAC agreed that further evaluation on the signal of infection due to viral transmission is warranted.

PRAC appointed Martin Huber as Rapporteur for the signal.

- **Summary of recommendation(s)**The MAHs for pancreatin-containing products should submit to EMA, within 60 days, a cumulative review of all cases of suspected viral infections with use of porcine pancreatin-containing products, a literature review on the risk of infection due to viral transmission associated with treatment with use of porcine pancreatin-containing products (including a critical discussion of the results from the studies *by Thornton et al., 2024*[3] and *Kamar et al., 2024*[4]). Considering the above, the MAHs should discuss patient populations at risk and the risk of viral transmission to humans, the manufacturing process and implemented measures used to minimise the potential of viral transmission, the causal relationship between risk of infection due to viral transmission and treatment with porcine pancreatin-containing products, as well as the need to amend the product information (PI) and/or the risk management plan (RMP) and for any safety communication tool, as warranted.
- A 120-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.2. Signals follow-up and prioritisation

None

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.

[3] Thornton et al. Porcine-derived pancreatic enzyme replacement therapy may be linked to chronic hepatitis E virus infection in cystic fibrosis lung transplant recipients. Gut. 2024 Apr 15:gutjnl-2023-330602. doi: 10.1136/gutjnl-2023-330602. Epub ahead of print. PMID: 38621922

[4] Kamar et al. Porcine-derived pancreatic enzyme replacement therapy: a cause of hepatitis E virus transmission? Gut. 2024 Jul 2:gutjnl-2024-332744. doi: 10.1136/gutjnl-2024-332744. Epub ahead of print. PMID: 38960583

5.1.1. Aficamten - (CAP MAA) - EMEA/H/C/006228

Scope (pre D-180 phase): Treatment of symptomatic obstructive hypertrophic cardiomyopathy (oHCM) in adult patients

5.1.2. Depemokimab - (CAP MAA) - EMEA/H/C/006446

Scope (pre D-180 phase): As an add-on maintenance treatment of asthma, and as an add-on treatment of inadequately controlled chronic rhinosinusitis with nasal polyps (CRSwNP)

5.1.3. Lutetium (^{177}Lu) chloride - (CAP MAA) - EMEA/H/C/006596

Scope (pre D-180 phase): Used only for the radiolabelling of carrier molecules that have been specifically developed and authorised for radiolabelling with Lutetium (^{177}Lu) chloride

5.1.4. Nogapendekin alfa inbakicept - (CAP MAA) - EMEA/H/C/006622

Scope (pre D-180 phase): Treatment of adult patients with BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumours

5.1.5. Tolebrutinib - (CAP MAA) - EMEA/H/C/006386

Scope (pre D-180 phase): Treatment of non-relapsing secondary progressive multiple sclerosis (nrSPMS) in adults

5.1.6. Trofinetide - (CAP MAA) - EMEA/H/C/006482, Orphan

Applicant: Comharsa Life Sciences Limited

Scope (pre D-180 phase): Treatment of Rett syndrome in adults and paediatric patients 2 years of age and older

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

See Annex I 15.2.

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

See also Annex I 15.3.

5.3.1. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0121

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Karin Bolin

Scope: Extension of indication to include treatment of paediatric ulcerative colitis for SIMPONI, based on results from study CNTO148UCO3003; this is a Phase 3 Randomized, Open-label Study to Assess the Efficacy, Safety, and Pharmacokinetics of Golimumab Treatment, a Human anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Paediatric Participants with Moderately to Severely Active Ulcerative Colitis. As a

consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. Version 28.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is updated in accordance with the latest EMA excipients guideline and aligned with the latest QRD template version 10.4.

Background

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

CHMP is evaluating a type II variation for Simponi, a centrally authorised product containing golimumab, to extend the indication to include treatment of paediatric ulcerative colitis. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure. For further background, see PRAC minutes April 2025.

Summary of advice

- The RMP for Simponi (golimumab) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 28.2 is submitted.
- PRAC discussed the Applicant's proposal to collect long-term safety data from paediatric patients with inflammatory bowel disease (IBD) who switch to golimumab during follow-up in the ongoing DEVELOP registry. PRAC requested the Applicant to provide additional details about: i) the possibility of including new Simponi-treated patients in the registry, ii) the approach for data collection, and iii) the plan about the report of the results from the Simponi-treated patients in the DEVELOP registry.

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

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

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

Background

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

CHMP is evaluating a type II variation for Jinarc, a centrally authorised product containing tolvaptan, to update the product information based on the final results from study 156-12-299 listed in the RMP. PRAC is responsible for providing advice to CHMP on the necessary

updates to the RMP to support this procedure. For further background, see PRAC minutes April 2025.

Summary of advice

- The RMP for Jinarc (tolvaptan) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 15.1 is submitted.
- PRAC considered that the product information[5] should be updated adequately to reflect the final results of the study, including the number of patients aged >65 years exposed to tolvaptan in the PASS study in order to clarify the extent of product use in elderly patients. Regarding the RMP, PRAC agreed to remove all missing information, however considered that the risk 'pregnancy outcome data' should be reflected in the RMP as an important potential risk under the term 'Reproductive toxicity'. Regarding the risk minimisation measures (RMMs), PRAC agreed to remove the educational materials for health care professionals, but considered that the educational material for patients should be maintained, and the patient alert card should be redefined as 'patient card' in line with the revised GVP XVI. Finally, PRAC agreed to remove the PASS from Annex II-D and consequently, to remove the product from the additional monitoring list.

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. Bevacizumab – ABEVMY (CAP); ALYMSYS (CAP); AVASTIN (CAP); AVZIVI (CAP); AYBINTIO (CAP); MVASI (CAP); OYAVAS (CAP); VEGZELMA (CAP); ZIRABEV (CAP) – EMA/PSUR/0000274402

Applicants: Amgen Technology (Ireland) Unlimited Company, Biosimilar Collaborations Ireland Limited, Celltrion Healthcare Hungary Kft., FGK Representative Service GmbH, Mabxience Research S.L., Pfizer Europe MA EEIG, Roche Registration GmbH, STADA Arzneimittel AG, Samsung Bioepis NL B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00000403/202502)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Abevmy, Alymsys, Avastin, Avzivi, Aybintio, Mvasi, Oyavas, Vegzelma and Zirabev, centrally authorised medicines containing bevacizumab and issued a recommendation on their marketing authorisation(s).

[5] SmPC sections 4.2 and 5.1

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of above-mentioned products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to include hyaline occlusive glomerular microangiopathy as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[6].
- All MAHs should include 'systemic ADRs following off-label intraocular administration in neonates' in the PSUR safety concerns as an important potential risk. In addition, all MAHs should review in their next PSUR whether the identified risks remain important or can be removed from the list of safety concerns in the PSUR. In addition, in the next PSUR, the MAHs should provide cumulative reviews of cases of *de novo* skin ulcer and of vasculitis, including data from spontaneous reports, clinical trials and literature, and discuss whether an update of the PI is warranted.

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

6.1.2. Bictegravir / Emtricitabine / Tenofovir alafenamide – BIKTARVY (CAP) – EMA/PSUR/0000274445

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010695/202502)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Biktarvy, a centrally authorised medicine containing bictegravir, emtricitabine, tenofovir alafenamide 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 Biktarvy (bictegravir/emtricitabine/tenofovir alafenamide) in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to amend the warning on 'weight and metabolic parameters' and consequently, to add 'weight increased' as an undesirable effect with a frequency 'common'. Moreover, the product information should be updated to add an interaction regarding co-administration with zinc and to add information on tenofovir alafenamide excretion in breastmilk. Therefore, the current terms of the marketing authorisation(s) should be varied[7].
- PRAC noted that the information on breastfeeding in the product information may require further revision, as additional data are available regarding the excretion of

[6] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[7] Update of SmPC sections 4.4, 4.5, 4.6 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

bictegravir and emtricitabine into breast milk, as well as their use during breastfeeding. The MAH should therefore review the current data on breastfeeding and propose an update to the relevant information in the PI as part of the next PSUR submission.

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. Efanesoctocog alfa – ALTUVOCT (CAP) – EMA/PSUR/0000274459

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00011062/202502)

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Altuvoct (efanesoctocog alfa) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning on hypersensitivity with the information that cases of occurrence of hypersensitivity reactions including anaphylaxis have been observed, with more detailed symptoms of hypersensitivity/anaphylaxis and to add hypersensitivity reactions, including anaphylaxis as undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[8].
- In the next PSUR, the MAH should provide a cumulative critical review of cases of serious and non-serious thromboembolic events.

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

6.1.4. Ribociclib – KISQALI (CAP) – EMA/PSUR/0000274416

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010633/202503)

Background

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

[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 CHMP for adoption of an opinion

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Kisqali (ribociclib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to amend the footnote on hepatotoxicity regarding the number of autoimmune hepatitis cases and to amend a sentence regarding adverse reactions so it correctly states that adverse reactions mentioned in the PI are also included from post-marketing experience. Therefore, the current terms of the marketing authorisation(s) should be varied[9].
- In the next PSUR, the MAH should provide a cumulative review of the association between palinopsia/visual perseveration and ribociclib, including data from literature, spontaneous case reports, clinical trials and non-interventional studies. The MAH should include a causality assessment and a discussion on potential mechanisms of action and on the need for an update of the PI.

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

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

See 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. Amlodipine / atorvastatin (NAP) – EMA/PSUR/0000274424

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00000177/202501)

Background

Amlodipine is a calcium channel blocker and atorvastatin is a statin (HMG-CoA reductase inhibitor). Amlodipine/atorvastatin fixed combination is indicated for the treatment of hypertension, subject to certain conditions.

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

Summary of recommendation(s) and conclusions

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of amlodipine/atorvastatin-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to include a warning/precaution regarding the increased risk of myopathy and/or rhabdomyolysis with the concomitant use of daptomycin and to add lichenoid drug reaction as an undesirable effect with a frequency 'rare'. Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAHs should provide a cumulative review of cases of lupus including data from clinical trials, post-marketing exposure and literature, and discuss the need for a PI update. In addition, the MAH should provide a cumulative review of cases of drug-drug interaction with ticagrelor.

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

6.3.2. Atenolol (NAP) – EMA/PSUR/0000274425

Applicants: various

PRAC Lead: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000259/202502)

Background

Atenolol is a β1-selective adrenergic receptor blocking agent and it is indicated for the control of hypertension, management of angina pectoris, control of cardiac arrhythmias, treatment of myocardial infarction (MI) and early and late intervention after MI, as well as for migraine prophylaxis and thyrotoxicosis.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing atenolol 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 atenolol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add a warning regarding the risk of severe hypoglycaemia with the concomitant use of beta-blockers and sulfonylureas. Therefore, the current terms of the marketing authorisation(s) should be varied[11].
- The MAH should submit a cumulative review cases related hyperglycaemia and new onset of diabetes for a possible association with atenolol treatment, including data from non-clinical, clinical setting and literature, including a discussion on possible mechanism

[10] Update of SmPC sections 4.4, 4.5 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position
[11] 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

for the association and on the need for an update of the PI. This will be part of a work-sharing variation for which Finland will be the Lead Member State (LMS).

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. Codeine (NAP) – EMA/PSUR/0000274397

Applicants: various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00000843/202501)

Action: For adoption

Background

Codeine is a centrally acting weak analgesic that belongs to opioid class of drugs, and it is indicated for the treatment of non-productive cough, mild to moderate pain of various causes and diarrhoea.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing codeine 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 codeine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to further minimise the risk of opioid use disorder (OUD), to include pancreatitis and sphincter of Oddi dysfunction as undesirable effects with frequency 'not known', as well as to add warnings regarding sleep-related breathing disorders and hyperalgesia. The PI should also be updated to reflect the drug-drug interaction with gabapentinoids. Moreover, the PI should be updated to add a new black box warning about the risk of dependence and addiction and to add a warning regarding the storage in a safe and secure place in the package leaflet. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAHs should maintain as safety concerns in the PSUR, the important identified risks of opioid toxicity (respiratory depression and sedation), opioid use disorder (abuse, misuse, dependence, addiction, tolerance, withdrawal), and effect on fertility as missing information.

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

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

6.3.4. Dorzolamide (NAP) – EMA/PSUR/0000274429

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00003168/202502)

Background

Dorzolamide is a potent inhibitor of human carbonic anhydrase II in the ciliary processes of the eye and it is indicated for the treatment of elevated intra-ocular pressure in patients with ocular hypertension, open-angle glaucoma, pseudo-exfoliative glaucoma and as adjunctive therapy to beta-blockers, or as monotherapy in patients unresponsive to beta-blockers or in whom betablockers are contraindicated, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing dorzolamide 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 dorzolamide-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add photophobia as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- In the next PSURs, all MAHs should continue to monitor cases of bradycardia, as well as the following safety concerns: severe hypersensitivity reactions, use during pregnancy and lactation, and use in paediatric population.

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

6.3.5. Gabapentin (NAP) – EMA/PSUR/0000274393

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00001499/202502)

Background

Gabapentin is an anticonvulsant indicated as monotherapy for the treatment of partial seizures with and without secondary generalisation in adults and adolescents aged 12 years and above, as adjunctive therapy for the treatment of partial seizures with and without secondary generalisation in adults and children aged 6 years and above, as well as for the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults.

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

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing gabapentin 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 gabapentin-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to include a warning regarding exacerbation of myasthenia gravis and to add exacerbation of myasthenia gravis as an undesirable effect with a frequency 'not known'. In addition, the PI should be updated to amend the warning/information regarding withdrawal reactions following dose reduction. Therefore, the current terms of the marketing authorisation(s) should be varied[14].
- In the next PSUR, all MAHs should provide cumulative reviews for the following potential risks, including data from literature and from post-marketing setting: cardiovascular disorders, withdrawal symptoms despite tapering in accordance with the existing product information (including causality assessment), impulse control disorders and related behavioural disorders (including causality assessment), cardiac arrhythmias, in particular atrial fibrillation, cutaneous leukocytoclastic vasculitis, dementia and cognitive disorders. The MAHs should discuss the need for an update of the PI 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.

6.3.6. Lisdexamfetamine (NAP) – EMA/PSUR/0000274437

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010289/202502)

Background

Lisdexamfetamine is a stimulant prodrug of dextroamphetamine, indicated as part of a comprehensive treatment programme for attention deficit/hyperactivity disorder (ADHD) in adults and in children aged 6 years and over when response to previous methylphenidate treatment is considered clinically inadequate.

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

Summary of recommendation(s) and conclusions

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of lisdexamfetamine containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAHs should discuss the effectiveness and usefulness of the additional risk minimisation measures that are in place for the respective lisdexamfetamine-containing products. This should include a discussion on whether the risks included in the educational material are sufficiently covered by the product information and clinical guidelines.

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

6.3.7. Prednisone (NAP) – EMA/PSUR/0000274401

Applicants: various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00002510/202501)

Background

Prednisone is a corticosteroid and it is indicated as an anti-inflammatory or immunosuppressive agent to treat a broad range of diseases such as rheumatoid arthritis, inflammatory bowel disease (IBD), asthma, allergies and other conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing prednisone 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 prednisone-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding thyrotoxic periodic paralysis in patients with underlying hyperthyroidism. Therefore, the current terms of the marketing authorisation(s) should be varied[15].

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

6.3.8. Propylthiouracil (NAP) – EMA/PSUR/0000274409

Applicants: various

PRAC Lead: Maia Uusküla

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

Scope: Evaluation of a PSUSA procedure (PSUSA/00002558/202501)

Background

Propylthiouracil is a thiourea antithyroid agent indicated for the treatment of Graves disease and hyperthyroidism.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing propylthiouracil 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 propylthiouracil-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing wording on the use in pregnancy and in women of childbearing potential. Therefore, the current terms of the marketing authorisation(s) should be varied[16].

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

6.3.9. Sodium citrate / sodium lauryl sulfoacetate, sodium citrate / sodium lauryl sulfoacetate / sorbitol (NAP) – EMA/PSUR/0000274413

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00002735/202501)

Background

Sodium citrate is an osmotic agent that increases intestinal osmotic pressure, thereby promoting water retention and softening the stool. Sodium lauryl sulfoacetate acts as a stool softener, mainly by re-distributing the water bound to hard faeces and exerting a softening effect on faeces and sorbitol is an osmotic laxative that is used in the management of constipation. As a combination, it is indicated for the symptomatic treatment of different types of constipation.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing sodium citrate/sodium lauryl sulfoacetate and sodium citrate/sodium lauryl sulfoacetate/sorbitol 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 sodium citrate/sodium lauryl sulfoacetate and sodium citrate/sodium lauryl sulfoacetate/sorbitol-containing medicinal products in the approved indication(s) remains unchanged.

[16] Update of SmPC section 4.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

- Nevertheless, the product information should be updated to include anaphylactic reaction as undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[17].

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

6.3.10. Trimethoprim (NAP) – EMA/PSUR/0000274411

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00003045/202501)

Background

Trimethoprim is a synthetic antimicrobial agent indicated for the treatment of susceptible infections caused by trimethoprim-sensitive organisms, including urinary tract infections (UTI) and respiratory tract infections, for the prophylaxis of recurrent UTI and acute exacerbations of chronic bronchitis.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing trimethoprim 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 trimethoprim-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include eosinophilia and systemic symptoms (DRESS) as undesirable effects with frequency 'not known', and hallucinations as undesirable effect with frequency 'very rare'. In addition, the product information should be updated to add 'first trimester of pregnancy' as contraindication. Therefore, the current terms of the marketing authorisation(s) should be varied[18].

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

6.3.11. Vancomycin (NAP) – EMA/PSUR/0000274422

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00003097/202501)

Background

[17] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position
[18] Update of SmPC sections 4.3, 4.4, 4.6 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

Vancomycin is an antibiotic indicated in the treatment of severe, potentially life-threatening infections due to susceptible gram-positive microorganisms which cannot be treated with or failed to respond to other effective, less toxic antimicrobial medicinal products, such as penicillin and cephalosporins.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing vancomycin 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 vancomycin-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to include haemolytic anaemia as an undesirable effect with a frequency 'not known'. In addition, the PI should be updated to include alanine aminotransferase increased and aspartate aminotransferase increased as undesirable effects with frequency 'common', as well as to add Kounis syndrome as a warning and as undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[19].
- In the next PSURs, all MAHs with products for intravenous administration are requested to provide a cumulative review regarding the possible role of vancomycin in the development of hypokalaemia, including data from literature, spontaneous case reports, randomised clinical trials and non-interventional studies. All MAHs should also discuss the need for update of the PI as warranted. In addition, all MAHs should provide a comprehensive review regarding the possible role of vancomycin in the development of drug-induced liver injury (DILI) outside the context of established severe cutaneous adverse reactions (SCARs) and discuss the need for update of the PI 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.

6.3.12. Warfarin (NAP) – EMA/PSUR/0000274420

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00003129/202501)

Background

Warfarin is an oral anticoagulant indicated for the prophylaxis and treatment of various thromboembolic disorders.

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

[19] 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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of warfarin-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, all MAHs should provide a cumulative review on interaction with oseltamivir leading to increased international normalised ratio (INR), including data from literature, spontaneous case reports, randomised clinical trials and non-interventional studies. The MAHs should discuss the need for an 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. Dapagliflozin – EDISTRIDE (CAP); FORXIGA (CAP) – EMA/PAM/0000289605

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Follow-up LEG (from EMEA/H/C/PSUSA/00010029/202410): Review of all cases related to the potential association between dapagliflozin exposure and prolonged ketoacidosis and prolonged glucosuria.

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 association between dapagliflozin exposure and prolonged ketoacidosis and prolonged glucosuria. 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 there is at least a reasonable possibility for a causal relationship between dapagliflozin for the treatment of type 2 diabetes and prolonged ketoacidosis and prolonged glucosuria.
- The MAH should submit to EMA, within 60 days, a variation[20] to update the product information (section 4.4) to amend the existing warning on ketoacidosis to indicate that ketoacidosis and glucosuria may be prolonged after discontinuation of dapagliflozin. This update aims to alert prescribers that extended monitoring and treatment may be required.

[20] Update of SmPC section 4.4.

- PRAC considered that the risk of prolonged ketoacidosis and prolonged glucosuria in patients with type 2 diabetes is also relevant for products containing dapagliflozin in fixed dose combinations (dapagliflozin/metformin and dapagliflozin/saxagliptin) as it is expected that the same risk as dapagliflozin is applicable also for dapagliflozin combination products.

6.4.2. Ravulizumab – ULTOMIRIS (CAP) – EMA/PAM/0000287237

Applicant: Alexion Europe

PRAC Rapporteur: Kimmo Jaakkola

Scope: PAM-LEG to address a question from the PRAC Rapporteur's PSUR Assessment report related to the Ultomiris PSUR #9 reporting period 01 Jan 2024 – 31 Dec 2024, procedure number

EMA/PSUR/0000257874 (EURD no.: PSUSA/00010787/202412) dated 10 July 2025. The MAH should submit a cumulative review of all available data concerning liver injury and hepatic enzyme elevations in ravulizumab treated patients until the DLP of this PSUR. In view of totality of the data, the MAH is requested to update the product information of ravulizumab (SmPC and PL), as warranted.

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 liver injury and hepatic enzyme elevations in ravulizumab treated patients. 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 agreed that the data are insufficient to establish causality between ravulizumab use and liver injury or hepatic enzyme elevations. Therefore, PRAC considered that no update to the product information is warranted at this stage. The MAH should continue to closely monitor this topic in future PSURs.

6.5. Variation procedure(s) resulting from PSUSA evaluation

None

6.6. Expedited summary safety reviews[21]

None

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

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[22]

See also Annex I 17.1.

7.1.1. Teduglutide – REVESTIVE (CAP) – EMA/PASS/0000269314

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: PASS amendment [107o]: Substantial amendment to a prospective, multi-center registry for patients with Short Bowel Syndrome (TED-R13-002)

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, submitted on 28 April 2025 an amended PASS protocol for Revestive (teduglutide) to amend the non-interventional imposed PASS protocol in accordance with Article 107o of Directive 2001/83/EC. For further background, see PRAC minutes July 2025.

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 11 in accordance with Article 107o of Directive 2001/83/EC, PRAC considered that the study is non-interventional and that the substantial amendments to the PASS protocol for Revestive (teduglutide) can be endorsed.
- The MAH should update, at the next regulatory opportunity, the milestone for the final study report in the RMP in line with the PASS protocol and the product information Annex IID. Furthermore, to minimise potential future confusion about milestones for interim reports, a brief clarification in the PASS protocol at the next regulatory opportunity could be added in relation to varying commitments between health authorities.

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[23]

See Annex I 17.2.

7.3. Results of PASS imposed in the marketing authorisation(s)[24]

See also Annex I 17.3.

[22] In accordance with Article 107n of Directive 2001/83/EC
[23] 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
[24] In accordance with Article 107p-q of Directive 2001/83/EC

7.3.1. Methylphenidate hydrochloride (NAP) – EMA/PASS/0000248031

Applicant(s): various

PRAC Rapporteur: Martin Huber

Scope: PASS 107q: Final study report for a multi-centre, observational, prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet retard according to normal standard clinical practice.

Background

Methylphenidate hydrochloride is a central nervous system (CNS) stimulant, indicated for the treatment of attention deficit hyperactivity disorder (ADHD) in children between 6 and 18 years of age and adults, as warranted.

In order to fulfil the obligation to submit the results of an imposed non-interventional post-authorisation safety study (PASS) in accordance with Article 107p of Directive 2001/83/EC, the MAH KG submitted on 29 January 2025 a PASS final study report to the EMA for methylphenidate hydrochloride. 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 study entitled 'A post-authorisation safety study to evaluate the long-term cardiovascular and psychiatric safety profile of methylphenidate in adult patients with attention deficit/hyperactivity disorder (ADHD) in European countries', PRAC considered that the benefit-risk balance of methylphenidate hydrochloride-containing products remains unchanged, and recommended that the terms of the marketing authorisation(s) for methylphenidate hydrochloride-containing products 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'. The MAH(s) should continue monitoring both cardiovascular and psychiatric risks and present any new information of interest in the upcoming PSURs. In light of the known limitation of spontaneous reporting, special focus should be given to published studies discussing psychiatric events in patients receiving methylphenidate.

7.3.2. Sodium valproate (NAP) – EMA/PASS/0000287665

Applicant(s): various

PRAC Rapporteur: Liana Martirosyan

Scope: valproate PASS results [107q]: Final study results for Drug Utilisation Study (DUS) extension of valproate and related substances in Europe, using databases.

Background

Sodium valproate and the related substances are antiepileptics indicated for the treatment of epilepsy, of bipolar disorders restricted to the treatment of manic episodes when lithium is contraindicated or not tolerated, and for the prophylaxis of migraine attacks, as warranted.

In order to fulfil the obligation to submit the results of an imposed non-interventional PASS in accordance with Article 107q of Directive 2001/83/EC, Sanofi-Aventis Recherche &

Développement, on behalf of the MAH's consortium, submitted on 17 July 2025 a PASS final study report v1.0 to the EMA for medicines containing substances related to valproate (sodium valproate, valproic acid, valproate semi-sodium, valpromide, valproate magnesium). PRAC discussed the final study results.

Summary of recommendation(s) and conclusions

- Based on the review of the final report of the non-interventional PASS, PRAC considered that a request for supplementary information (RSI) was necessary before a final recommendation could be issued.
- The MAH(s) should submit, within 90 days, to EMA the responses to the RSI . A 60 days-assessment timetable will be followed.
- In addition, the MAH(s) which have an RMP in place should submit an updated RMP via a variation procedure to the relevant national competent authority for assessment in order to remove the category 1 drug utilisation study (DUS) from the RMP.

7.4. Results of PASS non-imposed in the marketing authorisation(s)[25]

See also Annex I 17.4.

7.4.1. Alpelisib – PIQRAY (CAP) – EMA/VR/0000275207

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Bianca Mulder

Scope: Submission of the final report for study CBYL719C2005, listed as a category 3 study in the RMP. This is a non-interventional Post-authorisation Safety Study (PASS)/survey that was conducted to assess healthcare professionals' knowledge on management of hyperglycemia when using alpelisib in selected EU/EEA countries. The Annex II has been updated accordingly. Version 9.0 of the RMP has also been submitted.

Background

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

As stated in the RMP of Piqray (alpelisib), the MAH conducted a non-imposed non-interventional PASS (CBYL719C2005) to assess the effectiveness of risk minimisation measures (RMMs) of Piqray (alpelisib). The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI). For further background, see PRAC minutes September 2025.

Summary of advice

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

[25] 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

medicinal product (educational material: healthcare professional guide) has been fulfilled, and therefore it is recommended to be deleted from the Annex IID and the RMP.

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

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: A grouped application consisting of:

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

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

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 Spikevax (COVID-19 mRNA vaccine), the MAH conducted a non-imposed non-interventional PASS (Study mRNA-1273-P904 (P904) and Study mRNA-1273-P905 (P905)) to further characterize the safety profile of Spikevax (COVID-19 mRNA vaccine). The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI). For further background, see PRAC minutes July 2025.

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 agreed that an update to the product information (SmPC section 4.6) is warranted based on the data from the pregnancy PASS and in line with the removal of this missing information from the RMP. In addition, PRAC agreed to update the frequency of the adverse reactions anaphylaxis and erythema multiforme from 'not known' to 'rare' based on the final results from study mRNA-1273-P904.

7.4.3. Natalizumab – TYSABRI (CAP) – EMA/VR/0000262419

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: A grouped application consisting of:

C.I.4: Update of sections 4.4 and 5.1 of the SmPC in order to update pharmacodynamic information based on final results from study 101MS411, listed as a category 3 study in the RMP; this is an observational study utilising data from the US Tysabri TOUCH programme and select EU MS registries to estimate the risk of progressive multifocal leukoencephalopathy (PML) and other serious opportunistic infections among patients who were exposed to an MS disease modifying treatment prior to treatment with Tysabri. The RMP version 32.2 has also been submitted.

C.I.4: Update of section 5.1 of the SmPC in order to update pharmacodynamic information based on final results from study IMA 06 02 (TOP) listed as a category 3 study in the RMP. This is an observational study to evaluate the long-term safety and impact on disease activity and progression of Tysabri as a single disease-modifying agent in patients with RRMS in a clinical practice 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.

As stated in the RMP of Tysabri (natalizumab), the MAH conducted the following non-imposed non-interventional PASS: study mRNA-1273-P904 (P904) and study mRNA-1273-P905 (P905). The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI). For further background, see PRAC minutes June 2025.

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 is recommended for approval.
- PRAC agreed with the update to the RMP to remove the important potential risk of malignancies and the missing information of progressive multifocal leukoencephalopathy (PML) risk following switch from disease-modifying therapies (DMTs) with immunosuppressant effect from the list of safety concerns. PRAC also agreed with the removal of the completed studies 101MS411 and IMA-06-02 from the RMP. In addition, PRAC agreed with the update to the product information to inform that data from an observational study demonstrated that there is no increased risk of PML for the group of patients switching to natalizumab from fingolimod, dimethyl fumarate, or teriflunomide when compared to the group of patients switching from either beta interferon or glatiramer acetate and that no information is available for other disease-modifying therapies. In addition, PRAC agreed to update the product information to remove information on malignancies and to include a high-level summary of the design and main study results of the Tysabri Observational Program (TOP, IMA-06-02) Study.

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

See Annex I 17.5.

7.6. New Scientific Advice

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

7.7. Ongoing Scientific Advice

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

7.8. 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.

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

8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1.

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2.

8.3. Renewals of the marketing authorisation

See Annex I 18.3.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

10.1.1. Voxelotor – OXBRYTA (CAP) - EMEA/H/A-20/1538/C/004869/0014

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jo Robays

Scope: PRAC consultation on a referral procedure under Article 20 of Regulation (EC) No 726/2004 regarding risk minimisation measures to effectively mitigate the risk of vaso-occlusive crises (VOC) in any subset of the authorised patient population for Oxbryta, at request of CHMP

Background

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

A referral procedure under Article 20 of Regulation (EC) No 726/2004 regarding risk minimisation measures to effectively mitigate the risk of VOC for Oxbryta (voxelotor) is under evaluation at CHMP. PRAC was requested to provide advice on this variation.

Summary of advice

- Based on the review of the available information, PRAC considered that the risk of VOC is an important identified risk of voxelotor that warrants effective risk minimisation measures (RMMs). Given that the underlying mechanisms contributing to the increased risk of VOC and death observed in the studies GBT440-032 and GBT440-042 conducted in sub-Saharan Africa (SSA) are not established, PRAC concluded that no risk factors or specific patient population at increased risk can be identified. Consequently, no targeted RMMs (e.g. warnings, contraindications or restrictions) to exclude such patients from treatment with voxelotor can be proposed. In addition, PRAC considered the potential effectiveness of a patient card and a Direct Healthcare Professional Communication (DHPC) and noted the latest MAH's proposal for close monitoring for improvement of haemolytic anaemia, a risk awareness dialogue form and a patient diary. However, it was concluded that these tools would not effectively minimise the risk of VOC and death, considering that close routine clinical monitoring is already standard practice for this patient population and more frequent clinical assessment is considered unlikely to be effective for prior detection and prevention of infections or VOCs. Thus, no RMMs that could effectively mitigate the risk of VOC and death in patients treated with voxelotor were identified by PRAC.

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Acetylsalicylic acid (NAP) - FI/H/xxxx/WS/190

Applicant(s): Bayer Oy (Aspirin, Aspirin Cardio, Aspirin Zipp)

PRAC Lead: Terhi Lehtinen

Scope: PRAC consultation on a worksharing variation procedure (FI/H/xxxx/WS/190) to update the product information to add Kounis syndrome as undesirable effect with a frequency 'not known', at request of Finland

Background

Acetylsalicylic acid is a non-steroidal anti-inflammatory drug (NSAID), indicated to relieve pain, fever, and inflammation associated with many conditions, including the flu, the common cold, neck and back pain, dysmenorrhea, headache, tooth pain, sprains, fractures, myositis, neuralgia, synovitis, arthritis, etc.

In the context of the evaluation of a worksharing variation procedure on updating the product information of acetylsalicylic acid-containing products, Finland requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC supported to update the product information to add Kounis syndrome as a warning and undesirable effect for acetylsalicylic acid products, as there is sufficient evidence to consider a causal association and it is in line with what was previously discussed within PSUSA/00002291/202412 procedure. As hypersensitivity reactions are not dose dependent, PRAC considered justified to implement the same wording for all acetylsalicylic acid products, including the ones used for cardiovascular prevention and treatment.

11.1.2. Ketoprofen (topical use) (NAP) - SE/H/xxxx/WS/961

Applicant: Sanofi AB (Orudis)

PRAC Lead: Karin Bolin

Scope: PRAC consultation on a worksharing variation procedure (SE/H/xxxx/WS/961) to update the product information of ketoprofen-containing medicinal products (topical use)

regarding the risk of embryo/fetal death secondary to cardiopulmonary and/or renal toxicity after exposure during pregnancy, at request of Sweden

Background

Ketoprofen is a nonsteroidal anti-inflammatory drug (NSAID) indicated, for topical use, for the treatment of signs and symptoms of mild to moderate local pain associated with muscle and/or joints injuries (e.g., sport injuries).

In the context of the evaluation of a worksharing variation procedure on updating the product information of ketoprofen (topical use)-containing products, Sweden requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC concluded that adequate information and contraindication in relation to the use in pregnancy was already included in the product information (SmPC sections 4.3 and 4.6) for topical ketoprofen, as previously recommended within PSUSA/00009205/202201 variation for topical ketoprofen formulations.

11.1.3. Levonorgestrel (NAP) - SE/H/xxxx/WS/888

Applicant: Bayer (Mirena, Jaydess, Kyleena)

PRAC Lead: Karin Bolin

Scope: PRAC consultation on a worksharing variation procedure (SE/H/xxxx/WS/888) to update the product information of Mirena in order to amend the current warning regarding the risk of breast cancer and to include this information in the product information of Jaydess and Kyleena, at request of Sweden

Background

Levonorgestrel is a second-generation progestin (synthetic progesterone) indicated for oral contraception, heavy menstrual bleeding (hypermenorrhoea, idiopathic menorrhagia). It is also indicated for the protection from endometrial hyperplasia during oestrogen replacement therapy.

In the context of the evaluation of a worksharing variation procedure on updating the product information of Jaydess and Kyleena, Sweden requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC supported that the existing warning in the product information (SmPC section 4.4) on the risk of breast cancer for Mirena is to be strengthened in order to reflect the current evidence considering that since the last PSUSA assessment for levonorgestrel (PSUSA/00010828/202305), newer epidemiological studies have been published showing a slightly increased risk of breast cancer in the levonorgestrel intrauterine device (LNG-IUD) users. PRAC also endorsed that the revised warning for Mirena is also applied in the product information of Jaydess and Kyleena. In particular, PRAC agreed that the warning on the risk of breast cancer for combined oral contraceptives included in the Mirena product information should be added to Jaydess and Kyleena, while the existing wording included in Mirena related to

the risk of breast cancer for progesteron-only preparations should be removed as it is now superseded by specific information added for LNG-IUD products. Specific information related to the risk of breast cancer for LNG-IUD should be added to the SmPC section 4.4 for Mirena, Jaydess and Kyleena to reflect the actual evidence on this risk but a quantification on the magnitude of this risk should not be reflected in view of the study limitations and uncertainties. The Package Leaflets for the three products should be amended on the risk of breast cancer accordingly.

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The Chair welcomed Veronika Macurova as the new alternate representing Czech Republic and Maria Martinez Gonzalez as the new alternate representing Spain. The Chair thanked Gabriele Maurer for her contribution as the alternate representing Germany.

12.1.2. Vote by proxy

Georgia Gkegka gave a proxy to Panagiotis Psaras, Annalisa Capuano gave a proxy to Maria Teresa Herdeiro, Maria Popova gave a proxy to Julia Pallos and Hedvig Nordeng gave the proxy to Patricia McGettigan, covering the entire meeting.

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. PRAC strategic review and learning meeting (SRLM) under the Danish presidency of the European Union (EU) Council – Copenhagen, Denmark, 10 – 12 November 2025 - agenda

PRAC lead: Marie Louise Schougaard Christiansen

PRAC was informed on the final agenda for the 'PRAC strategic review and learning meeting (SRLM)', to be held on 10-12 November 2025 in Copenhagen, Denmark, under the Danish presidency of the Council of the European Union (EU). The topics to be discussed cover artificial intelligence in pharmacovigilance, real world data and enhancing adverse events reporting.

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. Marketing authorisation applications (MAA) forecast for 2025 – planning update dated Q2/Q3 2025

The EMA Secretariat presented for information to PRAC a quarterly updated report on marketing authorisation applications (MAA) planned for submission (the business 'pipeline') in Q2 and Q3 2025. PRAC noted the information.

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Petar Mas

The EMA Secretariat presented the changes to the EURD List: new, amended, merged and deleted entries. PRAC noted the information.

12.10.3. PSURs repository

None

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

In line with the criteria for plenary presentation of updates to the EURD List adopted by PRAC in December 2021, PRAC endorsed the draft revised EURD list, version October 2025, reflecting the PRAC's comments impacting on the data lock point (DLP) and PSUR submission frequencies of the substances/combinations. PRAC endorsed the newly allocated Rapporteurs for upcoming PSUSAs in accordance with the principles previously endorsed by PRAC (see PRAC minutes April 2013).

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

12.11. Signal management

12.11.1. Signals and safety analytics project – update on activities

The EMA Secretariat presented to PRAC an update on the progress of the signals and safety analytics project, including a clear overview of the next steps and the planned go-live. A demo of the new system will be presented during the First EMA/HMA multi-stakeholder forum on EudraVigilance and signal detection | European Medicines Agency (EMA). PRAC noted the information.

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

12.14.2. Tools, educational materials and effectiveness measurement of risk minimisations

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

12.15.2. Post-authorisation Safety Studies – non-imposed PASS

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. DARWIN EU impact study to measure the effectiveness of risk minimisation measures implemented for medicines containing nomegestrol or chlormadinone for the risk of meningioma – regulatory follow-up

PRAC lead: Petar Mas

The PRAC Sponsor (Petar Mas) presented the results of the first part of the DARWN EU® study "Impact of risk minimisation measures related to the risk of meningioma in women using nomegestrol or chlormadinone" (EUPAS1000000455). This pilot study was conducted under the remit of the PRAC Impact Strategy following referral EMEA/H/A-31/1510 introducing risk minimisation measures (RMM) in 2022 that restricted the use of high-dose products to second- or third-line treatment at the lowest effective dose for the shortest duration and contraindicated the use in patients with current or past meningioma. The study investigated how prescribing of nomegestrol and chlormadinone containing medicines (as single active ingredients and combinations products) has changed following these EU-wide label changes. In line with the process for regulatory follow-up on impact research, the PRAC Sponsor's critical appraisal of the results was discussed.

PRAC concluded that there were no substantial changes in prescribing of nomegestrol or chlormadinone following the 2022 RMM which could be attributed to the fact that the majority of observed exposures in this study involved low-dose products, whereas the 2022 RMM were predominantly directed at high-dose products. PRAC agreed that there was no need for regulatory follow-up or stakeholder communication at this point in time and to proceed with the planned second part (routine repeated study) only if additional data sources with high-dose nomegestrol and/or chlormadinone exposure can be identified in DARWIN EU®.

12.21. Others

12.21.1. Code of conduct of the European Medicines Agency – provisions for members and experts of scientific committees

At the ORGAM meeting held on 16 October 2025, the EMA Secretariat presented to PRAC the provisions for members and experts of scientific committees as part of the code of conduct of the European Medicines Agency. PRAC noted the information.

12.21.2. Council for International Organizations of Medical Sciences (CIOMS) – Report on severe cutaneous adverse reactions (SCAR)

The EMA Secretariat presented to PRAC the key elements of the published report on severe cutaneous adverse reactions (SCAR) of the Council for International Organizations of Medical Sciences (CIOMS). PRAC noted the information.

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

PRAC lead: Ulla Wändel Liminga

At the ORGAM meeting held on 16 October 2025, the EMA Secretariat presented to PRAC the finalised GVP Guideline on Product- or Population-Specific Considerations III: Pregnancy and Breastfeeding, following the commenting phase. PRAC adopted the guidance, which will now be presented to the CMDh for endorsement before proceeding through the standard internal EMA processes prior to its publication on the EMA website.

12.21.4. IRIS regulatory procedure management transition - update

At the ORGAM meeting held on 16 October 2025, the EMA Secretariat presented to PRAC an updated plan and engagement activities to support the preparation of the transition to IRIS for initial marketing authorisation applications and pre-submission activities, including an overview of activities for 2026. PRAC noted the information.

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

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

At the ORGAM meeting held on 16 October 2025, the PRAC Lead presented the revised PRAC guidance on SCARs. PRAC agreed that the information in the Annex should be shared with the MAHs when relevant. The guidance will also be presented to CHMP for information. The PRAC members were invited to send their comments on the proposed changes in writing by 31 October 2025.

Post-meeting note: The PRAC SCAR guidance was adopted by PRAC on 31 October 2025.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[26]

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[27].

14.1. New signals detected from EU spontaneous reporting systems

None

[26] 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

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

14.2. New signals detected from other sources

None

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

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

15.1.1. Etanercept - (CAP MAA) - EMEA/H/C/006738

Scope: Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, axial spondyloarthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, plaque psoriasis, paediatric plaque psoriasis

15.1.2. Golimumab - (CAP MAA) - EMEA/H/C/006621

Scope (pre D-180 phase): Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis and ulcerative colitis.

15.1.3. Ranibizumab - (CAP MAA) - EMEA/H/C/006502

Scope (pre D-180 phase): Treatment of 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. Emtricitabine / Rilpivirine / Tenofovir disoproxil – EVIPLERA (CAP) – EMA/VR/0000287296

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of two variations:

C.I.11.b: Submission of an updated RMP version 16.1 in order to propose the removal of 'Missing information' (Safety in pregnancy) and the removal of a Category 3 Additional Pharmacovigilance Activity (Antiretroviral Pregnancy Registry [APR]).

C.I.11.b: Submission of an updated RMP version 16.1 in order to propose the removal of Specific Adverse Reaction Follow-up Questionnaires related to bone and renal risks.

15.2.2. Mavacamten – CAMZYOS (CAP) – EMA/VR/0000275832

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of an updated RMP version 6.0 in order to introduce a change in the time of assessment of the primary objective from 52-week to 48-week of the ODYSSEY-HCM study (CV027031), listed as a category 3 study in the RMP. Additionally, the opportunity is taken to include a change to the submission due date of the ODYSSEY-HCM final clinical study report from July 2025 to June 2026.

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

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

15.3.1. Aflibercept – EYLEA (CAP) – EMA/VR/0000264981

Applicant: Bayer AG

PRAC Rapporteur: Zoubida Amimour

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

C.I.6: Extension of indication to include the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch, central and hemiretinal RVO) for EYLEA, based on results from study 22153 (QUASAR); this is a randomized, double-masked, active-controlled Phase 3 study of the efficacy and safety of aflibercept 8 mg in macular edema secondary to retinal vein occlusion. 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 accordingly. The RMP version 36.1 has also been submitted.

C.I.4: Update of section 4.2 of the SmPC in order to change posology recommendations of the approved indications neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME) based on the results from study 22153 (QUASAR) and post-hoc analysis of the pivotal studies 20968 (PULSAR), 21091 (PHOTON) and Phase II study 21086 (CANDELA).

15.3.2. Asciminib – SCEMBLIX (CAP) – EMA/VR/0000265010

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: A grouped application consisting of:

C.I.6.a: Extension of indication to include treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP) for SCEMBLIX, based on primary and key secondary analysis results from study CABL001J12301 (ASC4FIRST, J12301); this is an ongoing Phase III, multi-center, open-label, randomized study of oral asciminib (80 mg once daily, q.d.) versus Investigator selected tyrosine kinase inhibitor (TKI) in patients with newly diagnosed Ph+ CML-CP, with

the primary and key secondary objectives to compare the major molecular response (MMR) rates at Week 48 and Week 96, respectively. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. RMP version 4.0 has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection.

C.I.4: Update of sections 4.2, 4.5, 5.1, 5.2 and 5.3 of the SmPC in order to introduce a new posology regimen based on results from studies CABL001J12301 and CABL001A2302 (ASC4OPT, A2302). CABL001A2302 is an ongoing Phase IIIb, multi-center, open-label, treatment optimization study of oral asciminib (80 mg daily, randomized to 40 mg b.i.d. or 80 mg q.d.) in patients with Ph+ CML-CP previously treated with two or more TKIs, with the primary objective to estimate the MMR rate at Week 48 of all the patients (40 mg b.i.d. and 80 mg q.d.) with no evidence of MMR at baseline. The Package Leaflet is updated accordingly. RMP version 4.0 has also been submitted.

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

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

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

15.3.4. Blinatumomab – BLINCYTO (CAP) – EMA/VR/0000286935

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Veronika Macurova

Scope: Update of sections 4.4, 4.8 of the SmPC in order to add a new warning on Haemophagocytic lymphohistiocytosis (HLH)/Immune effector-cell-associated haemophagocytic lymphohistiocytosis-like syndrome (IEC-HS) following the evolving understanding of cytokine release syndrome and HLH/IEC-HS; the Package Leaflet is updated accordingly. The RMP version 20.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes to the PI.

15.3.5. Cemiplimab – LIBTAYO (CAP) – EMA/VR/0000264999

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adjuvant treatment of adult patients with Cutaneous Squamous Cell Carcinoma (CSCC) at high risk of recurrence after surgery and radiation for LIBTAYO, based on interim results from study R2810-ONC-1788; this is a phase 3, randomized, placebo-controlled, double-blind study of adjuvant cemiplimab versus placebo after surgery and radiation therapy in patients with high risk CSCC; As a

consequence, sections 4.1, 4.2, 4.8, 5.1, and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.2 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the warnings for the excipients proline and polysorbate to reflect EU guidance (Section 4.4), and also updated Annex IID of the PI in line with the updates made to the RMPv4.2 to consolidate the aRMMs.

15.3.6. COVID-19 mRNA vaccine – KOSTAIVE (CAP) – EMA/VR/0000284897

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.5, 4.8 and 5.1 of the SmPC in order to add information based on final results from study ARCT-2303-01 listed as a category 3 study in the RMP; this is a Phase 3 observer-blind, randomized controlled study to evaluate the immunogenicity, reactogenicity, and safety of Kostaive administered concomitantly with quadrivalent influenza vaccines in adults. The Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted. In addition, the MAH is taking the opportunity to implement editorial changes to the PI.

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Extension of indication to include, for SOTYKTU, alone or in combination with conventional synthetic disease modifying antirheumatic drugs (DMARDs), the treatment of active psoriatic arthritis (PsA) in adults who have had an inadequate response or who have been intolerant to a prior DMARD therapy, based on results from the following phase 3 studies: Study IM011-054 (POETYK PsA-1); this is a phase 3, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of deucravacitinib in participants with active psoriatic arthritis who are naïve to biologic disease-modifying anti-rheumatic drugs, and Study IM011-055 (POETYK PsA-2); this is a multi-center, randomized, double-blind, placebo-controlled phase 3 study to evaluate the efficacy and safety of BMS-986165 in participants with active psoriatic arthritis (PsA) who are naïve to biologic disease modifying anti-rheumatic drugs or had previously received TNFα inhibitor treatment. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet, as well as introduce administrative changes to the PI.

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

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of moderate to severe chronic spontaneous urticaria (CSU) in children aged 2 to 11 years whose disease is inadequately controlled by H1 antihistamines and who are naive to anti-IgE therapy for CSU for

DUPIXENT, based on the results from study PKM16982; this is a multi-center, single-arm study to investigate the pharmacokinetics and safety of dupilumab in male and female participants ≥2 years to <12 years of age with uncontrolled chronic spontaneous urticaria (CSU). Consequently, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 14.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template.

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

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication for IMFINZI to include in combination with FLOT chemotherapy as neoadjuvant and adjuvant treatment, followed by adjuvant IMFINZI monotherapy, for the treatment of adults with resectable gastric or gastro-oesophageal junction adenocarcinoma , based on interim results from study MATTERHORN, (D910GC00001); this is a randomized, double-blind, placebo-controlled, phase 3 study of neoadjuvant-adjuvant durvalumab and FLOT chemotherapy followed by adjuvant durvalumab in patients with resectable gastric and gastroesophageal junction cancer (GC/GEJC). As a consequence, sections 4.1, 4.2, 4.5, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 14.0 of the RMP has also been submitted.

15.3.10. Guselkumab – TREMFYA (CAP) – EMA/X/0000248626

Applicant: Janssen Cilag International

PRAC Rapporteur: Gabriele Maurer

Scope:

Extension application to add a new strength of 45 mg (100 mg/ml) in a pre-filled syringe (glass) in pre-filled pen (VarioJect) grouped with an extension of indication (C.I.6.a) to include treatment of moderate to severe plaque psoriasis in children and adolescents from the age of 6 years who are candidates for systemic therapy based on results from study CNTO1959PSO3011. This is a Phase 3, Multicenter, Randomized, Placebo- and Active Comparator-Controlled Study Evaluating the Efficacy, Safety, and Pharmacokinetics of Subcutaneously Administered Guselkumab for the Treatment of Chronic Plaque Psoriasis in Pediatric Participants (≥6 To <18 Years of Age). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 10.3 of the RMP has also been submitted.

15.3.11. Inebilizumab – UPLIZNA (CAP) – EMA/VR/0000257358

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: A grouped application consisting of:

C.I.6 (Extension of indication): Extension of indication to include add-on to standard therapy for the treatment of adult patients with generalised myasthenia gravis (gMG) for Uplizna, based on primary analysis results from Study MINT (VIB0551.P3.S1); this is a pivotal phase 3 multicentre, randomised, double-blind, placebo-controlled, parallel-cohort study to evaluate the efficacy and safety of inebilizumab in adults subjects with myasthenia gravis. As a consequence, sections 4.1, 4.2, 4.4 ,4.5, 4.6, 4.8, 5.1, 5.2, and 7 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.4.

A.6: Update of the ATC code of inebilizumab to L04AG10 in line with the 2024 ATC INDEX.

15.3.12. Insulin aspart – KIRSTY (CAP) – EMA/VR/0000285173

Applicant: Biosimilar Collaborations Ireland Limited

PRAC Rapporteur: Mari Thorn

Scope: Quality

15.3.13. Insulin icodec – AWIQLI (CAP) – EMA/VR/0000268356

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Sonja Radowan

Scope: Update of sections 4.4, and 5.1 of the SmPC in order to update information related to medication errors based on post-marketing data and data from clinical trials; the Package Leaflet (PL) is updated accordingly. The RMP version 2.0 has also been submitted in order to add new identified risk of "Medication errors with accidental overdose, due to erroneous transfer of dosing habits from other once-weekly injectable antidiabetic medicines”. In addition, "ankle swelling" was reworded to "swelling around ankles" in the PL.

15.3.14. Lebrikizumab – EBGLYSS (CAP) – EMA/VR/0000249804

Applicant: Almirall S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of:

C.I.4: Update of sections 4.8, and 5.1 of the SmPC in order to update information on clinical efficacy and the long-term safety based on final results from study J2T-DM-KGAA (ADjoin) listed as a category 3 study in the RMP; this is a long-term study to assess the long-term safety and efficacy of lebrikizumab in patients with moderate-to-severe atopic dermatitis over 100 weeks, which was ongoing at the time of the MAA submission. The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to introduce the changes following PEI linguistic review and editorial changes to the PI.

C.I.4: Update of section 5.1 of the SmPC in order to update information on clinical efficacy based on final results from study J2T-AP-KGBQ (Advantage); this is a randomised, double-blind, placebo-controlled phase 3 clinical trial to assess the efficacy and safety of lebrikizumab in combination with topical corticosteroids up to 52 weeks in patients with

moderate to-severe atopic dermatitis who were not adequately controlled with ciclosporin or non-eligible for cyclosporine.

15.3.15. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/VR/0000272242

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2, 4.4, 4.7 and 4.8 of the SmPC in order to update the post-treatment safety monitoring information based on clinical trials and real-world data. The Package leaflet section is updated in accordance. Version 8.0 of the RMP has also been submitted. In addition, the MAH the opportunity to update Annex II.

15.3.16. Meningococcal Group A, C, W and Y conjugate vaccine – MENQUADFI (CAP) – EMA/VR/0000281377

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication for MENQUADFI to include the active immunisation of patients from 6 weeks of age based on final results from study MET58 and additional supportive clinical studies. Study MET58 is a Phase 3, immunogenicity and Safety Study of an Investigational Quadrivalent Meningococcal Conjugate Vaccine when Administered Concomitantly with Routine Pediatric Vaccines in Healthy Infants and Toddlers in Europe. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated Risk Management Plan (RMP) version 4.0 is also included.

15.3.17. Methylthioninium chloride – METHYLTHIONINIUM CHLORIDE PROVEBLUE (CAP) – EMA/VR/0000265559

Applicant: Provepharm

PRAC Rapporteur: Karin Bolin

Scope: Submission of the final report from study PVP-2016005; this is an Open-label, Parallel group, Population-matched, Single-Dose Study to Investigate the Influence of Hepatic Impairment on the Pharmacokinetics and safety of ProvayBlue (methylene blue). The RMP version 3.4 has also been submitted.

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

Applicant: Janssen Cilag International

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include AKEEGA with prednisone or prednisolone for the treatment of adult patients with metastatic hormone-sensitive prostate cancer (mHSPC) and HRR-mutations (germline and/or somatic, based on interim results from study 67652000PCR3002 (AMPLITUDE); this is a phase 3 randomized, placebo-controlled, double-blind study of niraparib in combination with abiraterone acetate and prednisone versus

abiraterone acetate and prednisone for the treatment of participants with deleterious germline or somatic homologous recombination repair (HRR) gene-mutated metastatic castration-sensitive Prostate cancer (mCSPC). As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. In addition, the MAH is requesting an additional year of market protection for a new indication.

15.3.19. Nirmatrelvir / Ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/II/0061/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: A grouped application comprised of a Type II Variation and a Type IB Variation, as follows:

Type II (C.I.6.a): Extension of indication to include treatment of coronavirus disease 2019 (COVID-19) in paediatric patients 6 years of age and older weighing at least 20 kg for PAXLOVID, based on the final analysis of Cohorts 1 and 2 from pivotal Study C4671026; this is a Phase 2/3, Interventional Safety, Pharmacokinetics, and Efficacy, Open-Label, Multi-Center, Single-Arm Study to Investigate Orally Administered PF 07321332 (Nirmatrelvir)/Ritonavir in Nonhospitalized Symptomatic Pediatric Participants With COVID-19 Who Are at Risk of Progression to Severe Disease. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 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.

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

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

15.3.21. Obinutuzumab – GAZYVARO (CAP) – EMA/VR/0000244907

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of adult patients with active lupus nephritis who are receiving standard therapy for GAZYVARO, based on results from study

Regency (CA41705). This is an ongoing, Phase III, randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of obinutuzumab administered at standard infusion rates in patients with ISN/RPS 2003 Class III or IV lupus nephritis treated with standard-of-care therapy.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11 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.

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

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Liana Martirosyan

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

15.3.23. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – MRESVIA (CAP) – EMA/VR/0000263124

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

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

C.I.4: Update of section 4.5 of the SmPC in order to add drug-drug interaction information of co-administration of mRESVIA (mRNA-1345) dispersion for injection, in its all-registered presentations, with a Standard dose, Seasonal Influenza Vaccine, based on data forthcoming from mRNA-1345-P302 part A clinical study. It is a Phase 3 study to evaluate safety and immunogenicity of mRNA-1345 for respiratory syncytial virus (RSV) when given alone or co-administered with a Seasonal Influenza vaccine or COVID-19 vaccine. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted.

C.I.4: Update of section 4.5 of the SmPC in order to add drug-drug interaction information of co-administration of mRESVIA (mRNA-1345) dispersion for injection, in its all-registered presentations, with COVID-19 Vaccine, based on data forthcoming from mRNA-1345-P302 part B clinical study. It is a Phase 3 study to evaluate safety and immunogenicity of mRNA-1345 for RSV when given alone or co-administered with a Seasonal Influenza vaccine or COVID-19 vaccine. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted.

C.I.4: Update of section 4.5 of the SmPC in order to add drug-drug interaction information of co-administration of mRESVIA (mRNA 1345) dispersion for injection, in its all-registered presentations, with a High-dose, Quadrivalent Seasonal Influenza vaccine in Adults ≥65 Years of Age, based on data forthcoming from mRNA-1345-P304 clinical study. It is a Phase 3 Study to evaluate the safety and immune response of mRNA-1345, when co-administered with a High-dose, Quadrivalent Seasonal Influenza vaccine. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted.

15.3.24. Rurioctocog alfa pegol – ADYNOVI (CAP) – EMA/VR/0000268348

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC in order to update clinical pharmacokinetic, efficacy, and safety information based on final results from study 261203, listed as a category 3 study in the RMP; this is a phase 3, prospective, multi-center, open label study to investigate safety, immunogenicity, and hemostatic efficacy of PEGylated Factor VIII (BAX 855) in previously untreated patients (PUPs); 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, to introduce editorial changes, and to bring the PI in line with the latest QRD template.

15.3.25. Secukinumab – COSENTYX (CAP) – EMA/VR/0000267996

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Submission of the final report from study CAIN457F2304E1, listed as a category 3 study in the RMP. This is a phase 3, long-term, open-label, efficacy, safety and tolerability in JPsA and ERA subtypes of JIA up to 4 years in patients with active JPsA and ERA subtypes of JIA and who completed the Phase III study CAIN457F2304. The RMP version 12.0 has also been submitted.

15.3.26. Seladelpar lysine dihydrate – LYVDELZI (CAP) – EMA/VR/0000282041

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Amelia Cupelli

Scope: Update of section 5.2 of the SmPC in order to update pharmacokinetic information based on final results from study CB8025-21838 listed as a category 3 study in the RMP. This is an open-label study following oral dosing of seladelpar to subjects with primary biliary cholangitis (PBC) and hepatic impairment. In addition, the MAH took the opportunity to introduce additional administrative changes and corrections to the PI. The RMP version 1.1 has also been submitted.

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

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope:

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

15.3.28. Serplulimab – HETRONIFLY (CAP) – EMA/VR/0000282407

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include HETRONIFLY in combination with carboplatin and pemetrexed is indicated for the first-line treatment of adult patients with locally advanced or metastatic non-squamous non-small cell lung carcinoma who do not have EGFR or ALK positive mutations based on interim results from study HLX10-002-NSCLC301; this is a pivotal Phase III clinical study, patients treated with serplulimab in combination with carboplatin and pemetrexed showed statistically significant and clinically meaningful benefits in the efficacy endpoint results compared with those who received placebo with carboplatin and pemetrexed. As a consequence, sections 4.1, 4.8, 5.1, 5.2 of of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.

15.3.29. Serplulimab – HETRONIFLY (CAP) – EMA/VR/0000284402

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include, in combination with fluoropyrimidine- and platinum-based chemotherapy, the first-line treatment of adult patients with unresectable, locally advanced/recurrent or metastatic oesophageal squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 for HETRONIFLY, based on results from study HLX10-007-EC301; this is a randomized, double-blind, multi-center, phase III clinical study comparing the clinical efficacy and safety of HLX10 or placebo combined with chemotherapy in first-line treatment of locally advanced/metastatic esophageal squamous cell carcinoma (ESCC) patients. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.2 of the RMP has also been submitted.

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

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

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

15.3.31. Sonidegib – ODOMZO (CAP) – EMA/VR/0000268112

Applicant: Sun Pharmaceutical Industries (Europe) B.V.

PRAC Rapporteur: Petar Mas

Scope: Update of sections 5.3 and 6.6 of the SmPC in order to update non-clinical safety information on carcinogenicity based on final results from studies 8371102 and BRT_17_037G_TN; this is a 26-Week Oral Gavage Carcinogenicity Study with LDE225 in Transgenic Mice (RasH2 [001178-T (hemizigous), CByB6F1-Tg(HRAS)2Jic]) and a 104-Week Carcinogenicity Study of LDE225 in Wistar Rats by Oral Route, respectively. Sections 5.3 and 6.6 of the SmPC were also updated to include a statement on risk to the environment in line with the commitment following EMEA/H/C/002839/IB/0056. The RMP version 8.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to introduce editorial changes, and to bring the PI in line with the latest QRD template.

15.3.32. Sugemalimab – CEJEMLY (CAP) – EMA/VR/0000261157

Applicant: Cstone Pharmaceuticals Ireland Limited

PRAC Rapporteur: Petar Mas

Scope: Extension of indication to include the treatment of unresectable stage III non-small-cell lung cancer (NSCLC) with no sensitising EGFR mutations, or ALK, ROS1 genomic tumour aberrations in adults whose disease has not progressed following concurrent or sequential platinum-based chemoradiotherapy for CEJEMLY, based on final results from study CS1001-301; this is a Phase III, multicentre, randomised, double-blind, placebo-controlled study assessing the efficacy and safety of sugemalimab as consolidation therapy versus placebo in participants with locally advanced or unresectable stage III NSCLC who have not progressed after concurrent or sequential chemoradiotherapy. 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 2.0 of the RMP has also been submitted.

15.3.33. Tafasitamab – MINJUVI (CAP) – EMA/VR/0000255975

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include in combination with lenalidomide and rituximab treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after at least one line of systemic therapy for MINJUVI, based on interim results from study INCMOR 0208-301 (inMIND); this is a phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of tafasitamab plus lenalidomide and

rituximab vs lenalidomide and rituximab in patients with relapsed/refractory (R/R) follicular lymphoma grade 1 to 3a or R/R marginal zone lymphoma. As a consequence, sections 4.1, 4.2, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.34. Tecovirimat – TECOVIRIMAT SIGA (CAP) – EMA/VR/0000244868

Applicant: Siga Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.5 of the SmPC in order to add drug-drug interaction information with Calcium acetate, Lanthanum carbonate, Sevelamer carbonate, and Sucroferric oxyhydroxide based on final results from study SIGA-246-023. This is a safety, tolerability, and efficacy study of 4 phosphate binders on tecovirimat in adults. The Package Leaflet has been updated accordingly. The RMP version 2.1 has also been submitted.

15.3.35. Tirzepatide – MOUNJARO (CAP) – EMA/VR/0000281937

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adolescents and children aged 10 years and above with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise for MOUNJARO, based on final results from study I8F-MC-GPGV (SURPASS-PEDS); this is a study to evaluate efficacy, safety, and pharmacokinetics/pharmacodynamics of tirzepatide compared to placebo in paediatric and adolescent participants with type 2 diabetes mellitus inadequately controlled with metformin, or basal insulin, or both. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.1 of the RMP has also been submitted.

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

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

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

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

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

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

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

16.1.1. Aprocitentan – JERAYGO (CAP) – EMA/PSUR/0000274466

Applicant: Idorsia Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00011067/202503)

16.1.2. Axitinib – INLYTA (CAP) – EMA/PSUR/0000274426

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010022/202501)

16.1.3. Baloxavir marboxil – XOFLUZA (CAP) – EMA/PSUR/0000274449

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010895/202502)

16.1.4. Bempedoic acid / Ezetimibe – NILEMDO (CAP); NUSTENDI (CAP) – EMA/PSUR/0000274450

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010841/202502)

16.1.5. Burosumab – CRYSVITA (CAP) – EMA/PSUR/0000274414

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010669/202502)

16.1.6. Cabotegravir – VOCABRIA (CAP) – EMA/PSUR/0000274453

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010900/202503)

16.1.7. Cabotegravir – APRETUDE (CAP) – EMA/PSUR/0000274427

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000116/202503)

16.1.8. Carglumic acid – CARBAGLU (CAP) – EMA/PSUR/0000274412

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00000564/202501)

16.1.9. Ciltacabtagene autoleucel – CARVYKTI (CAP) – EMA/PSUR/0000274460

Applicant: Janssen Cilag International

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00011000/202502)

16.1.10. Cipaglucosidase alfa – POMBILITI (CAP) – EMA/PSUR/0000274442

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00011047/202503)

16.1.11. Dexamethasone – OZURDEX (CAP) – EMA/PSUR/0000274395

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00000985/202501)

16.1.12. Eptinezumab – VYEPTI (CAP) – EMA/PSUR/0000274456

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010966/202502)

16.1.13. Ex vivo expanded autologous human corneal epithelial cells containing stem cells – HOLOCLAR (CAP) – EMA/PSUR/0000274435

Applicant: Holostem S.R.L.

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00010352/202502)

16.1.14. Fedratinib – INREBIC (CAP) – EMA/PSUR/0000274467

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010909/202502)

16.1.15. Fenofibrate / Simvastatin – CHOLIB (CAP) – EMA/PSUR/0000274431

Applicant: Viatris Healthcare Limited

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00010096/202502)

16.1.16. Fosdenopterin – NULIBRY (CAP) – EMA/PSUR/0000274447

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00011017/202502)

16.1.17. Fruquintinib – FRUZAQLA (CAP) – EMA/PSUR/0000274462

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011069/202503)

16.1.18. Ganaxolone – ZTALMY (CAP) – EMA/PSUR/0000274432

Applicant: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00000093/202503)

16.1.19. Imlifidase – IDEFIRIX (CAP) – EMA/PSUR/0000274446

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010870/202502)

16.1.20. Influenza vaccine (surface antigen, inactivated, adjuvanted) – FLUAD (CAP); FLUAD TETRA (CAP) – EMA/PSUR/0000274436

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010300/202503)

16.1.21. influenza vaccine (surface antigen, inactivated, prepared in cell cultures) – FLUCELVAX (CAP); FLUCELVAX TETRA (CAP) – EMA/PSUR/0000274448

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010737/202503)

16.1.22. Miglustat – OPFOLDA (CAP) – EMA/PSUR/0000274388

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00000077/202503)

16.1.23. Mitapivat – PYRUKYND (CAP) – EMA/PSUR/0000274443

Applicant: Agios Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011025/202502)

16.1.24. Momelotinib – OMJJARA (CAP) – EMA/PSUR/0000274423

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00000263/202503)

16.1.25. Nitisinone – ORFADIN (CAP) – EMA/PSUR/0000274398

Applicant: Swedish Orphan Biovitrum International AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00002169/202502)

16.1.26. Nivolumab / Relatlimab – OPDUALAG (CAP) – EMA/PSUR/0000274454

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011018/202503)

16.1.27. Odronextamab – ORDSPONO (CAP) – EMA/PSUR/0000274458

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00011074/202502)

16.1.28. Omaveloxolone – SKYCLARYS (CAP) – EMA/PSUR/0000274406

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000245/202502)

16.1.29. Oritavancin – TENKASI (CAP) – EMA/PSUR/0000274430

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010368/202503)

16.1.30. Pegfilgrastim – CEGFILA (CAP); FULPHILA (CAP); GRASUSTEK (CAP); NEULASTA (CAP); NYVEPRIA (CAP); PELGRAZ (CAP); PELMEG (CAP); STIMUFEND (CAP); ZIEXTENZO (CAP) – EMA/PSUR/0000274399

Applicants: Accord Healthcare S.L.U., Amgen Europe B.V., Biosimilar Collaborations Ireland Limited, Fresenius Kabi Deutschland GmbH, Juta Pharma GmbH, Mundipharma Corporation (Ireland) Limited, Pfizer Europe MA EEIG, Sandoz GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00002326/202501)

16.1.31. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)– MOSQUIRIX (Art 58)[28] – EMA/PSUR/0000273313

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.1.32. Polihexanide – AKANTIOR (CAP) – EMA/PSUR/0000274457

Applicant: SIFI S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011082/202502)

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

16.1.33. Ponesimod – PONVORY (CAP) – EMA/PSUR/0000274452

Applicant: Laboratoires Juvise Pharmaceuticals

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00010940/202503)

16.1.34. Rilpivirine – REKAMBYS (CAP) – EMA/PSUR/0000274451

Applicant: Janssen Cilag International

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010901/202503)

16.1.35. Rimegepant – VYDURA (CAP) – EMA/PSUR/0000274465

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00010997/202502)

16.1.36. Ruxolitinib – JAKAVI (CAP) – EMA/PSUR/0000274417

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010015/202502)

16.1.37. Sodium thiosulfate – PEDMARQSI (CAP) – EMA/PSUR/0000274389

Applicant: Norgine B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00000066/202503)

16.1.38. Solriamfetol – SUNOSI (CAP) – EMA/PSUR/0000274441

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure (PSUSA/00010831/202503)

16.1.39. Sparsentan – FILSPARI (CAP) – EMA/PSUR/0000274455

Applicant: Vifor France

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00011060/202502)

16.1.40. Spesolimab – SPEVIGO (CAP) – EMA/PSUR/0000274439

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00011033/202503)

16.1.41. Teclistamab – TECVAYLI (CAP) – EMA/PSUR/0000274444

Applicant: Janssen Cilag International

PRAC Rapporteur: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00011010/202502)

16.1.42. Tildrakizumab – ILUMETRI (CAP) – EMA/PSUR/0000274440

Applicant: Almirall S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010720/202503)

16.1.43. Tivozanib – FOTIVDA (CAP) – EMA/PSUR/0000274415

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00010636/202502)

16.1.44. Valoctocogene roxaparvovec – ROCTAVIAN (CAP) – EMA/PSUR/0000274464

Applicant: Biomarin International Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011009/202502)

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

16.2.1. Ciclosporin – IKERVIS (CAP); VERKAZIA (CAP); VEVIZYE (CAP); NAP – EMA/PSUR/0000274428

Applicants: Laboratoires Thea, Santen Oy, various

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010362/202503)

16.2.2. Dexrazoxane – SAVENE (CAP); NAP – EMA/PSUR/0000274404

Applicants: Cnx Therapeutics Ireland Limited, various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00001001/202502)

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

16.3.1. Cyclophosphamide (NAP) – EMA/PSUR/0000274403

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000901/202501)

16.3.2. Dienogest / ethinylestradiol (prolonged-release tablet) (NAP) – EMA/PSUR/0000274463

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00011084/202503)

16.3.3. Glipizide (NAP) – EMA/PSUR/0000274392

Applicants: various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00001535/202501)

16.3.4. Hydroxyethyl starch / sodium chloride (NAP) – EMA/PSUR/0000274390

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00001694/202503)

16.3.5. Influenza vaccine (split virion, inactivated) (non centrally authorised products) (NAP) – EMA/PSUR/0000274438

Applicants: various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010298/202503)

16.3.6. Influenza vaccine (surface antigen, inactivated) (NAP) – EMA/PSUR/0000274391

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00001744/202503)

16.3.7. Interferon gamma (NAP) – EMA/PSUR/0000274394

Applicants: various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00001760/202501)

16.3.8. Lorazepam (NAP) – EMA/PSUR/0000274396

Applicants: various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00001909/202501)

16.3.9. Mesterolone (NAP) – EMA/PSUR/0000274418

Applicants: various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00010551/202501)

16.3.10. Pimozide (NAP) – EMA/PSUR/0000274421

Applicants: various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00002413/202502)

16.3.11. Potassium para-aminobenzoate (NAP) – EMA/PSUR/0000274434

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010130/202502)

16.3.12. Sevoflurane (NAP) – EMA/PSUR/0000274405

Applicants: various

PRAC Lead: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00002698/202501)

16.3.13. Tofisopam (NAP) – EMA/PSUR/0000274410

Applicants: various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00002982/202501)

16.3.14. Xipamide, triamterene / xipamide (NAP) – EMA/PSUR/0000274419

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00003133/202501)

16.4. Follow-up to PSUR/PSUSA procedures

None

16.5. Variation procedure(s) resulting from PSUSA evaluation

None

16.6. Expedited summary safety reviews[29]

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)[30]

17.1.1. 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.

17.1.2. 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

[29] 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

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

and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of Ketoconazole ESTEVE.

17.1.3. 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)[31]

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

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

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

17.2.2. Etrasimod – VELSIPITY (CAP) – EMA/PAM/0000287646

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Bolin

Scope: Study C5041046 - non-imposed non-interventional PASS protocol amendment: An Active Surveillance, Post-Authorization Safety Study to Characterize the Safety of Etrasimod in Patients with Ulcerative Colitis Using Real-World Data in the European Union

17.2.3. Inotersen – TEGSEDI (CAP) – EMA/PAM/0000286818

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: The MAH Akcea Therapeutics Ireland Limited submitted a revised PASS protocol version 3.0 to the European Medicines Agency (EMA) for Inotersen (Tegsedi). The PAM refers to A Retrospective, Non-interventional, Multi-centre Study of TEGSEDI-treated Patients to Evaluate Real-world Adherence to, and Effectiveness of the Recommendations for Platelet Monitoring, Dose Adjustment, and Steroid Initiation to Manage Risk of Thrombocytopenia

17.2.4. Romosozumab – EVENITY (CAP) – EMA/PAM/0000264559

Applicant: UCB Pharma

[31] 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

PRAC Rapporteur: Tiphaine Vaillant

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

17.2.5. Romosozumab – EVENITY (CAP) – EMA/PAM/0000264555

Applicant: UCB Pharma

PRAC Rapporteur: Tiphaine Vaillant

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

17.2.6. Spesolimab – SPEVIGO (CAP) – EMA/PAM/0000254921

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Zoubida Amimour

Scope: Updated protocol of PASS 1368-0128 - A 5-year active surveillance, post-authorisation safety study to characterise the safety of spesolimab for flare treatment in patients with GPP. Response to MEA 003.2 RSI adopted on 30 January 2025.

17.2.7. Sutimlimab – ENJAYMO (CAP) – EMA/PAM/0000287395

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Jan Neuhauser

Scope: Revised Study Protocol v. 3.0 for sutimlimab A Survey of Healthcare Professionals in Europe to Evaluate the Effectiveness of the ENJAYMO Physician’s Guide (HCP Survey, CEF-0205) a multinational, non-interventional, cross-sectional survey study.

17.2.8. Sutimlimab – ENJAYMO (CAP) – EMA/PAM/0000287412

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Jan Neuhauser

Scope: Revised Registry Study Protocol v. 6 for sutimlimab Cold Agglutinin Disease Real World Evidence Registry (CADENCE, OBS16454) a multinational, multi-center, observational, prospective, longitudinal disease registry. Former MEA 003.1-2

17.2.9. Tisagenlecleucel – KYMRIAH (CAP) – EMA/PAM/0000258545

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of protocol of the MEA Category 3 PASS CCTL019B2402 study entitiled 'A Non-Interventional Study (NIS) PASS to characterize secondary malignancies of T-cell origin following tisagenlecleucel therapy'

17.3. Results of PASS imposed in the marketing authorisation(s)[32]

17.3.1. 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.

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

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

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Karin Bolin

Scope: A grouped application comprised of:

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

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

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

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

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

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

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

17.4.3. COVID-19 mRNA vaccine – COMIRNATY (CAP) – EMA/VR/0000282346

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the final report for the non-interventional study C4591038, listed as category 3 study in the RMP. This is a Post Conditional approval active surveillance study among individuals in Europe receiving the Pfizer BioNTech Coronavirus Disease 2019 (COVID-19) vaccine. Sub-study to investigate natural history of post-vaccination myocarditis and pericarditis.

17.4.4. COVID-19 mRNA vaccine – SPIKEVAX (CAP) – EMA/VR/0000282182

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of final report from study mRNA-1273-P910 listed as category 3 study in the RMP. This is a multi-database observational study that utilized routinely collected secondary data in the European region to investigate the natural course of myocarditis and pericarditis following administration of Moderna vaccines targeting SARS-CoV-2 in terms of morbidity and identified relevant prognostic factors.

17.4.5. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) – EMA/VR/0000263592

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Sonja Radowan

Scope: Update of sections 4.4 and 4.8 of the SmPC to add "Guillain-Barre syndrome" to the list of adverse drug reactions with frequency "very rare" based on the results from study EPI-ZOSTER-032 VS US DB, listed as a category 3 study in the RMP. This is a non-interventional PASS to evaluate the safety of Shingrix in adults ≥ 65 years of age in the United States. The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted.

17.4.6. Laronidase – ALDURAZYME (CAP) – EMA/VR/0000282056

Applicant: Sanofi B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Submission of the final report from PASS ALID01803 listed as a category 3 study in the RMP. This is an observational, open-label study of the effects of Aldurazyme (laronidase) treatment on lactation in postpartum women with Mucopolysaccharidosis I (MPS I) and their breastfed infants. This study is to determine whether laronidase activity was present in the breast milk of mothers with MPS I disease and wether Aldurazyme affected the growth, development, and immunologic response of breastfed infants. The RMP version 2.0 has also been submitted.

17.4.7. 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 irritable bowel syndrome (IBS) predominantly with constipation (IBS-C) (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.

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

17.5.1. Blinatumomab – BLINCYTO (CAP) – EMA/PAM/0000287482

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Veronika Macurova

Scope: Submission of the second interim study report for Blincyto (blinatumomab) non-interventional post-authorisation safety study PASS 20180130 (category 1): Evaluation of Long-term Safety in Paediatric Patients With B-precursor Acute Lymphoblastic Leukemia (ALL) who Have Been Treated with Either Blinatumomab or Chemotherapy, Followed by Transplantation listed within the EU Risk Management Plan.

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

Applicant: Janssen Cilag International

PRAC Rapporteur: Jo Robays

Scope: Post-authorization Safety Study Survey to Evaluate the Effectiveness of the Ciltacabtagene Autoleucel HCP Educational Program and the Product Handling Training

17.5.3. COVID-19 mRNA vaccine – COMIRNATY (CAP) – EMA/PAM/0000286143

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the 5th Interim CSR for study C4591036; this is a category 3 study to characterize the clinical course, risk factors, long-term sequelae, and quality of life in children and young adults <21 years with acute post-vaccine myocarditis.

17.5.4. Givosiran – GIVLAARI (CAP) – EMA/PAM/0000266973

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission within 3 months after PSUSA finalisation all available data, whether these are CIOMS forms, TQ responses or other follow-up information, eCRFs or other documents that may apply on all potential DILI cases up to a DLP of January 31, 2025 as well as the complete assessment of the MAH on these cases as part of a post-authorisation measure.

17.5.5. Guselkumab – TREMFYA (CAP) – EMA/PAM/0000256444

Applicant: Janssen Cilag International

PRAC Rapporteur: Gabriele Maurer

Scope: Interim study results for PsoBest Registry - German Registry on the Treatment of Psoriasis with Biologics and Systemic Therapeutic

17.5.6. Nirmatrelvir / Ritonavir – PAXLOVID (CAP) – EMA/PAM/0000287758

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Following the CHMP outcome for Post-Authorisation Measure MEA 008.2 (first Interim Report for PASS C4671037 (analysis to characterise the safety profile of Paxlovid during pregnancy and breastfeeding women)), the company addresses the request to consider the inclusion of additional data sources. Additionally, the company is submitting the revised Interim Report 1 with corrections due to identified data errors in a database.

17.5.7. Nirmatrelvir / Ritonavir – PAXLOVID (CAP) – EMA/PAM/0000289516

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Following the CHMP outcome for Post-Authorisation Measure MEA 009.3, the MAH is hereby submitting the responses to the Request for Supplementary Information to the interim report of study PASS C4671047 to characterise the safety profile of Paxlovid in patients with COVID-19 and moderate or severe hepatic impairment or moderate or severe renal impairment. In addition, the request to consider the inclusion of additional data sources is addressed.

17.5.8. Odevixibat – BYLVAY (CAP) – EMA/PAM/0000287652

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: PAM MEA: Second interim study report for the registry-based PASS A4250-019 (Prospective Registry-Based Study of the Long-Term Safety of Odevixibat in Patients with Progressive Familial Intrahepatic Cholestasis (PFIC))

17.5.9. Respiratory syncytial virus vaccine (bivalent, recombinant) – ABRYSVO (CAP) – EMA/PAM/0000286222

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Assessment of the first interim report of the PASS category 3 to evaluate the safety of Abrysvo in all pregnant women and their offspring including immunocompromised pregnant women and high-risk pregnancies (C3671026)

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. Dinutuximab beta – QARZIBA (CAP) – EMA/S/0000282178

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Annual reassessment of the marketing authorisation

18.1.2. Ebola vaccine (Ad26.ZEBOV-GP [recombinant]) – ZABDENO (CAP) – EMA/S/0000281512

Applicant: Janssen Cilag International

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual reassessment of the marketing authorisation

18.1.3. Ebola vaccine (MVA-BN-Filo [recombinant]) – MVABEA (CAP) – EMA/S/0000281447

Applicant: Janssen Cilag International

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual reassessment of the marketing authorisation

18.1.4. Eladocagene exuparvovec – UPSTAZA (CAP) – EMA/S/0000293355

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Belzutifan – WELIREG (CAP) – EMA/R/0000290222

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

18.2.2. Etranacogene dezaparvovec – HEMGENIX (CAP) – EMA/R/0000288354

Applicant: CSL Behring GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.3. Exagamglogene autotemcel – CASGEVY (CAP) – EMA/R/0000290395

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.4. Repotrectinib – AUGTYRO (CAP) – EMA/R/0000282425

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Conditional renewal of the marketing authorisation

18.2.5. Seladelpar lysine dihydrate – LYVDELZI (CAP) – EMA/R/0000290389

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Amelia Cupelli

Scope: Conditional renewal of the marketing authorisation

18.2.6. Selpercatinib – RETSEVMO (CAP) – EMA/R/0000286890

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Abiraterone acetate – ABIRATERONE KRKA (CAP) – EMA/R/0000284809

Applicant: KRKA tovarna zdravil d.d. Novo mesto

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

18.3.2. Berotralstat – ORLADEYO (CAP) – EMA/R/0000282356

Applicant: Biocryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: 5-year renewal of the marketing authorisation

18.3.3. Fedratinib – INREBIC (CAP) – EMA/R/0000264185

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Radowan

Scope: 5-year renewal of the marketing authorisation

18.3.4. Lenalidomide – LENALIDOMIDE KRKA (CAP) – EMA/R/0000272358

Applicant: KRKA tovarna zdravil d.d. Novo mesto

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.5. Salmeterol / Fluticasone propionate – SEFFALAIR SPIROMAX (CAP) – EMA/R/0000280812

Applicant: Teva B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

18.3.6. Thiotepa – THIOTEPA RIEMSER (CAP) – EMA/R/0000282361

Applicant: Esteve Pharmaceuticals GmbH

PRAC Rapporteur: Tiphaine Vaillant

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 October PRAC meeting, which was held in-

person. Participants marked with "a" attended the plenary session while those marked with "b" attended the ORGAM.

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

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Ulla Wändel Liminga [a,b]	Chair	Sweden	No interests declared	
Jan Neuhauser [a,b]	Member*	Austria	No interests declared	
Sonja Radowan [a]	Alternate*	Austria	No interests declared	
Jean-Michel Dogné [a,b]	Member	Belgium	No restrictions applicable to this meeting	
Jo Robays [a]	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva [a,b]	Member*	Bulgaria	No interests declared	
Petar Mas [a]	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi [a,b]	Alternate*	Croatia	No interests declared	
Elena Kaisis [b]	Member	Cyprus	No interests declared	
Panagiotis Psaras [a]	Alternate	Cyprus	No interests declared	
Eva Jirsová [a,b]	Member	Czechia	No interests declared	
Veronika Macurova	Alternate	Czechia	No interests declared	
Marie Louise Schougaard Christiansen [a]	Member	Denmark	No interests declared	
Karin Erneholm [a,b]	Alternate	Denmark	No interests declared	
Maia Uusküla [a]	Member	Estonia	No interests declared	
Krõõt Aab [a]	Alternate*	Estonia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Terhi Lehtinen [a,b]	Member	Finland	No interests declared	
Kimmo Jaakkola [a,b]	Alternate*	Finland	No interests declared	
Tiphaine Vaillant [a,b]	Member	France	No interests declared	
Zoubida Amimour [a,b]	Alternate	France	No participation in discussion, final deliberations and voting on:	15.2.2. - EMA/VR/00002 75832 15.3.7. - EMA/VR/00002 82554 15.3.15. - EMA/VR/00002 72242 15.3.20.– EMA/VR/00002 82199 16.1.14.– EMA/PSUR/000 0274467 16.1.26. – EMA/PSUR/000 0274454 18.2.4. – EMA/R/000028 2425 18.3.3.– EMA/R/000026 4185
Gabriele Maurer [a]	Alternate	Germany	No interests declared	
Georgia Gkegka [a]	Member*	Greece	No interests declared	
Maria Poulianiti [a]	Alternate*	Greece	No restrictions applicable to this meeting	
Julia Pallos [a,b]	Member	Hungary	No participation in discussion, final	15.2.2.– EMA/VR/00002 75832

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			deliberations and voting on:	15.3.7.– EMA/VR/00002 82554 15.3.15.– EMA/VR/00002 72242 15.3.20. - EMA/VR/00002 82199 16.1.14.– EMA/PSUR/000 0274467 16.1.26. - EMA/PSUR/000 0274454 18.2.4. - EMA/R/000028 2425 18.3.3. - EMA/R/000026 4185
Melinda Palfi [a,b]	Alternate*	Hungary	No interests declared	
Guðrún Stefánsdóttir [a]	Member	Iceland	No participation in discussion, final deliberations and voting on:	6.1.1.– EMA/PSUR/000 0274402 15.3.4.– EMA/VR/00002 86935 15.3.11.– EMA/VR/00002 57358 16.1.30. EMA/PSUR/000 0274399 17.5.1.– EMA/PAM/0000 287482
Rhea Fitzgerald [a,b]	Member	Ireland	No interests declared	
Eamon O Murchu [a]	Alternate	Ireland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Amelia Cupelli [a,b]	Member	Italy	No interests declared	
Zane Neikena [a,b]	Member	Latvia	No interests declared	
Diana Litenboka [a]	Alternate*	Latvia	No interests declared	
Rugile Pilviniene [a]	Member	Lithuania	No restrictions applicable to this meeting	
Anne-Cecile Vuillemin [a,b]	Member	Luxembourg	No interests declared	
Magdalena Wielowieyska [a,b]	Alternate*	Luxembourg	No participation in discussion, final deliberations and voting on:	6.3.6.– EMA/PSUR/0000274437 7.1.1.– EMA/PASS/0000269314 15.3.36. – EMA/VR/0000255408 16.1.17.– EMA/PSUR/0000274462
John Joseph Borg [a]	Member	Malta	No restrictions applicable to this meeting	
Liana Martirosyan [a,b]	Member (Vice-Chair)	Netherlands	No interests declared	
Bianca Mulder [a,b]	Alternate	Netherlands	No interests declared	
David Olsen [a,b]	Member	Norway	No participation in discussion, final deliberations and voting on:	11.1.1. - FI/H/xxxx/WS/190 11.1.3. - SE/H/xxxx/WS/888 15.3.1.– EMA/VR/0000264981

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				16.3.9.– EMA/PSUR/0000274418
Pernille Harg [a,b]	Alternate*	Norway	No interests declared	
Adam Przybylkowski [a]	Member*	Poland	No restrictions applicable to this meeting	
Katarzyna Ziolkowska [a,b]	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins [a,b]	Member	Portugal	No interests declared	
Carla Torre [a]	Alternate*	Portugal	No restrictions applicable to this meeting	
Roxana Dondera [a]	Member	Romania	No interests declared	
Irina Sandu [a,b]	Alternate*	Romania	No interests declared	
Anna Mareková [a,b]	Member*	Slovakia	No interests declared	
Miroslava Gocova [a]	Alternate	Slovakia	No interests declared	
Marjetka Plementas [a,b]	Alternate	Slovenia	No interests declared	
Maria del Pilar Rayon [a,b]	Member	Spain	No interests declared	
Maria Martinez Gonzalez [a,b]	Alternate	Spain	No interests declared	
Mari Thorn [a,b]	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin [a,b]	Alternate	Sweden	No restrictions applicable to this meeting	
Milou-Daniel Drici [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Maria Teresa Herdeiro [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Patricia McGettigan [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Hedvig Marie Egeland Nordeng [a]	Member*	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark [a]	Member*	Independent scientific expert	No restrictions applicable to this meeting	
Roberto Frontini [a]	Member	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	6.3.6.– EMA/PSUR/0000274437 7.1.1.– EMA/PASS/0000269314 15.3.36.– EMA/VR/0000255408 16.1.17. – EMA/PSUR/0000274462
Martin Votava [a,b]	Alternate*	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Yiannoula Koulla [a,b]	Member	Patients' Organisation Representative	No interests declared	
Laurence de Fays [a]	Expert	Belgium	No interests declared	
Ines Husajina [a]	Expert	Croatia	No interests declared	
Lara Miletić [a]	Expert	Croatia	No interests declared	
Lora Pavlinović [a]	Expert	Croatia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Alexander Braathen [a]	Expert	Denmark	No interests declared	
Kirsten Egebjerg Juul [a]	Expert	Denmark	No interests declared	
Kristina Laursen [a]	Expert	Denmark	No interests declared	
Nicklas Hasselblad Lundstrøm [a]	Expert	Denmark	No interests declared	
Cecilie Louise Pedersen [a],[b]	Expert	Denmark	No participation in discussion, final deliberations and voting on:	15.3.13.– EMA/VR/00002 68356 16.1.12.– EMA/PSUR/000 0274456
Moritz Sander [a]	Expert	Denmark	No restrictions applicable to this meeting	
Aynur Sert [a]	Expert	Denmark	No interests declared	
Ditte Søgaard [a]	Expert	Denmark	No interests declared	
Emma Stadsbjerg [a]	Expert	Denmark	No restrictions applicable to this meeting	
Stine Wieland [a]	Expert	Denmark	No restrictions applicable to this meeting	
Katrin Kurvits [a]	Expert	Estonia	No restrictions applicable to this meeting	
Heili Tikk [a]	Expert	Estonia	No interests declared	
Helve Vestman [a]	Expert	Estonia	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Maria Paile-Hyvärinen [a]	Expert	Finland	No interests declared	
Guillaume Belliard [a]	Expert	France	No interests declared	
Pauline Dayani [a]	Expert	France	No interests declared	
Ludivine Martin [a]	Expert	France	No interests declared	
Dennis Lex [a,b]	Expert	Germany	No interests declared	
Dario Ortiz [a]	Expert	Germany	No interests declared	
Negar Babae [a]	Expert	Netherlands	No interests declared	
Hanja de Kooter [a]	Expert	Netherlands	No restrictions applicable to this meeting	
Sonia Roldan Munoz [a]	Expert	Netherlands	No restrictions applicable to this meeting	
Patrick Vrijlandt [a]	Expert	Netherlands	No restrictions applicable to this meeting	
Inge Zomerdijk [a]	Expert	Netherlands	No interests declared	
Joao Fernandes [a]	Expert	Portugal	No restrictions applicable to this meeting	
Charlotte Backman [a,b]	Expert	Sweden	No interests declared	
Jolanta Gulbinovic [a]	Expert	Sweden	No interests declared	
A representative from the European Commission attended the meeting				
Observers from Health Canada attended the meeting.				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

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

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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