20 October 2025
EMA/PRAC/326133/2025
Human Medicines Division

Pharmacovigilance Risk Assessment: Committee (PRAC)

Minutes of PRAC meeting on 01-04 September 2025

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

The Chairperson opened the 01-04 September 2025 meeting by welcoming all participants. The meeting was held remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates and experts and on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics. Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. Roberto Frontini declared a new or additional competing interest regarding Takeda Germany. 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 thanked the departing members/alternates for their contributions to the Committee.

1.2. Agenda of the meeting on 01-04 September 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 07-10 July 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 07-10 July 2025 were published on the EMA website on 10 September 2025 (EMA/PRAC/272191/2025).

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

3.1.1. Levamisole (NAP) – EMA/REF/0000293746

Applicant(s): various

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

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

Background

Levamisole is an anthelmintic and it is indicated in adults and children for the treatment of infections caused by the following parasitic worms: *Ascaris lumbricoides, Necator americanus, Ancylostoma duodenale, Strongyloides stercoralis and Trichostrongylus colubriformis.*

The Romanian Medicines Agency (ANMDMR) sent a letter of notification dated 28 August 2025 triggering a referral under Article 31 of Directive 2001/83/EC for the review of levamisole-containing products following concerns regarding leukoencephalopathy.

Discussion

PRAC noted the notification letter from the ANMDMR.

PRAC appointed Roxana Dondera as Rapporteur and Barbara Kovacic Bytyqi as Co-Rapporteur for the procedure.

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

Summary of recommendation(s)/conclusions

- The Committee adopted a list of questions to the MAHs of levamisole-containing products and a timetable for the procedure.
- PRAC discussed the option to conduct a public hearing in the context of the Article 31 procedure on medicinal products containing levamisole, according to the pre-defined criteria set out in the rules of procedure[1] (EMA/11523/2023 Rev.2). It was agreed by the Committee that at this stage in the assessment, in light of the currently available data and the need to determine the suitable approach to stakeholder engagement, a public hearing would not be appropriate. PRAC can come back to reconsider this at a later stage of the procedure as needed.

[1] Rules of procedure on the organisation and conduct of public hearings at PRAC

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

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

None

3.5. Others

3.5.1. Chikungunya vaccine (live) – IXCHIQ (CAP) – EMA/REF/0000269473

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer; PRAC Co-rapporteur: Jean-Michel Dogné

Scope: PRAC response to European Commission letter regarding the impact of additional cases of serious adverse events on the review of the benefit-risk balance, following notification by the European Commission (EC) of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data

Summary of conclusions

PRAC noted the decision by the US Food and Drug Administration (FDA) to suspend the use of Ixchiq in the United States of America on 22 August 2025. This regulatory action took into consideration 4 additional cases of serious adverse events that became available after the PRAC assessment under the Article 20 procedure was finalised (PRAC recommendation issued on 10 July 2025). See PRAC minutes July 2025.

Following a review of these cases and subsequent discussion during the PRAC September plenary meeting, PRAC confirmed that these additional cases do not impact the overall benefit-risk conclusion established during the Article 20 procedure, which remains favourable, subject to the recommended amendments to the product information. As a consequence, PRAC maintained its previously adopted recommendation that the marketing authorisation for Ixchiq should be varied.

PRAC highlighted that any additional information that may become available in the future will be assessed in accordance with established pharmacovigilance processes for the product, as appropriate.

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

4. Signals assessment and prioritisation[3]

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

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

See also Annex I 14.1.

4.1.1. Amlodipine (NAP)

Applicant(s): various

PRAC Rapporteur: Karin Erneholm

Scope: Signal of subacute cutaneous lupus erythematosus

EPITT 20203 – New signal

Lead Member State: DK

Background

Amlodipine is a calcium ion influx inhibitor (slow channel blocker or calcium ion antagonist) of the dihydropyridine group and it is indicated for the first line treatment of hypertension and myocardial ischaemia, whether due to fixed obstruction (stable angina) and/or to vasospasm/vasoconstriction (Prinzmetal's or variant angina) of the coronary vasculature.

During routine signal detection activities, a signal of subacute cutaneous lupus erythematosus was identified by Denmark, based on cases retrieved from EudraVigilance and the literature. Denmark confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

PRAC appointed Karin Erneholm as Rapporteur for the signal.

Having considered the available evidence including cases from EudraVigilance and the literature, PRAC has concluded that the current evidence is insufficient to establish a causal relationship between amlodipine and subacute cutaneous lupus erythematosus to further warrant an update of the product information and/or risk management plan at present.

Summary of recommendation(s)

- The MAHs of amlodipine-containing products (as monocomponent) should submit a cumulative review of subacute cutaneous lupus erythematosus in the next PSUR (DLP 07/03/2027).

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

4.1.2. Folic acid (NAP)

Applicant(s): various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of increased risk of cancer with high-dose folic acid (⩾1mg)

EPITT 20183 – New signal

Lead Member State: DK

Background

Folic acid (vitamin B9) is indicated for the prevention and treatment of folic acid deficiency, and for the prevention of neural tube defects in the developing foetus.

A signal of potentially increased risk of cancer with high-dose folic acid (≥1mg) was identified by Ireland, based on two epidemiological studies by *Vegrim et al. (2022[4] and 2024[5])* regarding mothers and children of mothers with epilepsy exposed to high-dose folic acid, respectively. Denmark confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

PRAC appointed Marie Louise Schougaard Christiansen as Rapporteur for the signal.

Having considered the evidence from the literature and PRAC's recommendation following the assessment of PSUSA/00000893/202411 (concluded at PRAC in July 2025) comprising a literature review and a discussion of the studies by *Vegrim et al. (2022 and 2024)* including the limitations identified in these studies (such as residual confounding, potential misclassification of exposure, lack of dose response relationship, and limited statistical power for rare outcomes), PRAC considered that there is insufficient evidence to conclude a potential risk of cancer associated with high-dose (≥1 mg) folic acid products.

Summary of recommendation(s)

- The MAHs of folic acid containing products should monitor new information regarding high-dose (≥1 mg) folic acid exposure and a potentially increased risk of cancer in the next PSUR.

4.2. Signals follow-up and prioritisation

4.2.1. Binimetinib – MEKTOVI (CAP) - EMEA/H/C/004579/SDA/007; cobimetinib – COTELLIC (CAP) - EMEA/H/C/003960/SDA/007; dabrafenib – TAFINLAR (CAP) - EMEA/H/C/002604/SDA/025, FINLEE (CAP) - EMEA/H/C/005885/SDA/004; encorafenib – BRAFTOVI (CAP) - EMEA/H/C/004580/SDA/007; trametinib – MEKINIST (CAP) - EMEA/H/C/002643/SDA/020, SPEXOTRAS (CAP) - EMEA/H/C/005886/SDA/003; vemurafenib – ZELBORAF (CAP) - EMEA/H/C/002409/SDA/040

Applicants: Novartis Europharm Limited (Finlee, Mekinist, Spexotras, Tafinlar), Pierre Fabre Medicament (Braftovi, Mektovi), Roche Registration GmbH (Cotellic, Zelboraf)

[4] Vegrim HM, Dreier JW, Alvestad S, et al. Cancer Risk in Children of Mothers With Epilepsy and High-Dose Folic Acid Use During Pregnancy. JAMA Neurol. 2022;79(11):1130–1138. doi:10.1001/jamaneurol.2022.2977

[5] Vegrim HM, Dreier JW, Igland J, Alvestad S, Gilhus NE, Gissler M, et al. High-dose folic acid use and cancer risk in women who have given birth: A register-based cohort study. Epilepsia. 2025; 66: 75–88. https://doi.org/10.1111/epi.18146

PRAC Rapporteur: Mari Thorn

Scope: Signal of tattoo associated skin reaction

EPITT 20160 – Follow-up to March 2025

Background

For background information, see PRAC minutes March 2025.

The MAH replied to the request for information on the signal of tattoo associated skin reaction and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance and literature, as well as the data submitted by the MAH, PRAC agreed that there is sufficient evidence to establish a causal association between trametinib or dabrafenib and tattoo associated skin reaction. Therefore, the product information (PI) of dabrafenib and trametinib-containing products should be updated to add tattoo associated skin reactions as an undesirable effect with a frequency 'not known'. In addition, PRAC concluded that the current evidence is insufficient to establish a causal relationship between vemurafenib, cobimetinib, encorafenib or binimetinib and tattoo-associated skin reactions reaction to further warrant an update to the PI and/or risk management plan at present.

Summary of recommendation(s)

- The MAH for Mekinist, Spexotras, Tafinlar and Finlee should submit to EMA, within 60 days, a variation to update the product information[6]. If more evidence becomes available in the future, the MAH of trametinib and dabrafenib-containing products should consider whether further updates of the PI regarding tattoo-associated skin reactions are necessary when the respective products are used in monotherapy or if the reactions are also relevant for the paediatric population. The MAH of Cotellic and Zelboraf, and the MAH of Braftovi and Mektovi, should monitor cases of tattoo-associated skin reactions in the next PSUR.

4.2.2. Dabigatran etexilate - DABIGATRAN ETEXILATE ACCORD (CAP); DABIGATRAN ETEXILATE TEVA (CAP); PRADAXA (CAP) - EMEA/H/C/000829/SDA/055; NAP

Applicant(s): Boehringer Ingelheim International GmbH, various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of splenic rupture

EPITT 20164 – Follow-up to May 2025

Background

For background information, see PRAC minutes May 2025.

The MAH of Pradaxa (Boehringer Ingelheim International GmbH) replied to the request for information on the signal of splenic rupture and the responses were assessed by the Rapporteur.

Discussion

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

Having considered the available evidence in EudraVigilance, the literature and the data submitted by the MAH, PRAC concluded that the current evidence is insufficient to establish a causal relationship between dabigatran and splenic rupture to further warrant an update to the product information and/or risk management plan at present.

Summary of recommendation(s)

- The MAH for Pradaxa (Boehringer Ingelheim International GmbH) should continue to monitor these events as part of routine pharmacovigilance.

4.2.3. Diazoxide (NAP)

Applicant(s): various

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of necrotising enterocolitis neonatal

EPITT 20163 – Follow-up to April 2025

Background

For background information, see PRAC minutes April 2025.

The MAHs replied to the request for information on the signal of necrotising enterocolitis neonatal and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance and the literature, including the data submitted by the MAHs, PRAC agreed that there is sufficient evidence to establish a causal association between necrotising enterocolitis neonatal and diazoxide. Therefore, the product information (PI) for diazoxide-containing products should be updated to add necrotising enterocolitis neonatal as a warning and as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAHs RPH Pharmaceuticals AB and Merck Sharp & Dohme B.V. should submit to national competent authorities, within 60 days, a variation to update the PI[7]. Taking into account the already existing wording in some nationally authorised products the text may need to be adapted by MAH(s) to individual products.

4.2.4. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/SDA/010

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of atypical haemolytic uraemic syndrome

EPITT 20169 – Follow-up to May 2025

Background

For background information, see PRAC minutes May 2025.

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

The MAH replied to the request for information on the signal of atypical haemolytic uraemic syndrome and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance and literature, including the data submitted by the MAH, PRAC agreed that there is sufficient evidence to establish a causal association between atypical haemolytic uraemic syndrome and dinutuximab beta. Therefore, the product information (PI) should be updated to add a warning on atypical haemolytic uraemic syndrome and to add atypical haemolytic uraemic syndrome as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAH for Qarziba (dinutuximab beta) should submit to EMA, within 60 days, a variation to update the PI[8].

4.2.5. Osimertinib - TAGRISSO (CAP) - EMEA/H/C/004124/SDA/009

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Signal of hepatitis B reactivation

EPITT 20172 – Follow-up to May 2025

Background

For background information, see PRAC minutes May 2025.

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

Discussion

Having considered the available evidence in EudraVigilance, literature and the data submitted by the MAH, PRAC agreed that there is sufficient evidence to establish a causal association between hepatitis B reactivation and osimertinib. Therefore, the product information (PI) should be updated to add hepatitis B Virus (HBV) reactivation as a warning and as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAH for Tagrisso (Osimertinib) should submit to EMA, within 60 days, a variation to update the PI[9].

4.2.6. Somatrogon - NGENLA (CAP) - EMEA/H/C/005633/SDA/005

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of lipoatrophy

EPITT 20173 – Follow-up to May 2025

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

Background

For background information, see PRAC minutes May 2025.

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

Discussion

Having considered the available evidence in EudraVigilance, literature and the data submitted by the MAH, PRAC agreed that there is sufficient evidence to establish a causal association between lipoatrophy and somatrogon. Therefore, the product information (PI) should be updated to add lipoatrophy as an undesirable effect with a frequency 'not known', and to amend sections on the method of administration as well as instructions for use to emphasise that the site of injection should be rotated at each administration to prevent lipoatrophy.

Summary of recommendation(s)

- The MAH for Ngenla (somatrogon) should submit to EMA, within 60 days, a variation to update the PI[10].

4.3. Variation procedure(s) resulting from signal evaluation

4.3.1. Leflunomide – ARAVA (CAP) – EMA/VR/0000279486

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: To update section 4.8 of the SmPC and section 4 of the PL to implement the signal recommendations on pulmonary nodule (EPITT no 20155) adopted at the 13 March 2025 PRAC meeting. In addition, the MAH took the opportunity to update the EU local representatives.

Background

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

In relation to previous recommendations on signal on pulmonary nodule, the MAH submitted to EMA a variation to update the product information (PI). PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

Summary of outcome(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed with update of the PI[11] to amend the existing warning related to respiratory reactions and to add pulmonary nodule as an undesirable effect with a frequency 'not known'.

[10] Update of SmPC sections 4.2 and 4.8. The package leaflet is updated accordingly.
[11] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly.

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

5.1.1. Blarcamesine - (CAP MAA) - EMEA/H/C/006475

Scope (pre D-180 phase): Treatment of Alzheimer's disease and dementia

5.1.2. Donidalorsen - (CAP MAA) - EMEA/H/C/006554, Orphan

Applicant: Otsuka Pharmaceutical Netherlands B.V.

Scope (pre D-180 phase): For routine prevention of recurrent attacks of hereditary angioedema (HAE)

5.1.3. Doxecitine / Doxribtimine - (CAP MAA) - EMEA/H/C/005119, PRIME, Orphan

Applicant: UCB Pharma

Scope (pre D-180 phase): Indicated for the treatment of paediatric and adult patients with thymidine kinase 2 deficiency (TK2d) with an age of symptom onset on or before 12 years

5.1.4. Germanium (^{68}Ge) chloride / Gallium (^{68}Ga) chloride - (CAP MAA) - EMEA/H/C/006639

Scope (pre D-180 phase): Indicated for in vitro radiolabelling of specific carrier molecules to be used for positron emission tomography (PET) imaging

5.1.5. Iloperidone - (CAP MAA) - EMEA/H/C/006561

Scope (pre D-180 phase): Treatment of schizophrenia, acute treatment of manic or mixed episodes associated with bipolar I disorder

5.1.6. Imlunestrant - (CAP MAA) - EMEA/H/C/006184

Scope (pre D-180 phase): Treatment of adult patients with advanced or metastatic breast cancer

5.1.7. COVID-19 mRNA vaccine - (CAP MAA) - EMEA/H/C/006428

Scope (pre D-180 phase): Active immunisation to prevent COVID 19 caused by SARS-CoV-2 in individuals 12 years of age and older.

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

Applicant: Novartis Europharm Limited, ATMP

Scope (pre D-120 phase): Treatment of 5q spinal muscular atrophy (SMA)

5.1.9. Teplizumab - (CAP MAA) - EMEA/H/C/005496, PRIME

Scope (pre D-180 phase): To delay both the onset of Stage 3 type 1 diabetes (T1D) and the progression of Stage 3 T1D

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

See also Annex I 15.2.

5.2.1. Fezolinetant – VEOZA (CAP) – EMA/VR/0000255134

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 4.0 in order to include Drug-Induced Liver Injury (DILI) as an important identified risk following PSUR procedure EMEA/H/C/PSUSA/00000231/202405 (EMA/PRAC/544509/2024).

Background

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

PRAC is evaluating a type II variation procedure for Veoza, a centrally authorised medicine containing fezolinetant, to update the RMP to reflect the inclusion of the DILI as an important identified risk in the RMP. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

Summary of advice

- The RMP version 4.2 for Veoza (fezolinetant) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.
- PRAC agreed with the inclusion of DILI as important identified risk in the RMP. In addition, PRAC noted the MAH's proposal for a feasibility assessment for a study to evaluate the effectiveness of risk minimisation measures (RMMs) for fezolinetant as additional pharmacovigilance activity. However, PRAC considered that, in case the planned feasibility assessment for a multi-database study in secondary data sources does not confirm the feasibility of such a PASS, alternative study designs should be proposed to evaluate the effectiveness of RMMs, and the RMP should be updated accordingly.

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

See also Annex I 15.3.

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

Applicant: Biocryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Extension application to introduce a new pharmaceutical form associated with new strengths (78 mg, 96 mg,108 and 132 film - coated granules). The new presentations are indicated to include treatment for paediatric patients aged 2 to less than 12 years. The extension application is grouped with a type II clinical variation (C.I.4). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 2.1 of the RMP has also been submitted.

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 line extension for Orladeyo, a centrally authorised product containing berotralstat. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

Summary of advice

- The RMP for Orladeyo (berotralstat) in the context of the procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 2.0 is submitted.
- PRAC considered that, as the new extended indication includes patients between 2 and 12 years of age, the 'long-term safety' should be characterised and evaluated in this patient population too. Moreover, PRAC was of the view that the MAH should discuss whether the extension of the ongoing category 3 NI-PASS (study 401) is feasible to the paediatric population and if not, the MAH should propose a pharmacovigilance activity to characterise further the long-term use in paediatric patients.

5.3.2. Burosumab – CRYSVITA (CAP) – EMA/VR/0000261369

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: A grouped application consisting of:

C.I.4: Update of sections 4.4, 4.5, and 4.8 of the SmPC in order to update safety information about Severe Hypercalcaemia in patients with Tertiary Hyperparathyroidism based on data from clinical trials and post-authorisation data sources; the Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted. In addition, the MAH took the opportunity (1) to improve the existing guidance in section 4.2 based on the accumulated clinical experience, (2) to introduce editorial changes to the PI, (3) to bring the PI in line with the latest QRD template, current guidelines, and PEI requests.

C.I.4: Update of section 4.8 of the SmPC in order to add urticaria to the list of adverse drug reactions (ADRs) with frequency common based on data from clinical trials and post-

authorisation data sources; the Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted.

Background

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

CHMP is evaluating a type II variation for Crysvita, a centrally authorised product containing burosumab. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure, including on the need for a direct healthcare professional communication (DHPC).

Summary of advice

- The RMP for Crysvita (burosumab) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 9.0 is submitted.
- PRAC endorsed the update of the safety concerns, including the reclassification of 'increased parathyroid hormone levels' from important potential risk to an identified risk not categorised as important, and the addition of 'severe hypercalcaemia in tertiary hyperparathyroidism patients' as important identified risk in the RMP. PRAC did not support the implementation of a revised follow-up questionnaire to collect additional information on hypercalcaemia and hyperparathyroidism with regard to the characterization of the new important identified risk 'severe hypercalcaemia in tertiary hyperparathyroidism patients'. In addition, PRAC concluded that the dissemination of a DHPC is warranted to inform the healthcare professionals about the risk of severe hypercalcaemia and the need for monitoring.

5.3.3. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/X/0149

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with a new strength (40 mg/ml).

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 line extension for Remsima, a centrally authorised product containing infliximab. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

Summary of advice

- The RMP version 17.2 for Remsima (infliximab) in the context of the procedure under evaluation by CHMP is considered acceptable.

- PRAC supported the addition of 'serious metabolic harms due to sorbitol exposure in patients with hereditary fructose intolerance (100mg and 350mg concentrate for solution for infusion only)' to the summary of safety concerns in the RMP. Consequently, PRAC supported the update of the patient card. Moreover, PRAC agreed the distribution of a direct healthcare professional communication (DHPC) together with a communication plan in order to inform the healthcare professionals (HCPs) about the new contraindication on hereditary fructose intolerance.

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. Apalutamide – ERLEADA (CAP) – EMA/PSUR/0000269021

Applicant: Janssen Cilag International

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00010745/202502)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Erleada, a centrally authorised medicine containing apalutamide 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 Erleada (apalutamide) in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add neutropenia and agranulocytosis as undesirable effects with a frequency 'common' and 'not known' respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAH should provide a cumulative review of thyroid dysfunction from all available sources, including preclinical, clinical, post-marketing but also scientific literature data, as well as a discussion on the need to update the PI, as warranted. The MAH should also provide an updated evaluation on the topic of ageusia and continue monitoring cases of medication errors for both dosages.
- The MAH is requested to submit, within 3 months, a cumulative review on the risk of laboratory interference leading to falsely elevated digoxin plasma levels as part of a

[12] 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.

dedicated procedure (LEG procedure) and discuss the need to update the PI, as warranted.

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

6.1.2. Brexucabtagene autoleucel – TECARTUS (CAP) – EMA/PSUR/0000268989

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010903/202501)

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Tecartus (brexucabtagene autoleucel) in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add status epilepticus as undesirable effect to the existing adverse reaction seizures with frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- In the next PSUR, the MAH should discuss the literature article by *Soravia A, et al. 2025*[14] concerning acute macular retinopathy, provide a review of any additional cases from clinical trials or post-marketing sources, and discuss the need to update the PI as warranted. In addition, the MAH should present a detailed analysis of myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML) cases, including the role of prior treatment and/or HCT, and discuss whether patients treated with brexucabtagene autolecleucel are at increased risk of MDS/AML.

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. Crovalimab – PIASKY (CAP) – EMA/PSUR/0000268996

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011071/202502)

[13] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[14] Soravia A, et al. A case of acute macular neuroretinopathy as atypical ICANS manifestation after CAR-T cell infusion. Leukemia & Lymphoma (2025) 66:565–566

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Piasky, a centrally authorised medicine containing crovalimab 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 Piasky (crovalimab) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide a comprehensive analysis of all gastroenteritis and discuss the need to update the product information (PI) as warranted.
- The MAH should remove the controlled access program in an upcoming regulatory procedure, and thus to submit, by end of 2025, a variation to update the Annex II of the PI and the RMP accordingly. However, no changes are recommended for the guide for healthcare professionals, patient/caregiver guide, patient card, vaccination/re-vaccination reminders.

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. Pirtobrutinib – JAYPIRCA (CAP) – EMA/PSUR/0000268970

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000155/202501)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Jaypirca, a centrally authorised medicine containing pirtobrutinib 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 Jaypirca (pirtobrutinib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add hepatic enzyme increased as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[15].
- In the next PSUR, the MAH should continue to closely monitor hypertension, cardiac failure, cardiac arrhythmia, use of pirtobrutinib during pregnancy and breastfeeding, for which the MAH should clearly discuss the causality of new cases from the reporting interval.

[15] 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.

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

6.1.5. Tezacaftor / Ivacaftor – SYMKEVI (CAP) – EMA/PSUR/0000269024

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00010730/202502)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Symkevi, a centrally authorised medicine containing tezacaftor/ivacaftor 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 Symkevi (tezacaftor/ivacaftor) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning regarding depression, and elevated transaminases and hepatic injury. 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.

6.1.6. Voclosporin – LUPKYNIS (CAP) – EMA/PSUR/0000268975

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011020/202501)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Lupkynis, a centrally authorised medicine containing voclosporin 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 Lupkynis (voclosporin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add fatigue as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[17].

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

The frequency of PSUR submission should be revised from six-monthly to 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 also Annex I 16.1.1.

6.2.1. Caspofungin – CANCIDAS (CAP); NAP – EMA/PSUR/0000268976

Applicants: Merck Sharp & Dohme B.V., various

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00000576/202412)

Background

Caspofungin is an antifungal indicated for the treatment of invasive candidiasis in adult or paediatric patients, of invasive aspergillosis in adult or paediatric patients who are refractory to or intolerant of amphotericin B, lipid formulations of amphotericin B and/or itraconazole, and as empirical therapy for presumed fungal infections (such as *Candida* or *Aspergillus*) in febrile, neutropenic adult or paediatric patients.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Cancidas, (a) centrally authorised medicine(s) containing caspofungin, and nationally authorised medicines containing caspofungin 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 caspofungin-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding the possibility of reduced caspofungin efficacy in patients undergoing continuous renal replacement therapy using polyacrylonitrile-derived membranes. Therefore, the current terms of the marketing authorisations should be varied[18].
- In the next PSUR, the MAH should continue to closely monitor cases of the following: severe cutaneous adverse reactions (SCARs) including drug reaction with eosinophilia and systemic symptoms (DRESS), cutaneous calcification, and lack of efficacy of caspofungin in renal replacement therapy (RRT).

PRAC agreed to the dissemination of a direct healthcare professional communication (DHPC) along with a communication plan about the potential for reduced efficacy of caspofungin in patients undergoing continuous RRT with polyacrylonitrile-derived membranes. The DHPC should be disseminated in Member States where caspofungin is currently on the market and polyacrylonitrile membrane is available.

[18] Update of SmPC section 4.4. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.

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

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

See also Annex I 16.2.1.

6.3.1. Botulinum neurotoxin type a (150 kd) free from complexing proteins (NAP) – EMA/PSUR/0000269022

Applicants: various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00009084/202412)

Background

Botulinum neurotoxin type a (150 kd) free from complexing proteins is a skeletal muscle relaxant and neuromuscular blocking agent, indicated for the symptomatic treatment in adults of blepharospasm and hemifacial spasm, cervical dystonia of a predominantly rotational form (spasmodic torticollis), spasticity of the upper limb, chronic sialorrhea due to neurological disorders, and in children and adolescents aged 2 to 17 years and weighing ≥ 12kg of chronic sialorrhea due to neurological/neurodevelopmental disorders. In addition, it is indicated for the temporary improvement in the appearance of upper facial lines in adults below 65 years when the severity of these lines has an important psychological impact for the patient: moderate to severe vertical lines between the eyebrows seen at maximum frown (glabellar frown lines), and/or moderate to severe lateral periorbital lines seen at maximum smile (crow's feet lines), and/or moderate to severe horizontal forehead lines seen at maximum contraction, as warranted.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing botulinum neurotoxin type a (150 kd) free from complexing proteins 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 botulinum neurotoxin type a (150 kd) free from complexing proteins-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add a warning that cases of iatrogenic botulism have been reported following injection of botulinum toxin products and action for patients and caregivers to take in the event of signs or symptoms consistent with spread of botulinum toxin effect. In addition, the PI should be updated to amend the existing warning on measures in cases of overdose in order to include management where the spread of toxin is suspected. Therefore, the current terms of the marketing authorisation(s) should be varied[19].

[19] Update of SmPC sections 4.4 and 4.9. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.

- In the next PSUR, the MAHs should provide a cumulative review on the use of botulinum toxin products during pregnancy, including all available data from all sources (clinical trials, literature, post-marketing setting) on pregnancy outcomes in women treated with botulinum toxin products during pregnancy taking also into consideration pregnancy outcomes in women suffering from foodborne or contamination-related botulism during pregnancy, as well as relevant data on botulinum toxin in breast milk. In addition, the MAHs should discuss the need to update the PI, as warranted. The MAHs should also closely monitor the effects of botulinum neurotoxin type a (150 kd) free from complexing proteins on bone health.

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

6.3.2. Botulinum toxin a (except for centrally authorised products) (NAP) – EMA/PSUR/0000268948

Applicants: various

PRAC Lead: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00000426/202412)

Background

Botulinum toxin a (except for centrally authorised products) is a skeletal muscle relaxant and neuromuscular blocking agent, indicated for the treatment of neurologic disorders (focal spasticity of the ankle and foot in ambulant paediatric cerebral palsy patients two years of age or older as an adjunct to rehabilitative therapy, focal spasticity of the wrist and hand in adult post stroke patients, focal spasticity of the ankle and foot in adult post stroke patients, blepharospasm, hemifacial spasm and associated focal dystonias, cervical dystonia (spasmodic torticollis), symptom relief in adults fulfilling criteria for chronic migraine in patients who have responded inadequately or are intolerant of prophylactic migraine medications), bladder disorders (idiopathic overactive bladder with symptoms of urinary incontinence, urgency and frequency in adult patients who have an inadequate response to, or are intolerant of, anticholinergic medication; urinary incontinence in adults with neurogenic detrusor overactivity resulting from neurogenic bladder due to stable sub-cervical spinal cord injury, or multiple sclerosis), and skin and skin appendage disorder (persistent severe primary hyperhidrosis of the axillae, which interferes with the activities of daily living and is resistant to topical treatment). In addition, it is indicated for the temporary improvement in the appearance of moderate to severe vertical lines between the eyebrows seen at maximum frown (glabellar lines) and/or, moderate to severe lateral canthal lines (crow’s feet lines) seen at maximum smile and/or, moderate to severe forehead lines seen at maximum eyebrow elevation, when the severity of the facial lines has an important psychological impact in adult patients, as warranted.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing botulinum toxin a (except for centrally authorised products) 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 botulinum toxin a (except for centrally authorised products)-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add a warning that cases of iatrogenic botulism have been reported following injection of botulinum toxin products and action for patients and caregivers to take in the event of signs or symptoms consistent with spread of botulinum toxin effect. In addition, the PI should be updated to amend the existing warning on measures in cases of overdose in order to include management where the spread of toxin is suspected. Therefore, the current terms of the marketing authorisation(s) should be varied[20].
- In the next PSUR, the MAHs should provide a cumulative review on the use of botulinum toxin products during pregnancy, including all available data from all sources (clinical trials, literature, post-marketing setting) on pregnancy outcomes in women treated with botulinum toxin products during pregnancy taking also into consideration pregnancy outcomes in women suffering from foodborne or contamination-related botulism during pregnancy, as well as relevant data on botulinum toxin in breast milk. In addition, the MAHs should discuss the need to update the PI, as warranted. The MAH AbbVie should continue close monitoring on bone and muscle health (muscle atrophy and fibrosis) cases, while the MAH Croma should also include possible distance spread of toxin (PDSOT) as a safety concern for the purposes of the PSUR.

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

6.3.3. Botulinum toxin a-haemagglutinin complex (NAP) – EMA/PSUR/0000268981

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00000427/202412)

Background

Botulinum toxin a-haemagglutinin complex is a is a skeletal muscle relaxant and neuromuscular blocking agent indicated for the symptomatic treatment of focal spasticity of upper limbs in adults, lower limbs in adults affecting the ankle joint, dynamic equinus foot deformity in ambulant paediatric cerebral palsy patients, two years of age or older, upper limbs in paediatric cerebral palsy patients, two years of age or older, for the management of urinary incontinence in adults with neurogenic detrusor overactivity due to spinal cord injury (traumatic or non-traumatic) or multiple sclerosis, who are regularly performing clean intermittent catheterisation, in adults for symptomatic treatment of spasmodic torticollis, blepharospasm, hemifacial spasm, and severe primary hyperhidrosis of the axillae, which does not respond to topical treatment with antiperspirants or antihidrotics, as warranted.

[20] Update of SmPC sections 4.4 and 4.9. 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 botulinum toxin a-haemagglutinin complex 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 botulinum toxin a-haemagglutinin complex-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 provide an updated cumulative review on the use of botulinum toxin products during pregnancy, including all available data from all sources (clinical trials, literature, post-marketing setting) on pregnancy outcomes in women treated with botulinum toxin products during pregnancy taking also into consideration pregnancy outcomes in women suffering from foodborne or contamination-related botulism during pregnancy, as well as relevant data on botulinum toxin in breast milk. In addition, the MAHs should discuss the need to update the product information (PI), as warranted. In addition, the MAHs should provide an update of cases of iatrogenic botulism and propose an update to the PI as per the PRAC recommendations for other botulinum toxins (see section 6.3.1 *Botulinum neurotoxin type a (150 kd) free from complexing proteins (NAP) – EMA/PSUR/0000269022* and section 6.3.2 *Botulinum toxin a (except for centrally authorised products) (NAP) – EMA/PSUR/0000268948*).

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

6.3.4. Bupropion (NAP) – EMA/PSUR/0000268977

Applicants: various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000461/202412)

Background

Bupropion is a selective norepinephrine–dopamine reuptake inhibitor (NDRI) antidepressant, indicated for the treatment of major depressive disorder (MDD) and of nicotine dependence as an aid to smoking cessation, as warranted.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing bupropion 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 bupropion-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning on hypersensitivity and add a warning regarding severe cutaneous adverse reactions (SCARs), as well as to add toxic epidermal necrolysis and drug reaction with eosinophilia

and systemic symptoms (DRESS) as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[21].

- In the next PSUR, the MAHs should provide a cumulative review of the overdose symptom of seizure cases, and continue to closely monitor cases of pulmonary hypertension and cardiac valve disorders.

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

6.3.5. Ciclosporin (systemic use) (NAP) – EMA/PSUR/0000269012

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00000745/202412)

Background

Ciclosporin (systemic use) is an immunosuppressive agent indicated for the following, as warranted: transplant indications include solid organ transplantation (prevention of graft rejection following kidney, liver, heart, combined heart-lung, lung or pancreas allogeneic transplantation and treatment of transplant rejection in patients previously receiving other immunosuppressive agents) and bone marrow transplantation (prevention of graft rejection following bone marrow transplantation, prevention or treatment of graft-versus-host disease (GVHD)), as well as non-transplantation indications like endogenous uveitis, nephrotic syndrome, rheumatoid arthritis, psoriasis and atopic dermatitis.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing ciclosporin (systemic use) 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 ciclosporin (systemic use)-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to amend the existing warning on breastfeeding. Therefore, the current terms of the marketing authorisation(s) should be varied[22].
- In the next PSUR, the MAHs should provide a cumulative review of cases of hyponatremia including any relevant literature articles, and to discuss any need to update the PI, as warranted.
- The MAH Teva is requested to submit, in the next RMP update, a variation to the relevant national competent authorities, to update the list of safety concerns and to remove the risks that are considered well characterized.

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

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. Dexketoprofen / tramadol (NAP) – EMA/PSUR/0000268986

Applicants: various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure (PSUSA/00010468/202501)

Background

Dexketoprofen/tramadol is a combination of a non-opioid analgesic and an opioid analgesic respectively, indicated for the treatment of the symptomatic short-term treatment of moderate to severe acute pain in adult patients whose pain is considered to require this combination.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing dexketoprofen/tramadol 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 dexketoprofen/tramadol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to reinforce the labelling on the risk of drug dependency/drug abuse (including a black box warning), to add the interactions with gabapentinoids, to add Kounis syndrome as a warning and an undesirable effect with a frequency 'not known', and fixed drug eruption as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[23].
- In the next PSUR, the MAHs should continue following any fatal cases, continue close monitoring of DRESS, cardiovascular and cerebrovascular adverse events, as well as sexual dysfunction. In addition, the MAHs should consider foetal toxicity as a risk to be followed in the PSURs.

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

6.3.7. Disodium hydrogen phosphate / sodium dihydrogen phosphate, phosphate sodium (NAP) – EMA/PSUR/0000268965

Applicants: various

PRAC Lead: Guðrún Stefánsdóttir

Scope: Evaluation of a PSUSA procedure (PSUSA/00002737/202501)

[23] 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.

Background

Disodium hydrogen phosphate/sodium dihydrogen phosphate, phosphate sodium is an osmotic laxative, indicated for constipation and for bowel evacuation before radiological exams or other diagnostic tests.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing disodium hydrogen phosphate/sodium dihydrogen phosphate, phosphate sodium 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 disodium hydrogen phosphate/sodium dihydrogen phosphate, phosphate sodium-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) of medicinal products Phospholax (disodium phosphate/sodium dyhidrogen phosphate) and Clisma Lax (sodium dihydrogen phosphate/disodium phosphate) should be maintained.
- Nevertheless, the product information of medicinal product Enemac (disodium phosphate heptahydrate/sodium dihydrogen phosphate monohydrate) should be updated to add a warning regarding the risk of elevated levels of sodium and phosphate in blood and diminished levels of calcium and potassium, and to add 'hyperphosphatemia, hypokalemia, hypernatremia, hypocalcemia and calcification of tissues' as an undesirable effect with a frequency 'rare'. Therefore, the current terms of the marketing authorisation(s) should be varied[24].

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. Levamisole (NAP) – EMA/PSUR/0000268962

Applicants: various

PRAC Lead: Roxana Dondera

Scope: Evaluation of a PSUSA procedure (PSUSA/00001845/202501)

Background

Levamisole is an anthelmintic and it is indicated in adults and children for the treatment of infections caused by the following parasitic worms: *Ascaris lumbricoides, Necator americanus, Ancylostoma duodenale, Strongyloides stercoralis and Trichostrongylus colubriformis.*

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing levamisole and issued a recommendation on their marketing authorisation(s) (see also PRAC minutes July 2025).

Summary of recommendation(s) and conclusions

[24] 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 levamisole-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- The above is without prejudice to a thorough review of levamisole-containing products within the ongoing referral procedure under Article 31 of Directive 2001/83/EC (EMA/REF/0000293746) to assess all available data and determine the impact of the new safety concerns on the benefit-risk balance of levamisole. Refer also to section 3.1.1 *Levamisole (NAP) – EMA/REF/0000293746*.
- In the next PSUR, the MAHs should provide information (PI) on the levamisole use in paediatric nephrotic syndrome, in colon cancer, recurrent aphthous ulcer and other product usage identified by the MAHs beyond the authorised indications, including a discussion on safety concerns associated with off-label use. In addition, the MAHs should present cases reported under SMQ Drug Abuse and Dependence (Narrow) and associated safety concerns, with fatal cases to be discussed separately. The MAHs should propose adequate risk minimisation measures, as warranted. Furthermore, the MAHs should provide a cumulative review of cases of angioedema and toxic epidermal necrolysis/severe cutaneous adverse reactions (SCARs) and discuss the need to update the PI as warranted.

The frequency of PSUR submission should be revised from ten-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.

6.3.9. Niflumic acid (NAP) – EMA/PSUR/0000268983

Applicants: various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00002157/202412)

Background

Niflumic acid is a non-steroidal anti-inflammatory drugs (NSAIDs), indicated for the treatment of adults and children over 12 years of age for short-term symptomatic relief of pain due to acute episodes of arthritis and non-articular rheumatism (e.g. tendinitis, bursitis), immediate treatment of pain during menstruation (dysmenorrhea) and inflammatory conditions in the field of ear-nose-throat (ENT) and stomatology (oral formulation). In addition, it is indicated as a long-term symptomatic relief of pain due to chronic, inflammatory rheumatic disorders (e.g. rheumatoid arthritis) (oral formulation) and as a short-term symptomatic relief of pain due to superficial tendinitis, sprains and contusions (topical formulation).

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

- Nevertheless, the product information should be updated to add a contraindication on the use of topical niflumic acid in third trimester of pregnancy and a warning about the risk of use in the first two trimesters. Therefore, the current terms of the marketing authorisation(s) should be varied[25].

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

6.3.10. Testosterone (all formulations apart from topical use) (NAP) – EMA/PSUR/0000269018

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00010631/202412)

Background

Testosterone (all formulations apart from topical use) is an androgen, anabolic steroid indicated for testosterone replacement therapy for male hypogonadism.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing testosterone (all formulations apart from topical use) 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 testosterone (all formulations apart from topical use)-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information of oil-based solutions should be updated to add pulmonary oil microembolism (POME) as a warning and an undesirable effect with a frequency 'rare', to add an interaction with sodium-glucose co-transporter 2 (SGLT-2) inhibitors and increase of haemoglobin and haematocrit levels. Therefore, the current terms of the marketing authorisation(s) should be varied[26].
- In the next PSUR, the MAHs provide cumulative reviews of cases of tendinopathies and ligament disorders (SMQ) and fracture risk, of acute kidney injury and of intracranial hypertension. The MAH(s) should also include pulmonary microembolism (POME) and thromboembolic risk secondary to haematocrit increase as important identified risks in the PSUR safety concerns. The MAH(s) with an RMP in place and with risk minimisation measures (aRMM) for POME should also review the effectiveness of the aRMM for POME and discuss the added benefit of maintaining the aRMMs. Finally, the MAHs should provide a review of usage/indications and safety profile of testosterone in women (XX genotype), including off-label use cases relevant to the SOCs 'cardiac disorders' and 'vascular disorders', as well as to discuss the relevant published literature including the

[25] Update of SmPC sections 4.3 and 4.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.
[26] 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.

studies by *Yelehe et al., 2022*[27] and *Coleman et al, 2022*[28] and any appropriate preventive and risk management measures, 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.

6.3.11. Testosterone (topical use) (NAP) – EMA/PSUR/0000268995

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00002908/202412)

Background

Testosterone (topical use) is an androgen, anabolic steroid indicated for testosterone replacement therapy for male hypogonadism.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing testosterone (topical use) 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 testosterone (topical use)-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add an interaction with sodium-glucose co-transporter 2 (SGLT-2) inhibitors and increase of haemoglobin and haematocrit levels. In addition, PRAC adopted, by majority, a recommendation to update the PI to amend a warning regarding actions following administration to prevent accidental transfer to pets; twenty-six members voted in favour of the recommendation whilst eight members[29] had a divergent view. The Icelandic and Norwegian PRAC members agreed with the recommendation. Therefore, the current terms of the marketing authorisation(s) should be varied[30].
- In the next PSUR, the MAHs provide cumulative reviews of cases of tendinopathies and ligament disorders (SMQ) and fracture risk, of acute kidney injury and of intracranial hypertension. The MAH(s) should provide a review of usage/indications and safety profile of testosterone in women (XX genotype), including off-label use cases relevant to the SOCs 'cardiac disorders' and 'vascular disorders', as well as to discuss the relevant

[27] Yelehe M, Klein M, El Aridi L, Maurier A, Gillet P, Feigerlova E. Adverse effects of gender-affirming hormonal therapy in transgender persons: Assessing reports in the French pharmacovigilance database. Fundam Clin Pharmacol. 2022 Dec;36(6):1115-1124. doi: 10.1111/fcp.12806

[28] Coleman, E., Radix, A. E., Bouman, W. P., Brown, G. R., de Vries, A. L. C., Deutsch, M. B. et al. (2022). Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. International Journal of Transgender Health, 23(sup1), S1–S259. https://doi.org/10.1080/26895269.2022.2100644

[29] Liana Martirosyan, Gabriele Maurer, Amelia Cupelli, Jean-Michel Dogné, Elena Kaisis, Ana Sofia Diniz Martins, Maria del Pilar Rayon, Yiannoula Koulla

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

published literature including the studies by *Yelehe et al., 2022*[31] and *Coleman et al, 2022*[32] and any appropriate preventive and risk management measures, 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

See Annex I 16.4.

6.5. Variation procedure(s) resulting from PSUSA evaluation

None

6.6. Expedited summary safety reviews[33]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[34]

See also Annex I 17.1.

7.1.1. rADAMTS13 – ADZYNMA (CAP) – EMA/PASS/0000253115

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Maia Uusküla

Scope: PASS 107n [PASS protocol]: A Post-Authorization Safety Study (PASS) to Further Evaluate Real-World Safety in Patients with Congenital Thrombotic Thrombocytopenic Purpura (cTTP) Treated with Adzynma

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 establishment of a PASS to be performed with Adzynma (rADAMTS13), was presented for review by PRAC. For further background, see PRAC minutes April 2025.

Endorsement/Refusal of the protocol

[31] Yelehe M, Klein M, El Aridi L, Maurier A, Gillet P, Feigerlova E. Adverse effects of gender-affirming hormonal therapy in transgender persons: Assessing reports in the French pharmacovigilance database. Fundam Clin Pharmacol. 2022 Dec;36(6):1115-1124. doi: 10.1111/fcp.12806

[32] Coleman, E., Radix, A. E., Bouman, W. P., Brown, G. R., de Vries, A. L. C., Deutsch, M. B. et al. (2022). Standards of Care for the Health of Transgender and Gender Diverse People, Version 8. International Journal of Transgender Health, 23(sup1), S1–S259. https://doi.org/10.1080/26895269.2022.2100644

[33] 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

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

- Based on the PRAC review of the PASS protocol version "Amendment 1" and in accordance with Article 107n(2)(a) of Directive 2001/83/EC, PRAC considers by consensus that the study is non-interventional and the PASS protocol for Adzynma (rADAMTS13) can be endorsed.

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[35]

See Annex I 17.1.1.

7.3. Results of PASS imposed in the marketing authorisation(s)[36]

See also Annex I 17.2.1.

7.3.1. Pitolisant – WAKIX (CAP) – EMA/PASS/0000281790

Applicant: Bioprojet Pharma

PRAC Rapporteur: Terhi Lehtinen

Scope: PASS results[107q]: A 5-year multi-center, observational PASS to document the utilisation of Wakix in the treatment of narcolepsy with or without cataplexy and to collect information on its long-term safety when used in routine medical practice.

Background

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

In order to fulfil the obligation to submit the results of an imposed non-interventional PASS in accordance with Article 107p of Directive 2001/83/EC, the MAH submitted on 13 June 2025 a PASS final study report for Wakix (pitolisant).

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 the benefit-risk balance of Wakix (pitolisant) remains unchanged. As a consequence, PRAC recommended that the terms of the marketing authorisation(s) for Wakix (pitolisant) should be varied to remove the PASS as an obligation 'to perform a post authorisation safety study (PASS) to assess the long term safety' from the 'conditions or restrictions with regard to the safe and effective use of the medicinal product'.

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

See also Annex I 17.3.1.

[35] 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
[36] In accordance with Article 107p-q of Directive 2001/83/EC
[37] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.4.1. 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' (HCP) 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.

Summary of advice

- Based on the available data and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be considered acceptable provided that the MAH submits satisfactory responses to a request for supplementary information (RSI).
- PRAC considered that study CBYL719C2005 could be considered completed and therefore can be removed from the RMP. However, PRAC agreed that the HCP educational materials should be maintained in the RMP as additional RMM, as well as in Annex II-D.

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

See Annex I 17.4.1.

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 18.2.1.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

Information related to this section cannot be released at the present time as it is deemed to

contain commercially confidential information.

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Carbamazepine (NAP) - DE/H/xxxx/WS/1998

Applicant: Novartis Pharma GmbH (Tegretal/Tegretol 100 mg/5 ml oral suspension)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a worksharing variation to update the product information (PI) of Tegretal/Tegretol oral suspension to restrict its use in newborns below 4 weeks of age in line with the core data sheet (CDS) version 3.2, on request of Germany

Background

Carbamazepine is an anticonvulsant indicated for the treatment of epilepsy, the paroxysmal pain of trigeminal neuralgia and for the prophylaxis of manic-depressive psychosis in patients unresponsive to lithium therapy.

In the context of the evaluation of a worksharing variation procedure on updating the PI of Tegretal/Tegretol oral suspension to restrict its use in newborns below 4 weeks of age, Germany requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC agreed that the product information of Tegretal/Tegretol oral Suspension (100 mg/5 ml) should be updated[38] to reflect the potential risk of increased exposure of propylene glycol or other alcohols following treatment in neonatal patients below 4 weeks of age, to introduce the relevant contraindication and warning. In addition, PRAC agreed with the direct healthcare professional communication (DHPC) letter and a communication plan to inform about this risk and restriction in use of the product.

11.1.2. Tofacitinib (NAP) - DE/H/8402/001-002/DC

PRAC Lead: Martin Huber

Scope: PRAC consultation on the evaluation of initial marketing authorisation applications (MAAs) under the decentralised procedure (DCP) for a generic medicinal product on request of Germany

Background

Tofacitinib is a selective inhibitor of the Janus kinase (JAK) family of kinases, indicated in combination with methotrexate (MTX) for the treatment of: moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying antirheumatic drugs (DMARDs), of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have

[38] Update of SmPC sections 4.3 and 4.4. The package leaflet to be updated accordingly.

been intolerant to a prior DMARD therapy. In addition, it is indicated for the treatment of adult patients with active ankylosing spondylitis (AS) who have responded inadequately to conventional therapy, with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent, and for the treatment of active polyarticular juvenile idiopathic arthritis (rheumatoid factor positive [RF+] or negative [RF-] polyarthritis and extended oligoarthritis), and juvenile psoriatic arthritis (PsA) in patients 2 years of age and older, who have responded inadequately to previous therapy with DMARDs.

In the context of the evaluation of initial MAAs under DCP, Germany requested PRAC advice on its assessment.

11.1.3. Valproate and related substances (NAP) - NL/H/xxxx/WS/988

Applicant: Sanofi B.V. (Depakine)

PRAC Lead: Liana Martirosyan

Scope: PRAC consultation on a worksharing variation to update the product information (PI) and the educational materials (healthcare professionals and patient guides) regarding the risk of being born small for gestational age (SGA) after in utero exposure, on request of The Netherlands

Background

Valproate and related substances (valproic acid, sodium valproate, valproate pivoxil, magnesium valproate, valproate semisodium, valproate bismuth, calcium valproate and valpromide) are indicated to treat epilepsy, bipolar disorders (BP) and, in some EU member states (MS), also indicated in the prophylaxis of migraine attacks.

In the context of the evaluation of a worksharing type II variation procedure on updating the PI and educational materials, The Netherlands requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC agreed on the proposed update of the product information to reflect the current scientific knowledge regarding SGA[39]. However, PRAC did not support an update of the conditions of the existing pregnancy prevention programme (PPP) with information on 'lower weight at birth for the gestational age', as the PPP should focus on the most important and serious risks observed during pregnancy, i.e. teratogenicity and neurodevelopmental disorders (NDD), and considering that the addition of information on less serious risks that generally not require a PPP would dilute the information for the risk that the PPP has been implemented. In addition, PRAC did not consider as risk proportionate to include information on SGA on the annual risk acknowledgment form (ARAF) for female patients that would warrant yearly discussions on this topic during annual reassessment, as SGA is not a risk that would generally require such measure, and this risk can be sufficiently minimized by routine risk minimisation measures (RMMs). However, since additional RMMs addressing risks in pregnancy are already in place for valproate, PRAC considered acceptable to reflect information on the risk of SGA in the core versions of the healthcare professional guide and patient guide for female patients, as these documents provide further background information on the risks associated with valproate exposure

[39] Update of SmPC section 4.6. The package leaflet to be updated accordingly.

during pregnancy, and background sections of these documents generally include the same (more detailed) information as reflected in the agreed updated product information.

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The PRAC Chair thanked Monica Martinez Redondo for her contribution as the alternate for Spain.

12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q2 2025

In line with the adopted PRAC best practice guidance (BPG) on Committee efficiency (see PRAC minutes May 2016 and PRAC minutes June 2018) and the adopted implementation plan for the BPG including goals to measure compliance with the recommendations (see PRAC minutes June 2016 and PRAC minutes June 2018), PRAC was informed on the quantitative measures collected for Q2 2025 of PRAC meetings.

12.1.3. Vote by proxy

None

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Healthcare Professionals Working Party (HCPWP) and Patients and Consumers Working Party (PCWP) - Nomination of PRAC representative(s)

PRAC lead: Ulla Wändel Liminga

Following a call for nomination of PRAC representatives for the PCWP and the HCPWP for a new three-year mandate, Roberto Frontini and Martin Votava were appointed as healthcare professional (HCP) PRAC representatives (as member and alternate, respectively) and Yiannoula Koulla was appointed as Patient PRAC Representative (as member) within the PCWP.

12.3.2. Summary of Product Characteristics Advisory Group (SmPC AG) – Nomination of PRAC Representative(s)

Following a call for expression of interest for a PRAC representative in the SmPC AG, PRAC endorsed the nomination of Amelia Cupelli.

12.4. Cooperation within the EU regulatory network

12.4.1. European Shortages Monitoring Platform overview for National Competent Authorities (NCAs)

The EMA Secretariat presented to PRAC an overview of the European Shortages Monitoring Platform (ESMP), including its objectives and key benefits it brings to the medicines network and public health. The presentation also emphasised the pivotal role played by NCAs as both contributors to and users of the ESMP. PRAC noted the information.

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2025 - update

PRAC lead: Ulla Wändel Liminga, Liana Martirosyan

The EMA Secretariat presented to PRAC a mid-year status update on the activities described in the PRAC work plan 2025. PRAC will initiate its work plan for 2026 taking into account the activities completed, progress made, priorities identified at the level of the Committee, EMA, Heads of Medicines Agencies (HMA) and the EU network.

12.8. Planning and reporting

12.8.1. PRAC workload statistics – Q2 2025

The EMA secretariat informed PRAC about the quarterly and cumulative figures to estimate the evolution of the PRAC workload for Q2 2025, by reflecting on the number of procedures and agenda items covered at each PRAC plenary meeting.

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. PSURs repository

None

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

Post-meeting note: following the PRAC meeting of September 2025, the updated EURD list was adopted by CHMP and CMDh at their September 2025 meetings and published on the EMA website, see: https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/pharmacovigilance-post-authorisation/periodic-safety-update-reports-psurs

12.11. Signal management

None

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

The PRAC was informed of 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: List of medicines under additional monitoring | European Medicines Agency (EMA)

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. Reflection Paper on Patient Experience Data (PED)

PRAC lead: Ulla Wändel Liminga, Carla Torre

The EMA Secretariat presented to PRAC the final draft reflection paper on PED, prior to the launch of public consultation. The reflection paper provides a framework for discussion on patient experience data, including on the types and sources of PED, and elaborates on the use and value of PED across the medicine lifecycle. It ultimately encourages stakeholders to embed PED across all stages of medicine development, including during safety monitoring. The document has been prepared and reviewed by a large multidisciplinary drafting group, including representatives from PRAC, CHMP and several working parties. PRAC endorsed the draft reflection paper.

13. Any other business

None

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

As per the agreed criteria for new signal(s), PRAC adopted without further plenary discussion the recommendation of the Rapporteur to request MAH(s) to submit a cumulative review following standard timetables[41].

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Cefazolin (NAP); cefazolin, lidocaine hydrochloride (NAP)

Applicant(s): various

PRAC Rapporteur: Sonja Radowan

Scope: Signal of Kounis syndrome

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

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

EPITT 20204 – New signal

Lead Member State: AT

14.1.2. Erdafitinib - BALVERSA (CAP)

Applicant: Janssen Cilag International

PRAC Rapporteur: Bianca Mulder

Scope: Signal of growth accelerated

EPITT 20194 – New signal

Lead Member State: NL

14.1.3. Galantamine (NAP)

Applicant(s): various

PRAC Rapporteur: Karin Bolin

Scope: Signal of nightmares

EPITT 20196 – New signal

Lead Member State: SE

14.1.4. Mepolizumab – NUCALA (CAP)

Applicant: GlaxoSmithKline Trading Services

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of alopecia

EPITT 20197 – New signal

Lead Member State: DE

14.1.5. Pegylated liposomal doxorubicin – CAELYX PEGYLATED LIPOSOMAL (CAP); CELDOXOME PEGYLATED LIPOSOMAL (CAP); ZOLSKETIL PEGYLATED LIPOSOMAL (CAP); NAP

Applicants: Accord Healthcare S.L.U. (Zolsketil pegylated liposomal), Baxter Holding B.V. (Caelyx pegylated liposomal, Celdoxome pegylated liposomal), various

PRAC Rapporteur: Eva Jirsová

Scope: Signal of renal-limited thrombotic microangiopathy

EPITT 20193 – New signal

Lead Member State: CZ

14.1.6. Pemetrexed – ALIMTA (CAP); ARMISARTE (CAP); PEMETREXED ACCORD (CAP); PEMETREXED FRESENUIS KABI (CAP); PEMETREXED MEDAC (CAP); PEMETREXED PFIZER (CAP); NAP

Applicants: Accord Healthcare S.L.U. (Pemetrexed accord), Actavis Group Ptc ehf. (Armisarte), Eli Lilly Nederland B.V. (Alimta), Fresenius Kabi Deutschland GmbH (Pemetrexed fresenuis kabi), Medac Gesellschaft für klinische Spezialpräparate mbH (Pemetrexed medac), Pfizer Europe MA EEIG (Pemetrexed pfizer), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Signal of lupus erythematosus

EPITT 20185 – New signal

Lead Member State: FR

14.1.7. Risankizumab – SKYRIZI (CAP)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of pemphigoid

EPITT 20192 – New signal

Lead Member State: NL

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. Autologous CD34+ haematopoietic stem cells transduced ex vivo with a lentiviral vector encoding human Wiskott-Aldrich syndrome protein - (CAP MAA) - EMEA/H/C/006525, Orphan

Applicant: Fondazione Telethon Ets, ATMP

Scope (pre D-180 phase): Treatment of patients with Wiskott-Aldrich Syndrome (WAS)

15.1.2. Denosumab - (CAP MAA) - EMEA/H/C/006492

Scope (pre D-180 phase): Treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures, treatment of bone loss associated with hormone ablation in

men with prostate cancer and treatment of bone loss associated with long-term systemic glucocorticoid therapy in adult patients

15.1.3. Denosumab - (CAP MAA) - EMEA/H/C/006797

Scope: Treatment of osteoporosis and bone loss

15.1.4. Insulin glargine - (CAP MAA) - EMEA/H/C/006136

Scope (pre D-180 phase): Treatment of diabetes mellitus

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. Aripiprazole - ARIPIPRAZOLE SANDOZ (CAP) - EMA/VR/0000272677; NAP

Applicant(s): Sandoz GmbH, various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: To update the RMP in line with the reference product of Aripiprazole Sandoz. In addition, the MAH has taken the opportunity to include the 20 mg tablets to the RMP in line with the approved SmPC and to reflect the change in MAH.

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

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Karin Erneholm

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

15.2.3. Darbepoetin alfa – ARANESP (CAP) – EMA/VR/0000267359

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 10.0 in order to remove the safety concern and risk minimisation measures regarding the 'Incorrect Use of the Pre-filled Pen Device Associated with Adverse Reactions, Including Underdose and Drug Dose Omission'. The Annex II is updated accordingly.

15.2.4. Denosumab – XGEVA (CAP) – EMA/VR/0000272344

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of an updated RMP version 37.0 in order to modify and update the list of safety concerns based on previously completed post-authorization safety studies, including registry study 20101102 and the long-term safety follow-up study 20140114.

15.2.5. Dolutegravir – TIVICAY (CAP); Dolutegravir / Abacavir / Lamivudine - TRIUMEQ (CAP); Dolutegravir / Lamivudine - DOVATO (CAP); Dolutegravir / Rilpivirine – JULUCA (CAP) - EMA/VR/0000278110

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: To update the RMP with the latest available post-authorisation exposure data and to include the 2024 Antiretroviral Pregnancy Registry data. To update the submission date for the final CSR for category 3 PASS study DOLOMITE-NEAT ID (208759) from 30 September 2025 to 30 September 2026 for Tivicay, Triumeq and Juluca.

15.2.6. Emtricitabine / Tenofovir disoproxil – TRUVADA (CAP) – EMA/VR/0000280828

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: A grouped application consisting of:

C.I.11: Submission of an updated RMP version 19.1 in order to remove targeted questionnaires (related to TDF) concerning (1) Renal events including tubulopathy, and (2) Bone events due to proximal renal tubulopathy/loss of BMD.

C.I.11: Submission of an updated RMP version 19.1 in order to remove missing information concerning Safety in pregnancy and lactation (related to TDF), and consequently remove 'Antiretroviral Pregnancy Registry' listed as a Category 3 Additional Pharmacovigilance Activity.

15.2.7. Fingolimod – FINGOLIMOD MYLAN (CAP) - EMA/VR/0000280709; NAP

Applicant(s): Mylan Pharmaceuticals Limited, various

PRAC Rapporteur: Tiphaine Vaillant

Scope: C.I.11.z - to implement changes to the Risk Management Plans for Fingolimod Mylan and Mulfiyna, following relevant updates to the Risk Management Plan of the innovator product Gilenya (Novartis Europharm Limited, EMEA/H/C/002202).

15.2.8. Idursulfase – ELAPRASE (CAP) – EMA/VR/0000279282

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of an updated RMP version 5.2 in order to reflect the completion of the Hunter Outcome Survey (HOS) study following procedure EMEA/H/C/PSUSA/00001722/202407; update the exposure data with information from the

ongoing study SHP-ELA-401; include template updates; remove all safety concerns, including missing information, in alignment with GVP Module V, Revision 2.

15.2.9. Pegfilgrastim – NEULASTA (CAP) – EMA/VR/0000274974

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an updated RMP version 11.0 in order to remove of Sickle cell crisis in patients with sickle cell disease and Glomerulonephritis as important identified risks.

15.2.10. Pregabalin – PREGABALIN SANDOZ (CAP) – EMA/VR/0000273334; NAP

Applicant(s): Hexal AG, various

PRAC Rapporteur: Liana Martirosyan

Scope: To align the RMP to the currently approved RMP of the reference product, e.g. removing the important identified risk of "Abuse and drug dependence".

15.2.11. Romiplostim – NPLATE (CAP) – EMA/VR/0000276333

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Monica Martinez Redondo

Scope: Update of section 4.8 of the SmPC in order to remove language regarding the testing for suspected neutralizing antibodies (Immunogenicity) following RMP update in EMEA/H/C/000942/II/0091.

15.2.12. Tenofovir disoproxil – VIREAD (CAP) – EMA/VR/0000280825

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Zoubida Amimour

Scope: Submission of an updated RMP version 26.2 in order to remove missing information concerning Safety in pregnancy and lactation, to remove 'Antiretroviral Pregnancy Registry' listed as a Category 3 Additional Pharmacovigilance Activity, and to implement PRAC agreed changes during procedure EMEA/H/C/PSUSA/00002892/202303 in relation to safety concerns associated with renal and bone adverse events.

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

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

15.3.1. Adalimumab - IDACIO (CAP) - EMEA/H/C/004475/II/0024/G

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Karin Bolin

Scope: Quality

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

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

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

15.3.3. Aflibercept – AHZANTIVE (CAP); BAIAMA (CAP) – EMA/VR/0000255900

Applicant: Formycon AG

PRAC Rapporteur: Zoubida Amimour

Scope: Quality

15.3.4. Aflibercept – OPUVIZ (CAP) – EMA/VR/0000280586

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Quality

15.3.5. Amivantamab – RYBREVANT (CAP) – EMA/X/0000268898

Applicant: Janssen Cilag International

PRAC Rapporteur: Gabriele Maurer

Scope: Extension application to add a new strength of 2400 mg and 3520 mg (solution for injection) grouped with the following variations:

C.I.4: Update of sections 4.2, 4.4, 4.8, 5.1, 5.2, 6.5 and 6.6 in order to include the Q3W dosing regimen based on data from relevant cohorts from the Phase 2 bridging study PALOMA-2 (NSC2002) and supported by data from the Phase 1 PALOMA study (NSC1003). The Package Leaflet and Labelling are updated accordingly. The RMP version 7.1 has also been submitted.

C.I.4: Update of sections 4.2, 4.4, 4.8, 5.1, 5.2, 6.5 and 6.6 in order to introduce a new Q4W dosing regimen based on data from the PALOMA-2 study (NSC2002) and supported by data from the Phase 1 PALOMA study (NSC1003). The Package Leaflet and Labelling are updated accordingly. The RMP version 7.1 has also been submitted.

15.3.6. Anakinra – KINERET (CAP) – EMA/VR/0000249038

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Karin Erneholm

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to include updated information on Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) following post-marketing safety surveillance; the Package Leaflet is updated accordingly. The RMP version 6.3 has also been submitted. In addition, the MAH took the opportunity to correct editorial errors, and to include wording regarding excipient polysorbate 80 in accordance with the updated annex to the European Commission guideline in the PI.

15.3.7. Asciminib – SCEMBLIX (CAP) – EMA/VR/0000280241

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final report from study CABL001A2301 listed as a category 3 study in the RMP; this is a phase 3, multicenter, open-label, randomized study of oral asciminib vs bosutinib in patients with CML-CP previously treated with two or more tyrosine kinase inhibitors. The RMP version 5.0 has also been submitted.

15.3.8. Avapritinib – AYVAKYT (CAP) – EMA/VR/0000275571

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with CYP3A substrates based on the final results from study BLU-285-1107 listed as a category 3 study in the RMP. This is a drug-drug interaction study to investigate the effect of 300 mg once daily avapritinib on the pharmacokinetics (PK) of midazolam in patients with unresectable or metastatic Gastrointestinal Stromal Tumors (GIST) and other Advanced Solid Tumors. The MAH also updated PBPK model to extend the clinical findings of Study BLU-285-1107 and simulate the effects of lower doses of avapritinib on the pharmacokinetics of midazolam and its metabolite. The package leaflet is updated accordingly. 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 version 10.4. The RMP version 5.0 has also been submitted.

15.3.9. Avelumab – BAVENCIO (CAP) – EMA/VR/0000261861

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add "Gastritis" to the list of adverse drug reactions (ADRs) with frequency "Not known" based on postmarketing data and literature. The Package Leaflet is updated accordingly. The RMP version 9.1 has also been submitted.

15.3.10. Budesonide / Formoterol - BIRESP SPIROMAX (CAP) – EMEA/H/C/WS2806/G; Budesonide / Formoterol - DUORESP SPIROMAX (CAP) - EMEA/H/C/WS2806/G

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: A grouped application consisting of:
C.I.6: Extension of the asthma indication to include the anti-inflammatory reliever (AIR) use for DuoResp Spiromax and BiResp Spiromax, based on the latest GINA report, the European Respiratory Society guidelines, and literature data. In addition, the Applicant referred to changes made for Symbicort (UK). As a consequence, sections 4.1, 4.2, 4.4, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI introduced editorial changes, and is brought in line with the latest QRD template version. The RMP version 4.0 has also been submitted.
C.I.2.a: To update sections 4.5, and 5.1 of the SmPC following assessment of the same change for the reference product Symbicort Turbohaler (SE/H/0229/001- 002) and also Symbicort (UK).

15.3.11. Dabrafenib – TAFINLAR (CAP); Trametinib - MEKINIST (CAP) – EMA/VR/0000271728

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of unresectable or metastatic melanoma with a BRAF V600 mutation and adjuvant treatment of Stage III melanoma with a BRAF V600 mutation for adolescents aged 12 years and older for TAFINLAR and MEKINIST, based on an extrapolation report using a modelling and simulation approach to demonstrate PK, PD and efficacy of dabrafenib and trametinib in adolescent patients. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. RMP versions 13.0 and 21.0 for Tafinlar and Mekinist, respectively, have also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI and to update list of local representatives in the Package Leaflet.

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

Applicant: Janssen Cilag International

PRAC Rapporteur: Amelia Cupelli

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

15.3.13. Dengue tetravalent vaccine (live, attenuated) - – DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (CAP); QDENGA (CAP) – EMA/VR/0000266281

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of:

C.I.13: Submission of the interim report from study DEN-301 Part 4 listed as a category 3 study in the RMP, and addressing PAM [MEA] and PAM [REC] #1. This is a phase 3, double-blind, randomized, placebo-controlled trial to investigate the efficacy, safety and immunogenicity of a Tetravalent Dengue Vaccine (TDV) administered subcutaneously in healthy children aged 4 -16 years old, investigating a TDV booster dose in the booster phase (Parts 4 and 5) of the trial. The RMP version 3.1 has also been submitted.

C.I.13: Submission of the final report from study DEN-303 listed as a category 3 study in the RMP, and addressing PAM [MEA], PAM [REC] #1 and PAM [P46]. This is a phase 3, follow-up trial to evaluate long-term safety and antibody persistence, and the impact of a booster dose of a Tetravalent Dengue Vaccine candidate in healthy adolescents and adults in areas non endemic for dengue. The RMP version 3.1 has also been submitted.

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

Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of paediatric population (adolescents aged 12 years and above) for FERACCRU, based on results from phase 1 study ST10-01-103, phase 3 study ST10-01-305 and a supportive phase 1 study ST10-01-104. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 9.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to implement editorial changes to the PI. Furthermore, the PI is brought in line with the latest QRD template version 10.4.

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

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

15.3.16. 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.

15.3.17. Ivacaftor / Tezacaftor / Elexacaftor – KAFTRIO (CAP) – EMA/VR/0000280845

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the 96-weeks of treatment report (Part A) for study VX20-445-112 (Study 112), listed as a category 3 study in the RMP; this is a Phase 3, open-label, extension study evaluating the long-term safety and efficacy of ELX/TEZ/IVA combination therapy in subjects with cystic fibrosis who are 2 years of age and older. The RMP version 10.1 has also been submitted.

15.3.18. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/II/0058, Orphan

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include the treatment of unresectable or metastatic, somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs) in adolescents aged 12 years and older for LUTATHERA based on primary analysis results from study CAAA601A32201 (also referred to as NETTER-P) as well as results from modelling and simulation analysis of PK and dosimetry data of Lutathera in adolescents. NETTER-P study is a Phase II, multicenter open-label study which evaluated the safety and dosimetry of Lutathera in adolescent patients with somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs) and pheochromocytoma and paragangliomas (PPGLs). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 11 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted.

15.3.19. Macitentan / Tadalafil – YUVANCI (CAP) – EMA/VR/0000280219

Applicant: Janssen Cilag International

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 4.8 of the SmPC in order to update safety information based on final results from Phase 3 study AC-077A301 A DUE (Open Label); this is a multi-center, double-blind, randomized, active-controlled, triple-dummy, parallel-group, group-sequential, adaptive study conducted to evaluate the efficacy and safety of Macitentan/Tadalafil Fixed

Dose Combination, versus macitentan or tadalafil monotherapy in participants with PAH. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to update the active metabolite to its INN name throughout the PI.

15.3.20. Maralixibat - LIVMARLI (CAP) - EMEA/H/C/005857/X/0016, Orphan

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to add a new strength (19 mg/ml oral solution). In addition, the MAH took the opportunity to implement editorial changes in sections 4.2 and 4.8. of the SmPC and Point 4 of PL of Livmarli, 9.5 mg/ml oral solution.

15.3.21. Marstacimab – HYMPAVZI (CAP) – EMA/VR/0000268024

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to add information regarding thromboembolic events and to add "thrombosis" to the list of adverse drug reactions (ADRs) with frequency uncommon based on a review of clinical data, post marketing data and literature. The Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes and corrections to the PI, including Annex II.

15.3.22. Mexiletine – NAMUSCLA (CAP) – EMA/X/0000258210

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Extension application to add new strengths of 62 mg and 83 mg grouped with an extension of indication to include the symptomatic treatment of myotonia in children and adolescents (from 6 to 18 years of age) with non-dystrophic myotonic disorders for NAMUSCLA, based on final results from study MEX-NM-301 as well as population pharmacokinetic analysis of mexiletine in healthy volunteers and myotonic patients; MEX-NM-301 is an open-label, multi-centre, single arm, interventional study to describe the steady-state PK, safety, and efficacy of mexiletine in paediatric patients (6 to <18 years of age) with myotonic disorders. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI and update the list of local representatives in the Package Leaflet.

15.3.23. Mitapivat - PYRUKYND (CAP) - EMEA/H/C/005540/X/0010/G, Orphan

Applicant: Agios Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new strength (100 mg film-coated tablet)

associated with a new orphan indication for the "treatment of adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassaemia". The extension application is grouped with a type II variation (C.I.4) to update of sections 4.2 and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from study AG348-C-024 listed as a category 3 study in the RMP; this is a Phase 1, Open-label, Single-dose, Pharmacokinetic Study of Mitapivat in Subjects with Moderate Hepatic Impairment Compared to Matched Healthy Control Subjects with Normal Hepatic Function. The RMP (version 1.1) is updated in accordance.

15.3.24. Mosunetuzumab - LUNSUMIO (CAP) - EMEA/H/C/005680/X/0015, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with two new strengths (5 mg and 45 mg) and new route of administration (subcutaneous use). The RMP (version 3.0) is updated in accordance.

15.3.25. Nivolumab – OPDIVO (CAP) – EMA/VR/0000279319

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 5.1 of the SmPC in order to add the final OS data based on final results from study CA209816. This is a randomized, Open-Label, Phase 3 Trial of Nivolumab plus Ipilimumab or Nivolumab plus Platinum-Doublet Chemotherapy versus Platinum-Doublet Chemotherapy in Early Stage NSCLC. The RMP version 47.0 has also been submitted. In addition, the MAH took the opportunity to update Annex II.

15.3.26. Nivolumab – OPDIVO (CAP) – EMA/VR/0000278256

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report for the OS final analysis from the post authorisation efficacy study (PAES) CA209577 listed as an obligation in the Annex II of the Product Information. This is a randomized, multicenter, double-blind phase 3 study of adjuvant nivolumab in subjects with resected oesophageal cancer or gastroesophageal cancer who have received CRT followed by surgery. The Annex II and the RMP (version 45.0) are updated accordingly.

15.3.27. Nonacog beta pegol – REFIXIA (CAP) – EMA/VR/0000249232

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update clinical information based on the latest data obtained from the completed clinical studies, including results from studies NN7999-3774 and NN7999-3895. The RMP version 6.0 has also been submitted.

15.3.28. Nusinersen - SPINRAZA (CAP) - EMEA/H/C/004312/X/0038, Orphan

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Karin Bolin

Scope: Extension application to add a new strength of 28 mg and 50 mg. The RMP (version 12.x) is updated in accordance (version 12.2 is under assessment in procedure EMEA/H/C/004312/II/0034/G).

15.3.29. Pegcetacoplan – ASPAVELI (CAP) – EMA/VR/0000248937

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of adults and adolescents aged 12 to 17 years with C3 glomerulopathy (C3G) or primary immune complex membranoproliferative glomerulopathy (IC-MPGN) for ASPAVELI, based on interim results from study APL2-C3G-310; this is a randomized, placebo-controlled, double-blinded, multicenter study to evaluate the safety and efficacy of twice-weekly s.c. infusions of pegcetacoplan in patients diagnosed with C3G or primary IC-MPGN and results from Phase 2 study APL2-C3G-204, an open-label, randomized, controlled study to evaluate the efficacy and safety of pegcetacoplan in posttransplant recurrence of C3G or primary IC-MPGN. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.2 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC. Furthermore, the PI is brought in line with the latest QRD template version 10.4.

15.3.30. Pembrolizumab – KEYTRUDA (CAP) – EMA/X/0000248795

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with two new strengths (790 mg and 395 mg) and new route of administration (subcutaneous use). The RMP (version 49.1) is updated in accordance.

15.3.31. Pembrolizumab – KEYTRUDA (CAP) – EMA/VR/0000245108

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include KEYTRUDA as monotherapy, for the treatment of resectable locally advanced head and neck squamous cell carcinoma (HNSCC), as neoadjuvant treatment, continued as adjuvant treatment in combination with radiation therapy with or without platinum-containing chemotherapy and then as monotherapy in adults, based on the results of study P689V01MK3475 (KEYNOTE-689); this is a Phase 3, randomised, open-label study evaluating pembrolizumab as neoadjuvant therapy and in combination with standard of care as adjuvant therapy for stage III or IVA, resectable, locoregionally advanced head and neck squamous cell carcinoma. Consequently, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in

accordance. The RMP version 48.1 has also been submitted. In addition, the MAH took the opportunity to introduce some minor editorial changes to the PI.

15.3.32. rADAMTS13 – ADZYNMA (CAP) – EMA/VR/0000255553

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Maia Uusküla

Scope: Submission of the final report from study 281102 listed as a Specific Obligation in the Annex II of the Product Information. This is a phase 3, prospective, randomized, controlled, open-label, multicentre study evaluating the safety and efficacy of TAK-755 (rADAMTS13) in the prophylactic and on-demand treatment of subjects with cTTP. In addition, results from the second interim analysis for Study 3002, which is a Phase 3b, prospective, open-label, multicenter, single treatment arm, continuation study of study 281102 was also submitted. The Annex II and the RMP version 1.1 are updated accordingly.

15.3.33. Recombinant respiratory syncytial virus pre-fusion F protein, adjuvanted with AS01E – AREXVY (CAP) – EMA/VR/0000276225

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus in adults 18 years of age and older for AREXVY, based on results from study 222253 (RSV OA=ADJ-025); this is a Phase 3b, open-label study to evaluate the non-inferiority of the immune response and to evaluate the safety of the RSVPreF3 OA investigational vaccine in adults 18-49 years of age at increased risk of respiratory syncytial virus disease, compared to older adults ≥60 years of age. As a consequence, sections 4.1, 4.6, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI.

15.3.34. Recombinant vesicular stomatitis virus (strain Indiana) with a deletion of the envelope glycoprotein, replaced with the Zaire Ebolavirus (strain Kikwit-1995) surface glycoprotein– ERVEBO (CAP) – EMA/VR/0000280470

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of:

C.I.4: To update sections 4.4, 4.8, 5.1 of the SmPC to include safety and immunogenicity data following the results from study referred to as V920-015 ACHIV, listed as a category 3 study in the RMP; this is a Phase 2 Randomized, Multi-Center Double-Blind, Placebo-Controlled Study to evaluate the safety and immunogenicity of the V920/Ervebo (rVSVΔG-ZEBOV-GP) Ebola virus vaccine candidate in HIV-Infected adults and adolescents. The RMP version 2.1 has also been submitted. In addition, the Applicant took the opportunity to remove the complete list of local representatives, as suggested by the EMA during the review

of specimens for the current ongoing renewal. Instead, the contact details of the MAH are included for ease of contact.

C.I.11.b: Submission of an updated RMP version 2.1 in order to summarize the safety and effectiveness of Ervebo administered in the context of Expanded Access Protocol (EAP) 5 compassionate ring vaccination study.

15.3.35. Respiratory syncytial virus vaccine (bivalent, recombinant) – ABRYSVO (CAP) – EMA/VR/0000254927

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update clinical efficacy and safety information on the use of Abrysvo in immunocompromised individuals, based on final results from Study C3671023 (substudy B); this is a Phase 3 clinical study designed to evaluate the safety, tolerability, and immunogenicity of Abrysvo in adults at high risk of severe RSV disease. Substudy B was conducted in approximately 200 immunocompromised participants who were 18 years of age and older and received 2 doses of RSVpreF 120 µg, with an interval of 1 month. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce a minor change to the PI.

15.3.36. Retifanlimab – ZYNYZ (CAP) – EMA/VR/0000247788

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include in combination with carboplatin and paclitaxel treatment of adult patients with metastatic or with inoperable locally recurrent squamous cell carcinoma of the anal canal (SCAC) for ZYNYZ, based on interim results from study INCMGA 0012-303 (POD1UM-303/InterAACT-2); this is a phase 3 global, multicenter, double-blind randomized study of carboplatin-paclitaxel with retifanlimab or placebo in participants with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal not previously treated with systemic chemotherapy. 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 1.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce editorial changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.37. Ritonavir – NORVIR (CAP) – EMA/VR/0000249795

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of:

Type II (C.I.6.a): To modify the approved therapeutic indication to reflect current clinical use as a pharmacokinetic enhancer of other antiretroviral products only. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8 and 5.1 of the SmPC. The Package Leaflet is updated

accordingly. The updated RMP version 8.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.

15.3.38. Selumetinib – KOSELUGO (CAP) – EMA/VR/0000245231

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication for KOSELUGO to include treatment of adults based on results from study D134BC00001 (KOMET). This is a phase III, multicentre, international study with a parallel, randomised, double-blind, placebo-controlled, 2 arm design that assesses efficacy and safety of selumetinib in adult participants with NF1 who have Symptomatic Inoperable Plexiform Neurofibromas. 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 4.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes to the SmPC. As part of the application the MAH is requesting a 1-year extension of the market protection.

15.3.39. Talquetamab – TALVEY (CAP) – EMA/VR/0000258454

Applicant: Janssen Cilag International

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add a new warning on Ataxia/Balance disorder based on post-marketing data. The Package Leaflet is updated accordingly. The RMP version 3.1 has also been submitted.

15.3.40. Talquetamab – TALVEY (CAP) – EMA/VR/0000264615

Applicant: Janssen Cilag International

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Submission of the interim report from study 64407564MMY1001 listed as a Specific Obligation in the Annex II of the Product Information. This is a phase 1/2, first-in-human, open-label, dose escalation study of talquetamab, a humanized GPRC5D x CD3 bispecific antibody, in subjects with relapsed or refractory multiple myeloma. Safety data were revised based on the 2-year follow-up analysis for the pivotal RP2D population The Annex II and the RMP version 3.2 are updated accordingly.

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

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

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

15.3.42. Tezepelumab – TEZSPIRE (CAP) – EMA/VR/0000245013

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include treatment of Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) for Tezspire, based on results from study WAYPOINT (D5242C00001); this is a global, multicentre, randomised, double-blind, parallel-group, placebo-controlled study that evaluated the efficacy and safety of tezepelumab compared with placebo in the treatment of CRSwNP. 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 4.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes and to update the PI and the Package Leaflet in accordance with the latest EMA excipients guideline.

15.3.43. Tirzepatide – MOUNJARO (CAP) – EMA/VR/0000271898

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Update of section 4.6 of the SmPC in order to include information on breast-feeding based on results from study I8F-MC-GPIN (GPIN); this was a Phase I, single-site, open-label, single-treatment arm, single-dose, lactation study, assessing pharmacokinetics of tirzepatide in breastmilk and plasma in healthy lactating women. The Package Leaflet is also updated accordingly. The RMP version 6.1 has also been submitted.

15.3.44. Tralokinumab – ADTRALZA (CAP) – EMA/VR/0000254976

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update clinical efficacy and safety information based on the final clinical trial report of the open-label extension PASS study LP0162-1337 (ECZTEND), listed as a category 3 study in the RMP. This is a phase 3 open-label, single-arm, multi-centre, long-term extension trial to evaluate the safety and efficacy of tralokinumab in subjects with moderate-to-severe atopic dermatitis who participated in previous tralokinumab clinical trials. The RMP has been updated to version 3.0. In addition, the MAH took the opportunity to update the PI according to the updated EU Excipient guideline to include a warning regarding polysorbate as well as to include minor editorial changes and to update the list of local representatives in the Package Leaflet.

15.3.45. Tucatinib – TUKYSA (CAP) – EMA/VR/0000280202

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study SGNTUC-016 listed as a category 3 study in the RMP. This is a randomized, double blind, phase 3 study of Tucatinib or Placebo in combination with Ado-Trastuzumab Emtansine (T-DM1) for subjects with unresectable locally

advanced or metastatic HER2+ Breast Cancer. Primary objective is to compare progression-free survival (PFS) by investigator per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 between treatment arms. The RMP version 2.0 has also been submitted.

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

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

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

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

16.1.1. Amifampridine – FIRDAPSE (CAP) – EMA/PSUR/0000269014

Applicant: Serb

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00000141/202412)

16.1.2. Avapritinib – AYVAKYT (CAP) – EMA/PSUR/0000268946

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010878/202501)

16.1.3. Baricitinib – OLUMIANT (CAP) – EMA/PSUR/0000268999

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010578/202502)

16.1.4. Birch bark extract – FILSUVEZ (CAP) – EMA/PSUR/0000268967

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure (PSUSA/00010446/202501)

16.1.5. Concentrate of proteolytic enzymes enriched in bromelain – NEXOBRID (CAP) – EMA/PSUR/0000269011

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010028/202412)

16.1.6. Danicopan – VOYDEYA (CAP) – EMA/PSUR/0000269006

Applicant: Alexion Europe

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00011056/202501)

16.1.7. Dapivirine – DAPIVIRINE VAGINAL RING 25 MG (CAP) – EMA/PSUR/0000267345 (Art 58[42])

Applicant: International Partnership For Microbicides

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUV Dapivirine)

16.1.8. Daridorexant – QUVIVIQ (CAP) – EMA/PSUR/0000269025

Applicant: Idorsia Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010993/202501)

16.1.9. Dasiglucagon – ZEGALOGUE (CAP) – EMA/PSUR/0000269023

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure (PSUSA/00011078/202501)

16.1.10. Decitabine / Cedazuridine – INAQOVI (CAP) – EMA/PSUR/0000268951

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000118/202501)

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

16.1.11. Defatted powder of *Arachis hypogaea L.*, semen (peanuts) – PALFORZIA (CAP) – EMA/PSUR/0000268968

Applicant: Stallergenes

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010902/202501)

16.1.12. Delgocitinib – ANZUPGO (CAP) – EMA/PSUR/0000269028

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011091/202501)

16.1.13. Dolutegravir – TIVICAY (CAP); Dolutegravir / Abacavir / Lamivudine - TRIUMEQ (CAP); Dolutegravir / Lamivudine - DOVATO (CAP) – EMA/PSUR/0000269008

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010075/202501)

16.1.14. Elbasvir / Grazoprevir – ZEPATIER (CAP) – EMA/PSUR/0000268984

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010519/202501)

16.1.15. Elranatamab – ELREXFIO (CAP) – EMA/PSUR/0000268954

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00000225/202502)

16.1.16. Entacapone – COMTAN (CAP); COMTESS (CAP); ENTACAPONE ORION (CAP) – EMA/PSUR/0000269013

Applicant: Orion Corporation

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00001223/202501)

16.1.17. Epinephrine – EURNEFFY (CAP) – EMA/PSUR/0000269019

Applicant: Alk-Abello A/S

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011081/202502)

16.1.18. Evinacumab – EVKEEZA (CAP) – EMA/PSUR/0000268966

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010945/202502)

16.1.19. Faricimab – VABYSMO (CAP) – EMA/PSUR/0000268993

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00011016/202501)

16.1.20. Gefapixant – LYFNUA (CAP) – EMA/PSUR/0000268941

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000132/202501)

16.1.21. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/PSUR/0000269003

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010990/202502)

16.1.22. Lonoctocog alfa – AFSTYLA (CAP) – EMA/PSUR/0000268994

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010559/202501)

16.1.23. Melphalan flufenamide – PEPAXTI (CAP) – EMA/PSUR/0000268987

Applicant: Oncopeptides AB

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00011013/202502)

16.1.24. Metreleptin – MYALEPTA (CAP) – EMA/PSUR/0000269015

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010700/202501)

16.1.25. Odevixibat – BYLVAY (CAP); KAYFANDA (CAP) – EMA/PSUR/0000268956

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010949/202501)

16.1.26. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted, prepared in cell cultures) – INCELLIPAN (CAP); Zoonotic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted, prepared in cell cultures) - CELLDEMIC (CAP)– EMA/PSUR/0000268985

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00011057/202501)

16.1.27. Perflutren – LUMINITY (CAP); OPTISON (CAP) – EMA/PSUR/0000268958

Applicants: GE Healthcare AS, Lantheus EU Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00002350/202412)

16.1.28. Pneumococcal polysaccharide conjugate vaccine (15 valent, adsorbed) – VAXNEUVANCE (CAP) – EMA/PSUR/0000268990

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010975/202501)

16.1.29. Quadrivalent influenza vaccine (recombinant, prepared in cell culture) – SUPEMTEK TETRA (CAP) – EMA/PSUR/0000268982

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00010886/202501)

16.1.30. Relugolix – ORGOVYX (CAP) – EMA/PSUR/0000268974

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00010994/202501)

16.1.31. Risdiplam – EVRYSDI (CAP) – EMA/PSUR/0000268972

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010925/202502)

16.1.32. Romosozumab – EVENITY (CAP) – EMA/PSUR/0000268947

Applicant: UCB Pharma

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00010824/202501)

16.1.33. Salmeterol / Fluticasone propionate – BROPAIR SPIROMAX (SRD[43]); SEFFALAIR SPIROMAX (CAP) – EMA/PSUR/0000268979

Applicant: Teva B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010928/202501)

16.1.34. Simoctocog alfa – NUWIQ (CAP); VIHUMA (CAP) – EMA/PSUR/0000268960

Applicant: Octapharma AB

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010276/202501)

16.1.35. Smallpox and monkeypox vaccine (live modified vaccinia virus Ankara) – IMVANEX (CAP) – EMA/PSUR/0000269020

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010119/202501)

16.1.36. Sodium phenylbutyrate – AMMONAPS (CAP); PHEBURANE (CAP) – EMA/PSUR/0000268988

Applicants: Eurocept International B.V., Immedica Pharma AB

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00002758/202412)

16.1.37. Sutimlimab – ENJAYMO (CAP) – EMA/PSUR/0000268980

Applicant: Recordati Rare Diseases

[43] European Commission decision for the withdrawal of the marketing authorisation, at the holder's request: 23 May 2025

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00011023/202502)

16.1.38. Tafasitamab – MINJUVI (CAP) – EMA/PSUR/0000269001

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010951/202501)

16.1.39. Talquetamab – TALVEY (CAP) – EMA/PSUR/0000268940

Applicant: Janssen Cilag International

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00000099/202502)

16.1.40. Tecovirimat – TECOVIRIMAT SIGA (CAP) – EMA/PSUR/0000268964

Applicant: Siga Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010971/202501)

16.1.41. Umeclidinium / Vilanterol – ANORO ELLIPTA (CAP); LAVENTAIR ELLIPTA (CAP) – EMA/PSUR/0000268953

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010264/202412)

16.1.42. Umeclidinium bromide – INCRUSE ELLIPTA (CAP); ROLUFTA ELLIPTA (CAP) – EMA/PSUR/0000268992

Applicants: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010263/202412)

16.1.43. Vericiguat – VERQUVO (CAP) – EMA/PSUR/0000269002

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010950/202501)

16.1.44. Verteporfin – VISUDYNE (CAP) – EMA/PSUR/0000269026

Applicant: Cheplapharm Arzneimittel GmbH

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00003110/202412)

16.1.45. Voxelotor – OXBRYTA (CAP) – EMA/PSUR/0000268973

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00010983/202502)

16.1.46. Ziconotide – PRIALT (CAP) – EMA/PSUR/0000269017

Applicant: Esteve Pharmaceuticals GmbH

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00003142/202412)

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

16.2.1. Macimorelin – GHRYVELIN (CAP); NAP – EMA/PSUR/0000268945

Applicants: Atnahs Pharma Netherlands B.V., various

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010746/202501)

16.2.2. Nitric oxide – INOMAX (CAP); NAP – EMA/PSUR/0000268961

Applicants: Linde Healthcare AB, various

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00002172/202412)

16.2.3. Sorafenib – NEXAVAR (CAP); NAP – EMA/PSUR/0000268978

Applicants: Bayer AG, various

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00002773/202412)

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

16.3.1. Alitretinoin (oral use) (NAP) – EMA/PSUR/0000269007

Applicants: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010710/202501)

16.3.2. Amino acid combinations / glucose / triglyceride combinations (e.g. olive oil, soya bean oil, fish oil)/ with or without electrolytes/ mineral compounds (i.v. application) - only for the drug Numeta (NAP) – EMA/PSUR/0000269010

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010190/202412)

16.3.3. Anthrax vaccine (NAP) – EMA/PSUR/0000268943

Applicants: various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010771/202412)

16.3.4. Bendamustine hydrochloride (NAP) – EMA/PSUR/0000269009

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00003162/202501)

16.3.5. Camellia sinensis, leaf, dry extract refined (derived from *Camellia sinensis, L.* O.KUNTZE) (topical use) (NAP) – EMA/PSUR/0000269000

Applicants: various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010569/202412)

16.3.6. Cefotaxime (NAP) – EMA/PSUR/0000268997

Applicants: various

PRAC Lead: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000599/202412)

16.3.7. Cyanocobalamin / diclofenac / pyridoxine / thiamine (NAP) – EMA/PSUR/0000269016

Applicants: various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00001041/202501)

16.3.8. Flumazenil (NAP) – EMA/PSUR/0000269027

Applicants: various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00001413/202412)

16.3.9. Flunitrazepam (NAP) – EMA/PSUR/0000268937

Applicants: various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00001418/202501)

16.3.10. Haloperidol (NAP) – EMA/PSUR/0000268939

Applicants: various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00001587/202501)

16.3.11. Human alfa1-proteinase inhibitor (apart from the centrally authorised product) (NAP) – EMA/PSUR/0000268942

Applicants: various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000108/202412)

16.3.12. Lidocaine / phenazone (NAP) – EMA/PSUR/0000268949

Applicants: various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00002359/202501)

16.3.13. Menotrophin (NAP) – EMA/PSUR/0000268950

Applicants: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00001972/202412)

16.3.14. Metamizole sodium / triacetonamine tosilate (NAP) – EMA/PSUR/0000268944

Applicants: various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure (PSUSA/00001999/202501)

16.3.15. Myristalkonium, benzalkonium (vaginal use only) (NAP) – EMA/PSUR/0000268969

Applicants: various

PRAC Lead: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure (PSUSA/00010987/202501)

16.3.16. Omega-3-acid ethyl esters (NAP) – EMA/PSUR/0000268957

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010312/202501)

16.3.17. Phenylephrine (ophthalmic formulations) (NAP) – EMA/PSUR/0000268963

Applicants: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00010402/202501)

16.3.18. Pirenoxine (NAP) – EMA/PSUR/0000268955

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00002431/202501)

16.3.19. Rosuvastatin / Omega-3-acid ethyl esters (NAP) – EMA/PSUR/0000268971

Applicants: various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010915/202501)

16.3.20. Roxithromycin (NAP) – EMA/PSUR/0000269004

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00002669/202412)

16.3.21. Tizanidine (NAP) – EMA/PSUR/0000269005

Applicants: various

PRAC Lead: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00002977/202412)

16.3.22. Typhoid vaccine (live, attenuated) (NAP) – EMA/PSUR/0000268991

Applicants: various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00003067/202412)

16.3.23. Valaciclovir (NAP) – EMA/PSUR/0000268998

Applicants: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00003086/202412)

16.3.24. Varicella- Zoster immunoglobuline (NAP) – EMA/PSUR/0000268952

Applicants: various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010266/202412)

16.4. Follow-up to PSUR/PSUSA procedures

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

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

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

16.5. Variation procedure(s) resulting from PSUSA evaluation

None

16.6. Expedited summary safety reviews[44]

None

[44] 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

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)[45]

17.1.1. Avapritinib – AYVAKYT (CAP) – EMA/PASS/0000282408

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: PASS amendment [107o]: BLU-285-1406: an observational study evaluating safety and efficacy of avapritinib in the first line treatment of patients with Platelet derived Growth Factor Alpha D842V mutated gastrointestinal stromal tumor.

17.1.2. Tofersen – QALSODY (CAP) – EMA/PASS/0000264233

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: PASS protocol [107n]: An observational registry-based study utilising data from two disease registry networks precision ALS and ALS/MND NHC to evaluate the long-term safety of tofersen in people with SOD1-ALS [MAH's response to EMEA/H/C/PSP/S/0109]

17.1.3. Topiramate (NAP) – EMA/PASS/0000281792

Applicant: Janssen Cilag International

PRAC Rapporteur: Karin Bolin

Scope: Topiramate PASS amendment [107o]: Substantial amendment to a PASS survey among healthcare professionals and patients to assess their knowledge and behaviour regarding the risks of topiramate use during pregnancy, the measures implemented to prevent pregnancy, and the receipt/use of educational materials as part of the pregnancy prevention program.

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[46]

17.2.1. Abaloparatide – ELADYNOS (CAP) – EMA/PAM/0000281538

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Karin Erneholm

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

Scope: Protocol amendment for Study EUPAS1000000613 (MEA 001: European non-interventional post-authorization safety study (PASS) to evaluate cardiovascular (CV) events in patients newly exposed to abaloparatide or teriparatide)

17.2.2. Capivasertib – TRUQAP (CAP) – EMA/PAM/0000281199

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Protocol amendment for study D3612R00020 (CAPIseid): a database study of the safety and effectiveness of TRUQAP (capivasertib) + fulvestrant in patients with advanced breast cancer and type 1 or type 2 diabetes. (NINI; RMP) along with MAH's responses to questions/comments raised as part of Truqap MEA 001.

17.2.3. Chikungunya vaccine (recombinant, adsorbed) – VIMKUNYA (CAP) – EMA/PAM/0000276447

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the protocol for the post-authorisation safety study BN-CV-317-011 (version 1.0) which is a category 3 study in the RMP. BN-CV-317-011 is an observational prospective study to evaluate the safety of Vimkunya in pregnant women and their offspring.

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

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

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

17.2.5. COVID-19 mRNA vaccine – COMIRNATY (CAP) – EMA/PAM/0000273399

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the interim clinical study report, Protocol and Amendment 2 and, the updated statistical Analysis Plan 1 for study C4591052; this is a post-authorisation safety observational study to determine whether there is an increased risk of pre-specified adverse events of special interests following the administration of Comirnaty bivalent BA.1 or Comirnaty bivalent BA.4-5 compared with not receiving any COVID-19 vaccine.

17.2.6. COVID-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP) – EMA/PAM/0000273311

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of a revised PASS protocol version 7.0 for study 2019nCoV-404 for COVID-19 vaccine (recombinant, adjuvanted) (Nuvaxovid)

17.2.7. COVID-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP) – EMA/PAM/0000273301

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of a revised PASS protocol version 7.0 for study 2019nCoV-402 for COVID-19 vaccine (recombinant, adjuvanted) (Nuvaxovid), to assess the safety of the Novavax COVID-19 vaccine in England using a self-controlled case series design (PASS using data from the Clinical Practice Research Datalink (CPRD) Aurum and linked databases)

17.2.8. Crovalimab – PIASKY (CAP) – EMA/PAM/0000281171

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Responses to the List of Questions raised in the assessment report of EMEA/H/C/006061/MEA/002 and submission of the revised draft NI-PASS protocol MO45473. This is a post-authorization safety study (PASS) to characterize safety events and special conditions such as pregnancy and infant outcomes, in paroxysmal nocturnal hemoglobinuria (PNH) patients treated with crovalimab within the IPIG registry (Study MO45473).

17.2.9. Danicopan – VOYDEYA (CAP) – EMA/PAM/0000285097

Applicant: Alexion Europe

PRAC Rapporteur: Martin Huber

Scope: Responses to the request for supplementary information (MEA 2.1). Submission of a revised protocol for the non-imposed non-interventional PASS study ALX-PNH-502 - an observational cohort study to assess long-term safety of danicopan add-on therapy in patients with paroxysmal nocturnal hemoglobinuria: analysis of IPIG-registry data.

17.2.10. Dimethyl fumarate – SKILARENCE (CAP) – EMA/PAM/0000280214

Applicant: Almirall S.A.

PRAC Rapporteur: Karin Bolin

Scope: Submission of amended protocol for the non-imposed (category 3) Post Authorisation Safety Study (PASS) M-41008-40, "An Observational Post-Authorisation Safety Study of Skilarence in European Psoriasis Registers"; Protocol, version 2.0, dated 27 May 2025; former MEA 001.9

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

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Amelia Cupelli

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

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

17.2.12. Etranacogene dezaparvovec – HEMGENIX (CAP) – EMA/PAM/0000248926

Applicant: CSL Behring GmbH

PRAC Rapporteur: Bianca Mulder

Scope: The MAH submitted a PASS protocol (version 1.0), which covers a Healthcare Professional Survey (HCP) to assess the effectiveness of the additional Risk Minimization Measures (aRMM) for Hemgenix (etranacogene dezaparvovec).

17.2.13. Human thrombin / Human fibrinogen – TACHOSIL (CAP) – EMA/PAM/0000247840

Applicant: Corza Medical GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Revised protocol for PASS PasTel: Short- and long-term safety evaluation of TachoSil in paediatric population

17.2.14. Marstacimab – HYMPAVZI (CAP) – EMA/PAM/0000255006

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of a study protocol for a category 3 study B7841016: A Post-Authorisation Safety Study to Evaluate the Safety of Marstacimab Among Patients with Severe Haemophilia A or B using Real-World Data in European Haemophilia Registers.

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

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

17.2.16. Tofacitinib – XELJANZ (CAP) – EMA/PAM/0000276269

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of interim report covering a study period from 01 January 2018 to 31 December 2023 and a protocol amendment v.5 for A3921403 (RMP Category 3 Study - A

Post-Authorisation Safety Study of the Utilisation and Prescribing Patterns of Xeljanz (tofacitinib) Using an Administrative Healthcare Database in France, SNDS); former MEA 025

17.2.17. Ustekinumab – STELARA (CAP) – EMA/PAM/0000281464

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Protocol amendment 4 for the Paediatric Psoriasis Registry, study CNTO1275PSO4056 - the observational PASS (EUPAS19506) of Ustekinumab in the treatment of paediatric patients aged 6 years and older with moderate to severe plaque psoriasis; former MEA 044

17.2.18. Vamorolone – AGAMREE (CAP) – EMA/PAM/0000274869

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: PASS protocol for a non-interventional, post-authorisation safety study to evaluate the safety of vamorolone (AGAMREE®) in patients with Duchenne muscular dystrophy in a real world setting.

17.2.19. Velaglucerase alfa – VPRIV (CAP) - EMA/PAM/0000248394

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated study protocol number TAK-669-4018 (v6.0) for a non-interventional (Cat.3) PASS EUPAS49598 for Vpriv 400 U, powder for solution for infusion: A Survey among Patients, Caregivers and Home Infusion Nurses based in the European Union to Assess their Awareness and Understanding of Educational Materials (EM) Supporting VPRIV Infusion at Home. Submission includes updated Patient and Caregiver Questionnaire v.6.0 and updated Home Infusion Nurse Questionnaire v.6.0. Former MEA/030.

17.3. Results of PASS imposed in the marketing authorisation(s)[47]

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

Applicants: Medice Arzneimittel Puetter GmbH & Co. KG

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.

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

17.4. Results of PASS non-imposed in the marketing authorisation(s)[48]

17.4.1. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence – STRIMVELIS (CAP) – EMA/VR/0000282021

Applicant: Fondazione Telethon Ets

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the final report from study STRIM-005. This is a non-interventional methodology study to investigate the utility of retroviral insertion site analysis in samples from subjects treated with Strimvelis gene therapy. The RMP version 8.0 has also been submitted.

Action: For adoption

17.4.2. Avelumab – BAVENCIO (CAP) – EMA/VR/0000244307

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the final report from study MS100070-0031 listed as a category 3 PASS in the RMP. This is a non-interventional cohort efficacy and safety study to assess the characteristics and management of patients with Merkel cell carcinoma (MCC) in Germany.

17.4.3. Dabigatran etexilate – PRADAXA (CAP) – EMA/VR/0000256456

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of the final report from the non-interventional paediatric PASS 1160.307, listed as a category 3 study in the RMP. This is an observational study to evaluate the safety of dabigatran etexilate for the treatment of venous thromboembolism (VTE) and prevention of recurrent VTE in paediatric patients from birth to less than 2 years of age in routine clinical practice setting. The RMP version 41.3 has also been submitted.

17.4.4. Deferasirox – EXJADE (CAP) – EMA/VR/0000280855

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section D of Annex II of the PI based on the submission of the final report from study CICL670E2422, listed as an imposed PASS in the Annex II. This is an observational study that evaluated the safety of deferasirox in the treatment of pediatric patients with non-transfusion-dependent iron overload. The RMP version 23.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

[48] 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

17.4.5. Fingolimod – GILENYA (CAP) – EMA/VR/0000257758

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: A grouped application consisting of:

C.I.4: Update of section 4.6 of the SmPC in order to update information on pregnancy based on final results from Gilenya Pregnancy Registry (study CFTY720D2404) listed as a category 3 study in the RMP; this is a non-interventional, prospective, observational study in pregnant MS patients with confirmed or suspected maternal exposure to fingolimod; the Package Leaflet is updated accordingly. The RMP version 21.0 has also been submitted. In addition, the MAH took the opportunity to bring editorial changes to the PI.

C.I.4: Update of section 4.6 of the SmPC in order to update information on pregnancy based on the fingolimod Pregnancy outcomes Intensive Monitoring (PRIM) program to collect pregnancy outcome data from the Novartis global pharmacovigilance (PV) database; the Package Leaflet is updated accordingly. The RMP version 21.0 has also been submitted.

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

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Mari Thorn

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

17.4.7. Radium-223 – XOFIGO (CAP) – EMA/VR/0000279392

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Submission of the final report from study 16913 (REASSURE) listed as a category 3 study in the RMP. This is a non-interventional safety study for the evaluation of long-term safety of Radium-223 used for the treatment of metastatic castration resistant prostate cancer.

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

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

and formatting changes to the PI and to align the wording used for the pre-filled syringe and the pre-filled pen, as well as to update the list of local representatives in the Package Leaflet.

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

17.5.1. Aflibercept – EYLEA (CAP) – EMA/PAM/0000278528

Applicant: Bayer AG

PRAC Rapporteur: Zoubida Amimour

Scope: Interim study report for FIREFLEYE NEXT Study #20275: An extension study to evaluate the long-term outcomes of subjects who received treatment for retinopathy of prematurity in Study 20090 (non-imposed/interventional/RMP).

17.5.2. Avatrombopag – DOPTELET (CAP) – EMA/PAM/0000281531

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Monica Martinez Redondo

Scope: Category 3, MEA EMEA/H/C/ 004722/MEA/0002: Post authorisation Safety Study (PASS) of Avatrombopag in Patients With Severe Chronic Liver Disease (CLD).

Progress report

17.5.3. Beclometasone / Formoterol / Glycopyrronium bromide – TRYDONIS (CAP) – EMA/PAM/0000274900

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: PASS CLI-05993BA1-05 (TRIBE): Second interim report and Statistical analysis plan (SAP) v. 3.0 - Multinational database cohort study to assess adverse cardiovascular and cerebrovascular outcomes in patients with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurized metered dose inhaler (pMDI).

17.5.4. Beclometasone / Formoterol / Glycopyrronium bromide – TRIMBOW (CAP) – EMA/PAM/0000274884

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: PASS CLI-05993BA1-05 (TRIBE): Second Interim Study and statistical analysis plan (SAP) v. 3.0 - Multinational database cohort study to assess adverse cardiovascular and cerebrovascular outcomes in patients with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurized metered dose inhaler (pMDI)

17.5.5. Brexucabtagene autoleucel – TECARTUS (CAP) – EMA/PAM/0000273165

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Protocol amendment 6 for Study KT-EU-472-6036 (Long-term, non-interventional study of recipients of Tecartus for treatment of adult patients relapsed or refractory (r/r) mantle cell lymphoma (MCL) or adult patients with r/r B-cell precursor acute lymphoblastic leukemia (ALL)

17.5.6. Burosumab – CRYSVITA (CAP) – EMA/PAM/0000273741

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Follow-up to the 1st Interim Study Report in Adult population, PASS EUPAS32190: Non-interventional Post-Authorisation Safety Study of Burosumab in the Treatment of Children >1 year of age, Adolescents and Adults with X linked Hypophosphataemia (protocol number 2019-36-EU-CRY).

17.5.7. COVID-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP) – EMA/PAM/0000281402

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the third interim study report 2019nCoV-405 (Study No EUPAS39096, Global Pregnancy and Infant Outcomes Study Using the COVID-19 Vaccines International Pregnancy Exposure Registry (C-VIPER))

17.5.8. Dimethyl fumarate – SKILARENCE (CAP) – EMA/PAM/0000280759

Applicant: Almirall S.A.

PRAC Rapporteur: Karin Bolin

Scope: 7th Study Progress Report (2025 Annual Progress Report): "An observational Post-Authorisation Safety Study of Skilarence in European Psoriasis Registers" M-41008-40; follow on from MEA 001.8

17.5.9. Diroximel fumarate – VUMERITY (CAP) – EMA/PAM/0000281622

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the second interim report of PASS 272MS403 An observational study utilising data from big MS data registries to evaluate the long-term safety of Vumerity and Tecfidera. Cat 3

17.5.10. Dolutegravir – TIVICAY (CAP) – EMA/PAM/0000276456

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: The 4th annual RESPOND (The International Cohort Consortium of Infectious Disease) study report from 2024 concerning dolutegravir (Tivicay), dolutegravir/abacavir/lamivudine (Triumeq) and dolutegravir/lamivudine (Dovato).

17.5.11. Dolutegravir / Abacavir / Lamivudine – TRIUMEQ (CAP) – EMA/PAM/0000276483

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: The 4th annual RESPOND (The International Cohort Consortium of Infectious Disease) study report from 2024 concerning dolutegravir (Tivicay), dolutegravir/abacavir/lamivudine (Triumeq) and dolutegravir/lamivudine (Dovato).

17.5.12. Dolutegravir / Lamivudine – DOVATO (CAP) – EMA/PAM/0000276335

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: The 4th annual RESPOND (The International Cohort Consortium of Infectious Disease) study report from 2024 concerning dolutegravir (Tivicay), dolutegravir/abacavir/lamivudine (Triumeq) and dolutegravir/lamivudine (Dovato).

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

Applicant: Estetra

PRAC Rapporteur: Martin Huber

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

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

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

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

17.5.15. Efgartigimod alfa – VYVGART (CAP) – EMA/PAM/0000279810

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the first annual progress report for ARGX-113-PASS-2208 study: Post-authorisation safety study to characterize the risks and missing information outlined in the risk management plan including serious infections, use of live/attenuated vaccines, use with monoclonal antibodies, long-term safety and use in immunocompromised patients and evaluate whether there are specific and/or unexpected patterns of adverse events.

17.5.16. Fremanezumab – AJOVY (CAP) – EMA/PAM/0000280795

Applicant: TEVA GmbH

PRAC Rapporteur: Terhi Lehtinen

Scope: The interim report for PASS Study TV48125-MH-40217 in line with the defined milestones mentioned in the respective protocol (v1.0) and risk management plan (v6.0).

17.5.17. Galcanezumab – EMGALITY (CAP) – EMA/PAM/0000275530

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Interim results of an ongoing non-interventional galcanezumab study I5Q-MC-B001, as agreed to in the RMP. This PAM covers responses to questions raised in MEA 004.3.

17.5.18. Lenalidomide – REVLIMID (CAP) – EMA/PAM/0000281668

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of an interim study report of study CC-5013-MM-034: A prospective non-interventional post-authorisation safety study (PASS) of lenalidomide in previously untreated adult multiple myeloma patients who are not eligible for transplant

17.5.19. Luspatercept – REBLOZYL (CAP) – EMA/PAM/0000280221

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Jo Robays

Scope: 5th annual report of Study No. ACE-536-LTFU-001.

To evaluate the long-term safety, including TEEs (only in the TD and non-TD β thalassaemia population with splenectomy), EMH masses (only in the TD and non-TD β-thalassaemia population), and progression to AML and/or other malignancies/ pre-malignancies, of luspatercept in patients who have participated in Acceleron or Celgene-sponsored luspatercept clinical trials.

17.5.20. Lutetium (177Lu) oxodotreotide – LUTATHERA (CAP) – EMA/PAM/0000279830

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Study No. A-LUT-T-E02-402: An International, Non-Interventional, Post-Authorization LongTerm Safety Study of Lutathera, in Patients with Unresectable or Metastatic, Well-Differentiated, Somatostatin Receptor Positive, Gastroenteropancreatic Neuroendocrine Tumours (SALUS study).

Eighth PASS Yearly PROGRESS REPORT, Study No. A-LUT-T-E02-402, SALUS Study

17.5.21. Natalizumab – TYSABRI (CAP) – EMA/PAM/0000281383

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the Annual interim report of the comparison between extended interval dosing (EID) versus standard interval dosing (SID) risk for PML from the TOUCH database and justification for cessation of EID vs. SID.

17.5.22. Neratinib – NERLYNX (CAP) – EMA/PAM/0000281194

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Bianca Mulder

Scope: Interim report of the NER7402 (NERLYFE) study, a category 3 PASS: a multicentre, multi-country, prospective, observational, post-authorisation safety study to describe the incidence of discontinuation due to diarrhoea within the first 3 months of a treatment with neratinib, in adult breast cancer patients treated in extended adjuvant in a real world setting.

Interim report for the combined NERLYFE/ELEANOR study, a category 3 PASS. The ELEANOR study is a multi-centric, multi-national, prospective, longitudinal, non-interventional study in Austria, Germany and Switzerland conducted with neratinib in patients with HER2+ breast cancer.

17.5.23. Octocog alfa – KOVALTRY (CAP) – EMA/PAM/0000273323

Applicant: Bayer AG

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the category 3 post-authorisation measure to evaluate adverse events of special interest in the PedNet registry with the submission of interim results of the PedNet Annual Report 2024 for Kovaltry

17.5.24. Ravulizumab – ULTOMIRIS (CAP) – EMA/PAM/0000280924

Applicant: Alexion Europe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Category 3 Study - Additional Pharmacovigilance Activity in the Risk Management Plan Submission of Paroxysmal Nocturnal Hemoglobinuria (PNH) Registry Biennial Report, Protocol M07-001, dated 12 Jun 2025.

This is the third biennial report for Ultomiris (ravulizumab).

17.5.25. Rurioctocog alfa pegol – ADYNOVI (CAP) – EMA/PAM/0000248808

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Bianca Mulder

Scope: 5th interim/progress report (dated 15 January 2025, with a data cut-off of 12 November 2024) for the ongoing Adynovi post-authorisation safety study (PASS) TAK-660-403 (EUPAS35698) which is a non-interventional, imposed study aimed to investigate the potential effects of PEG accumulation in the choroid plexus of the brain and other tissues/organs.

17.5.26. Siponimod – MAYZENT (CAP) – EMA/PAM/0000280344

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Fourth interim study report of Study CBAF312A2411: Evaluation of pregnancy and infant outcomes in Mayzent patients using PRegnancy outcomes Intensive Monitoring (PRIM) data.

17.5.27. Solriamfetol – SUNOSI (CAP) – EMA/PAM/0000280836

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Julia Pallos

Scope: Submission of the sixth progress report (version 1.0) dated 9 May 2025 for JZP865-401 'A post-authorisation safety study (PASS) to evaluate cardiovascular events in adult patients with obstructive sleep apnoea (OSA) treated with solriamfetol'.

17.5.28. Sutimlimab – ENJAYMO (CAP) – EMA/PAM/0000273920

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Jan Neuhauser

Scope: 3rd Annual interim report for the sutimlimab Cold Agglutinin Disease Real World Evidence Registry (CADENCE, OBS16454) a multinational, multi-center, observational, prospective, longitudinal disease registry; former MEA 003.2

17.5.29. Upadacitinib – RINVOQ (CAP) – EMA/PAM/0000280404

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Annual progress report for PASS P20-199: Drug utilisation study of upadacitinib in Europe to evaluate the effectiveness of additional risk minimisation measures among patients with Rheumatoid Arthritis.

17.5.30. Velaglucerase alfa – VPRIV (CAP) – EMA/PAM/0000281221

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Martin Huber

Scope: Submission of the 14th Annual 2025 Study Results of Gaucher Disease Outcome Survey (GOS): An Observational, International, Multi-center, Long-term Registry of Patients with Gaucher Disease. GOS registry study discontinuation requested.

17.5.31. Venetoclax – VENCLYXTO (CAP) – EMA/PAM/0000255427

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: To provide targeted tumour lysis syndrome (TLS) assessment reports on a biannual basis through 2023, and annually from Q1 2024 onwards, as per the RMP v8.1, to ensure close monitoring of the important identified risk of TLS, and the evaluation of the impact of newly implemented risk minimisation measures for TLS, on adherence to both already existing and updated recommendation added to the SmPC, the impact of the DHPC distributed to hematologists, and the patient card.

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. Tofersen – QALSODY (CAP) – EMA/S/0000275049

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Adagrasib – KRAZATI (CAP) – EMA/R/0000281723

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Conditional renewal of the marketing authorisation

18.2.2. Brexucabtagene autoleucel – TECARTUS (CAP) – EMA/R/0000278705

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.3. Loncastuximab tesirine – ZYNLONTA (CAP) – EMA/R/0000281443

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Jirsová

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. Sotorasib – LUMYKRAS (CAP) – EMA/R/0000285162

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Conditional renewal of the marketing authorisation

18.2.6. Spesolimab – SPEVIGO (CAP) – EMA/R/0000272399

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Zoubida Amimour

Scope: Conditional renewal of the marketing authorisation

18.2.7. Trastuzumab deruxtecan – ENHERTU (CAP) – EMA/R/0000282648

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Atidarsagene autotemcel – LIBMELDY (CAP) – EMA/R/0000257479

Applicant: Orchard Therapeutics (Netherlands) B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: 5-year renewal of the marketing authorisation

18.3.2. Baloxavir marboxil – XOFLUZA (CAP) – EMA/R/0000265299

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Radowan

Scope: 5-year renewal of the marketing authorisation

18.3.3. Bevacizumab – OYAVAS (CAP) – EMA/R/0000278081

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Karin Erneholm

Scope: 5-year renewal of the marketing authorisation

18.3.4. Bevacizumab – ALYMSYS (CAP) – EMA/R/0000276471

Applicant: Mabxience Research S.L.

PRAC Rapporteur: Karin Erneholm

Scope: 5-year renewal of the marketing authorisation

18.3.5. Cenobamate – ONTOZRY (CAP) – EMA/R/0000273504

Applicant: Aziende Chimiche Riunite Angelini Francesco A.C.R.A.F. S.p.A.

PRAC Rapporteur: Jo Robays

Scope: 5-year renewal of the marketing authorisation

18.3.6. Defatted powder of Arachis hypogaea L., semen (peanuts) – PALFORZIA (CAP) – EMA/R/0000264359

Applicant: Stallergenes

PRAC Rapporteur: Terhi Lehtinen

Scope: 5-year renewal of the marketing authorisation

18.3.7. Fenfluramine – FINTEPLA (CAP) – EMA/R/0000256601

Applicant: UCB Pharma

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

18.3.8. Hepatitis B surface antigen – HEPLISAV B (CAP) – EMA/R/0000271891

Applicant: Dynavax GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: 5-year renewal of the marketing authorisation

18.3.9. Icosapent ethyl – VAZKEPA (CAP) – EMA/R/0000275813

Applicant: Amarin Pharmaceuticals Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

18.3.10. Insulin aspart – KIRSTY (CAP) – EMA/R/0000276245

Applicant: Biosimilar Collaborations Ireland Limited

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.11. 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

18.3.12. Ofatumumab – KESIMPTA (CAP) – EMA/R/0000276182

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

18.3.13. Remimazolam – BYFAVO (CAP) – EMA/R/0000278275

Applicant: Paion Pharma GmbH

PRAC Rapporteur: Eamon O Murchu

Scope: 5-year renewal of the marketing authorisation

18.3.14. Risdiplam – EVRYSDI (CAP) – EMA/R/0000275338

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

18.3.15. Somapacitan – SOGROYA (CAP) – EMA/R/0000278080

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

18.3.16. Sunitinib – SUNITINIB ACCORD (CAP) – EMA/R/0000269316

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Amelia Cupelli

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 01-04 September 2025 PRAC meeting, which was held remotely.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Ulla Wändel Liminga	Chair	Sweden	No interests declared	
Jan Neuhauser	Member	Austria	No interests declared	
Sonja Radowan	Alternate	Austria	No interests declared	
Jean-Michel Dogné	Member	Belgium	No restrictions applicable to this meeting	
Jo Robays	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva	Member	Bulgaria	No interests declared	
Petar Mas	Member	Croatia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Barbara Kovacic Bytyqi	Alternate	Croatia	No interests declared	
Elena Kaisis	Member	Cyprus	No interests declared	
Panagiotis Psaras	Alternate	Cyprus	No interests declared	
Eva Jirsová	Member	Czechia	No interests declared	
Marie Louise Schougaard Christiansen	Member	Denmark	No interests declared	
Karin Erneholm	Alternate	Denmark	No interests declared	
Maia Uusküla	Member	Estonia	No interests declared	
Krõõt Aab	Alternate	Estonia	No interests declared	
Terhi Lehtine	Member	Finland	No interests declared	
Kimmo Jaakkola	Alternate	Finland	No interests declared	
Tiphaine Vaillant	Member	France	No interests declared	
Zoubida Amimour	Alternate	France	No participation in discussion, final deliberations and voting on:	15.3.25. EMA/VR/00002 79319 15.3.26. EMA/VR/00002 78256 16.1.21. EMA/PSUR/000 0269003 17.5.18. EMA/PAM/0000 281668 17.5.19. EMA/PAM/0000 280221 18.2.1. EMA/R/000028 1723

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				18.2.4. EMA/R/000028 2425
Martin Huber	Member	Germany	No interests declared	
Gabriele Maurer	Alternate	Germany	No interests declared	
Georgia Gkegka	Member	Greece	No interests declared	
Maria Poulianiti	Alternate	Greece	No participation in discussion, final deliberations and voting on:	4.2.2. EMEA/H/C/000 829/SDA/055; NAP 16.3.11. EMA/PSUR/000 0268942
Julia Pallos	Member	Hungary	No participation in discussion, final deliberations and voting on:	15.3.25. EMA/VR/00002 79319 15.3.26. EMA/VR/00002 78256 16.1.21. EMA/PSUR/000 0269003 17.5.18. EMA/PAM/0000 281668 17.5.19. EMA/PAM/0000 280221 18.2.1. EMA/R/000028 1723 18.2.4. EMA/R/000028 2425
Guðrún Stefánsdóttir	Member	Iceland	No participation in discussion, final deliberations and voting on:	15.2.3. EMA/VR/00002 67359 15.2.4. EMA/VR/00002 72344 15.2.9.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				EMA/VR/00002 74974 15.2.11. EMA/VR/00002 76333 15.3.15. EMEA/H/C/005 818/II/0012 18.2.5. EMA/R/000028 5162
Rhea Fitzgerald	Member	Ireland	No interests declared	
Eamon O Murchu	Alternate	Ireland	No interests declared	
Amelia Cupelli	Member	Italy	No interests declared	
Zane Neikena	Member	Latvia	No interests declared	
Diana Litenboka	Alternate	Latvia	No interests declared	
Rugile Pilviniene	Member	Lithuania	No restrictions applicable to this meeting	
Lina Seibokiene	Alternate	Lithuania	No interests declared	
Anne-Cecile Vuillemin	Member	Luxembourg	No interests declared	
John Joseph Borg	Member	Malta	No restrictions applicable to this meeting	
Benjamin Micallef	Alternate	Malta	No interests declared	
Liana Martirosyan	Member	Netherlands	No interests declared	
Bianca Mulder	Alternate	Netherlands	No interests declared	
David Olsen	Member	Norway	No participation in discussion, final	6.3.10. EMA/PSUR/000 0269018 16.1.43. EMA/PSUR/000 0269002

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			deliberations and voting on:	16.2.3. EMA/PSUR/0000268978 17.4.6. EMA/VR/0000279392 17.5.1. EMA/PAM/0000278528 17.5.23. EMA/PAM/0000273323
Pernille Harg	Alternate	Norway	No interests declared	
Adam Przybylkowski	Member	Poland	No restrictions applicable to this meeting	
Ana Sofia Diniz Martins	Member	Portugal	No interests declared	
Carla Torre	Alternate	Portugal	No restrictions applicable to this meeting	
Roxana Dondera	Member	Romania	No interests declared	
Irina Sandu	Alternate	Romania	No interests declared	
Anna Mareková	Member	Slovakia	No interests declared	
Miroslava Gocova	Alternate	Slovakia	No interests declared	
Polona Golmajer	Member	Slovenia	No interests declared	
Maria del Pilar Rayon	Member	Spain	No interests declared	
Monica Martinez Redondo	Alternate	Spain	No interests declared	
Mari Thorn	Member	Sweden	No restrictions	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			applicable to this meeting	
Karin Bolin	Alternate	Sweden	No restrictions applicable to this meeting	
Annalisa Capuano	Member	Independent scientific expert	No restrictions applicable to this meeting	
Milou-Daniel Drici	Member	Independent scientific expert	No restrictions applicable to this meeting	
Maria Teresa Herdeiro	Member	Independent scientific expert	No restrictions applicable to this meeting	
Patricia McGettigan	Member	Independent scientific expert	No restrictions applicable to this meeting	
Hedvig Marie Egeland Nordeng	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark	Member	Independent scientific expert	No restrictions applicable to this meeting	
Roberto Frontini	Member	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	7.1.1. EMA/PASS/0000253115 14.1.13. Galantamine (NAP) 15.2.8. EMA/VR/0000279282 15.3.13. EMA/VR/0000266281 15.3.32.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				EMA/VR/0000255553 17.2.19. EMA/PAM/0000248394 17.4.5. EMEA/H/C/000899/II/0061 17.5.30. EMA/PAM/0000281221
Yiannoula Koulla	Member	Patients' Organisation Representative	No interests declared	
Els Beghein	Expert	Belgium	No interests declared	
Piyush Jain	Expert	Belgium	No interests declared	
Chloé Wyndham-Thomas	Expert	Belgium	No restrictions applicable to this meeting	
Marian Hjortlund Allon	Expert	Denmark	No interests declared	
Alexander Braathen	Expert	Denmark	No interests declared	
Rita Chan Andersen	Expert	Denmark	No restrictions applicable to this meeting	
Nicklas Hasselblad Lundstrøm	Expert	Denmark	No interests declared	
Signe Hertz Hansen	Expert	Denmark	No interests declared	
Mette Hjorslev Knudgaard	Expert	Denmark	No interests declared	
Kirsten Egebjerg Juul	Expert	Denmark	No interests declared	
Lærke Nilausen	Expert	Denmark	No restrictions applicable to this meeting	
Helle Gerda Olsen	Expert	Denmark	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Moritz Sander	Expert	Denmark	No restrictions applicable to this meeting	
Per Sindahl	Expert	Denmark	No interests declared	
Indrek Soosaar	Expert	Estonia	No interests declared	
Helve Vestman	Expert	Estonia	No restrictions applicable to this meeting	
Henning Brohmann	Expert	Germany	No interests declared	
Dennis Lex	Expert	Germany	No interests declared	
Karin Seifert	Expert	Germany	No interests declared	
Tamás László Balázsa	Expert	Hungary	No interests declared	
Zsuzsanna Biro-Sandor	Expert	Hungary	No interests declared	
Clare Foley	Expert	Ireland	No interests declared	
Sheena Kennedy	Expert	Ireland	No restrictions applicable to this meeting	
Emer Maloney	Expert	Ireland	No interests declared	
Giulia Gritti	Expert	Italy	No interests declared	
Talip Eroglu	Expert	Netherlands	No restrictions applicable to this meeting	
Sara Khosrovani	Expert	Netherlands	No interests declared	
Sophia Venzke	Expert	Netherlands	No interests declared	
Anita Volkers	Expert	Netherlands	No interests declared	
Joao Fernandes	Expert	Portugal	No restrictions applicable to this meeting	
Ruxandra-Ana Moldoveanu	Expert	Romania	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Iulia-Maria Stanescu	Expert	Romania	No restrictions applicable to this meeting	
Roxana Stefania Udrescu	Expert	Romania	No interests declared	
María Martínez	Expert	Spain	No interests declared	
Charlotte Backman	Expert	Sweden	No interests declared	
Jolanta Gulbinovic	Expert	Sweden	No interests declared	
Maria Luttgen	Expert	Sweden	No restrictions applicable to this meeting	
Karin Nylén	Expert	Sweden	No interests declared	
Miriam Taekema	Expert	Sweden	No interests declared	
A representative from the European Commission attended the meeting				
Observers from WHO attended the meeting.				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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