12 December 2025
EMA/PRAC/375420/2025
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 27-30 October 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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

1. Introduction

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

The Chairperson opened the 27-30 October 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. No new or additional competing interests were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

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

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

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

1.2. Agenda of the meeting on 27-30 October 2025

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

1.3. Minutes of the previous meeting on 29 September – 02 October 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 29 September – 02 October 2025 were published on the EMA website on 21 November 2025 (EMA/PRAC/352486/2025).

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

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

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

See Annex I 14.1.

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

4.2. Signals follow-up and prioritisation

4.2.1. Adalimumab – AMGEVITA (CAP); AMSPARITY (CAP); HEFIYA (CAP); HUMIRA (CAP) - EMEA/H/C/000481/SDA/128; HUKYNDRA (CAP); HULIO(CAP); HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP); LIBMYRIS (CAP); YUFLYMA (CAP)

Applicant: AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita), Biosimilar Collaborations Ireland (Hulio), Celltrion Healthcare Hungary Kft. (Yuflyma), Fresenius Kabi Deutschland GmbH (Idacio), Pfizer Europe MA EEIG (Amsparity), Samsung Bioepis NL B.V. (Imraldi), Sandoz GmbH (Hefiya, Hyrimoz), STADA Arzneimittel AG (Hukyndra, Libmyris)

PRAC Rapporteur: Karin Bolin

Scope: Signal of morphoea

EPITT 20166 – Follow-up to May 2025

Background

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

Discussion

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

Summary of recommendation(s)

- The MAHs of adalimumab containing products with an obligation to submit PSURs should monitor this topic and present any new cases of morphoea received after 12 May 2025 in the next PSUR (data lock point 31 December 2025).

4.2.2. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/SDA/018; NAP

Applicant: Pfizer Europe MA EEIG, various

PRAC Rapporteur: Martin Huber

Scope: Signal of cutaneous vasculitis

EPITT 20184 – Follow-up to July 2025

Background

The MAH of Bosulif (bosutinib) replied to the request for information on the signal of cutaneous vasculitis and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance, literature and the responses of the MAH of Bosulif (bosutinib), PRAC agreed that there is sufficient evidence to support a causal association between bosutinib and cutaneous vasculitis. Therefore, the product information should be updated to add cutaneous vasculitis as an undesirable effect with a frequency 'uncommon'.

Summary of recommendation(s)

- The MAHs of bosutinib containing products should submit to EMA and/or to the relevant National Competent Authorities (NCAs) of the Member States, within 60 days, a variation to amend[3] the product information.

4.2.3. Datopotamab deruxtecan - DATROWAY (CAP) - EMEA/H/C/006547/SDA/002

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Mari Thorn

Scope: Signal of anaphylactic reaction

EPITT 20181 – Follow-up to July 2025

Background

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

Discussion

Having considered the available evidence in EudraVigilance, literature and the responses of the MAH, PRAC agreed that there is sufficient evidence to support a causal association between datopotamab deruxtecan and anaphylactic reaction. Therefore, the product information should be updated to include a warning on anaphylactic reactions and to add anaphylactic reaction as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAH for Datroway (datopotamab deruxtecan) should submit to EMA, within 60 days, a variation to amend[4] the product information.

4.2.4. Epcoritamab - TEPKINLY (CAP) - EMEA/H/C/005985/SDA/005

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Signal of hypogammaglobulinaemia

EPITT 20174 – Follow-up to June 2025

Background

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

Discussion

Having considered the available evidence in EudraVigilance, literature and the responses of the MAH, PRAC agreed that there is sufficient evidence to support a causal association between epcoritamab and hypogammaglobulinaemia. Therefore, the product information should be updated to include hypogammaglobulinaemia as a warning and as an undesirable effect with a frequency 'very common' for all grades and 'uncommon' for grades 3-4.

[3] Update of section 4.8. The package leaflet is updated accordingly.
[44] Update of sections 4.4 and 4.8. The package leaflet is updated accordingly.

Summary of recommendation(s)

- The MAH for Tepkinly (epcoritamab) should submit to EMA, within 60 days, a variation to amend[5] the product information.

4.2.5. Sulfasalazine (NAP)

Applicant(s): various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of idiopathic intracranial hypertension (Pseudotumor cerebri)

EPITT 20188 – Follow-up to July 2025

Background

The MAH Pfizer replied to the request for information on the signal of idiopathic intracranial hypertension (Pseudotumor cerebri) and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance, literature and the response of the MAH, PRAC has concluded that the current evidence is insufficient to establish a causal relationship between sulfasalazine and idiopathic intracranial hypertension (pseudotumor cerebri syndrome) to further warrant an update to the product information and/or risk management plan at present.

Summary of recommendation(s)

- The MAHs of sulfasalazine containing medicinal products should monitor this topic in the next PSUR and present and discuss new cases of idiopathic intracranial hypertension (pseudotumor cerebri syndrome) assessed as possibly or probably related to treatment, including case narratives and a causality assessment.

4.3. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

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

5.1.1. Acellular pertussis vaccine (CAP MAA) - EMEA/H/C/006304

Scope (pre opinion phase): Indicated for booster immunisation against pertussis of individuals 12 years of age and older, passive protection against pertussis in early infancy following maternal immunisation during pregnancy

5.1.2. Estetrol (CAP MAA) - EMEA/H/C/006213

Scope (pre D-180 phase): Hormone replacement therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women

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

Scope (pre D-210 phase): Treatment of schizophrenia, acute treatment of manic or mixed episodes associated with bipolar I disorder

5.1.4. Semaglutide (CAP MAA) - EMEA/H/C/006426

Scope (pre D-180 phase): Treatment of non-cirrhotic metabolic dysfunction-associated steatohepatitis with liver fibrosis

5.1.5. Trivalent influenza vaccine (recombinant, prepared in cell culture) (CAP MAA) - EMEA/H/C/006674

Scope (pre D-180 phase): Immunisation for the prevention of influenza disease

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

See also Annex I 15.2.

5.2.1. 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 tenofovir disoproxil fumarate) concerning (1) Renal events including tubulopathy, and (2) Bone events due to proximal renal tubulopathy/loss of bone mineral density.

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 tenofovir disoproxil fumarate), and consequently remove 'Antiretroviral Pregnancy Registry' listed as a Category 3 Additional Pharmacovigilance Activity.

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 Truvada, a centrally authorised medicine containing emtricitabine/tenofovir disoproxil, to update the RMP to remove the targeted questionnaires concerning renal and bone events and to remove missing information concerning safety in pregnancy and lactation, and consequently to remove 'Antiretroviral Pregnancy Registry' listed as a category 3 study 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 20.0 for Truvada (emtricitabine/tenofovir disoproxil) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.
- PRAC agreed with the removal of specific adverse reaction follow-up questionnaires related to bone events and renal toxicity and considered that the events related to these two risks should continue to be closely monitored through routine pharmacovigilance. In addition, PRAC agreed with the removal of safety in pregnancy and safety in lactation from the list of safety concerns in the RMP, as well as with the removal of the 'Antiretroviral Pregnancy Registry' listed as a category 3 study in the RMP. These two aspects will continue to be monitored through routine pharmacovigilance and captured in future PSURs. Finally, PRAC noted that the product information on breastfeeding may require further revision, considering the current data available regarding the excretion of emtricitabine and tenofovir disoproxil into breast milk, as well as their use during breastfeeding. Therefore, the MAH should review the current data on breastfeeding and propose an update to the relevant information in the product information as part of the next PSUR submission.

5.2.2. Leflunomide – ARAVA (CAP) – EMA/VR/0000264105

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of an updated RMP version 6.0 in order to address query raised by PRAC EMEA/H/C/PSUSA/00001837/202309 on the effectiveness and usefulness of the additional risk minimization measures (aRMMs) specifically related to the safety concerns hepatic reactions, blood cytopenia, and infections.

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 Arava, a centrally authorised medicine containing leflunomide, to update the RMP regarding the effectiveness and usefulness of the additional risk minimization measures (aRMMs) specifically related to the safety concerns hepatic reactions, blood cytopenia, and infections. 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 for Arava (leflunomide) in the context of the variation procedure under evaluation by PRAC and CHMP could be considered acceptable provided that an update to RMP version 6.0 is submitted.
- PRAC concluded that the following safety concerns should be removed from the RMP: hepatic reactions, blood cytopenia, and infections. Consequently, PRAC considered that these concerns should be removed from the additional risk minimisation measures (aRMMs) for healthcare professionals and that these risks can be adequately monitored in PSURs. In addition, PRAC generally endorsed the proposed revisions to Annex II-D; however, certain amendments were requested to the key elements of the patient information sheet and the healthcare professional guide. Furthermore, PRAC considered that the MAH should further evaluate and discuss the necessity of implementing additional risk minimisation measures directed at healthcare professionals to address teratogenicity and male-mediated fetal toxicity.

5.2.3. 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.

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 Viread, a centrally authorised medicine containing tenofovir disoproxil, to update the RMP 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. 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 27.0 for Viread (tenofovir disoproxil) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.
- PRAC agreed to remove the 'safety in pregnancy and lactation' as missing information from the list of safety concerns, as well as to remove the 'Antiretroviral Pregnancy Registry' (APR) as category 3 study from the RMP. Additionally, PRAC agreed to remove from the RMP the following safety concerns: safety in patients with renal impairment, renal toxicity and bone events due to proximal renal tubulopathy/loss of bone mineral

density (BMD). Moreover, PRAC supported the removal of additional pharmacovigilance activities and specific adverse reaction follow-up questionnaires related to bone events and renal toxicity and considered that the events related to these two risks should continue to be closely monitored through routine pharmacovigilance. Finally, PRAC noted that the product information on breastfeeding may require further revision, considering the current data available regarding the excretion of emtricitabine and tenofovir disoproxil into breast milk, as well as their use during breastfeeding. Therefore, the MAH should review the current data on breastfeeding and propose an update to the relevant information in the product information as part of the next PSUR submission.

5.2.4. Valoctocogene roxaparvovec – ROCTAVIAN (CAP) – EMA/VR/0000294531

Applicant: Biomarin International Limited

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an updated RMP version 1.6 in order to remove the Biodistribution study investigating vertical transmission of the AAV5 vector in female mice listed as category 3 study in RMP.

Background

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

PRAC is evaluating a type II variation procedure for Roctavian, a centrally authorised medicine containing valoctocogene roxaparvovec, to update the RMP to remove the biodistribution study investigating vertical transmission of the AAV5 vector in female mice listed as category 3 study. 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.

S**ummary of advice**

- The RMP version 1.6 for Roctavian (valoctocogene roxaparvovec) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.
- PRAC agreed to remove the biodistribution study investigating vertical transmission of the AAV5 vector in female mice listed as category 3 study in the RMP.

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

See also Annex I 15.3.

5.3.1. Finerenone – KERENDIA (CAP) – EMA/X/0000248026

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new strength 40 mg for film-coated tablets grouped with a type II variations C.I.6: Extension of indication to include the treatment of symptomatic chronic heart failure with left ventricular ejection fraction (LVEF) ≥ 40% in adults for KERENDIA, based on final results from the phase 3 study FINEARTS-HF (20103); this is a randomized, double-blind, placebo-controlled phase 3 study evaluating the efficacy and safety of finerenone on morbidity and mortality in participants with symptomatic heart failure with left ventricular ejection fraction (LVEF) ≥40%.; Type II variation C.I.13: Submission of the final report from non-clinical study T105281-7, R-14405 - Juvenile toxicology study in rats; Type IB variation C.I.z: Minor correction of numbers in the currently approved SmPC due to a previously communicated GCP violation affecting the FIDELIO-DKD and FIGARO-DKD trials.

As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 5.3, 6.1, 6.6 and 8 of the SmPC are updated. The Labelling and Package Leaflet are updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial and administrative changes to the PI and to bring it in line with the latest QRD template version 10.4.

Background

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

CHMP is evaluating a line extension procedure for Kerendia, a centrally authorised product containing finerenone, to introduce a new strength 40 mg for film-coated tablets, and to extend the indication to include the treatment of symptomatic chronic heart failure with left ventricular ejection fraction (LVEF) ≥ 40% in adults. 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 Kerendia (finerenone) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 3.2 is submitted.
- PRAC considered that no updates of the list of safety concerns are needed. Regarding the pharmacovigilance plan, PRAC agreed that routine pharmacovigilance activities are sufficient to further characterise the safety profile of the medicinal product. Finally, PRAC concluded that routine risk minimisation measures (RMMs) are sufficient to minimise the risks of the medicinal product.

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. Apremilast – OTEZLA (CAP) – EMA/PSUR/0000282235

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Evaluation of a PSUSA procedure (PSUSA/00010338/202503)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Otezla, a centrally authorised medicine containing apremilast 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 Otezla (apremilast) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the current warning regarding psychiatric disorders and to add anxiety and mood altered as undesirable effects with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[6].
- In the next PSUR, the MAH should closely monitor cases of hepatic disorders, with a focus on cases with hepatic enzyme increase related terms, and provide a critical appraisal of relevant cases, including cases with laboratory data, suggestive of drug-induced liver injury (DILI), and with a fatal outcome.

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

6.1.2. Dimethyl fumarate – TECFIDERA (CAP); diroximel fumarate - VUMERITY (CAP) – EMA/PSUR/0000282247

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010143/202503)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tecfidera and Vumerity, centrally authorised medicines containing dimethyl fumarate and diroximel fumarate respectively, 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 Tecfidera and Vumerity in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.

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

- In the next PSUR, the MAH should further assess a possible association between Vumerity or Tecfidera and tachyarrhythmia, as well as between Vumerity or Tecfidera and gastrointestinal perforation, ulcer, haemorrhage and obstruction, and discuss any new findings. In addition, the MAH should continue to monitor cases of malignancies (including but not limited to non-melanoma skin cancer) as important potential risk in the PSUR and report new significant information, as well as include any newly available literature on breastfeeding.

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

6.1.3. Dimethyl fumarate – SKILARENCE (CAP) – EMA/PSUR/0000282230

Applicant: Almirall S.A.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010647/202503)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Skilarence, a centrally authorised medicine containing dimethyl fumarate 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 Skilarence (dimethyl fumarate) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should further assess whether there is any association between Skilarence and gastrointestinal perforation, ulcer, haemorrhage and obstruction and discuss any new findings.

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

6.1.4. Epcoritamab – TEPKINLY (CAP) – EMA/PSUR/0000282231

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Evaluation of a PSUSA procedure (PSUSA/00000107/202503)

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Tepkinly (epcoritamab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning of haemophagocytic lymphohistiocytosis (HLH) and to add HLH as undesirable effect with a frequency 'uncommon' for all grades, and frequency 'rare' for grade 3-4. Therefore, the current terms of the marketing authorisation(s) should be varied[7].
- In the next PSUR, the MAH should provide a critical analysis of long-term cases related to cutaneous malignancies, considering the physiopathology of the underlying disease. The MAH should also provide an analysis of cases of cytokine release syndrome, including cases of HLH and immune effector cell-associated haemophagocytic lymphohistiocytosis-like syndrome (IEC-HS), considering the appropriate definition to be used in each case. In addition, the MAH should provide an analysis of cases of infections not listed in the product information to assess any new risk aspects, explain possible reasons for prophylactic failure in fatal cases despite antimicrobial use, and describe actions taken with epcoritamab when infection is suspected.

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. Nemolizumab – NEMLUVIO (CAP) – EMA/PSUR/0000282252

Applicant: Galderma International

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011111/202503)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Nemluvio, a centrally authorised medicine containing nemolizumab 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 Nemluvio (nemolizumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add bullous pemphigoid as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[8].
- In the next PSUR, the MAH should further monitor the risk of eczematous reactions, focusing on new/more severe aspects of eczematous reactions beyond the ones presented in the product information, including monitoring of cases of dermatitis exfoliative generalised. In addition, the MAH should carefully review the cases reporting device malfunctioning and analyse if these cases are indicative of product issues, and if actions are needed to address them.

[7] Update of SmPC sections 4.4 and 4.8 The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[8] 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. The frequency of submission of the subsequent PSURs should be changed from 6-monthly to yearly and the list of Union reference dates (EURD list) will be updated accordingly.

6.1.6. Olipudase alfa – XENPOZYME (CAP) – EMA/PSUR/0000282268

Applicant: Sanofi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00011003/202503)

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Xenpozyme (olipudase alfa) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing warning regarding hypersensitivity/anaphylaxis and the descriptive text of the existing adverse reaction: infusion-associated reactions (IARs), including hypersensitivity/anaphylactic reaction. Therefore, the current terms of the marketing authorisation(s) should be varied[9].
- In the next PSUR, the MAH should provide an evaluation of the risk of medication errors in the home setting using data from all sources, and outline a plan to collect further information on desensitisation procedures and their outcomes.

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

6.1.7. Retifanlimab – ZYNYZ (CAP) – EMA/PSUR/0000282291

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011059/202503)

Background

[9] Update of SmPC sections 4.4 and 4.8. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Zynyz, a centrally authorised medicine containing retifanlimab 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 Zynyz (retifanlimab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding patients with pre-existing autoimmune disease. Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAH should assess causality for new cases of immune-mediated, infusion-related, and anaphylactic reactions, and monitor and discuss new cases of autoimmune disease flares, scleroderma, systemic sclerosis, morphea, related adverse events, and thrombotic microangiopathy (TMA).

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.

6.1.8. Sotatercept – WINREVAIR (CAP) – EMA/PSUR/0000282250

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00011076/202503)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Winrevair, a centrally authorised medicine containing sotatercept 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 Winrevair (sotatercept) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add pericardial effusion as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[11].
- In the next PSUR, the MAH should continue monitoring cases of severe thrombocytopenia without an alternative cause or prostacyclin analogue association, as well as serious bleeding cases with prior or concurrent telangiectasia. In addition, as pericardial effusion is now considered an important identified risk in the PSUR, the MAH should provide an updated review covering severity, risk factors, dose dependency, appropriate management, frequency, potential mechanism of action, and discuss whether the product information should be updated.

[10] 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
[11] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

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

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

See Annex I 16.2.

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

See also Annex I 16.3.

6.3.1. Clomipramine (NAP) – EMA/PSUR/0000282228

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000811/202503)

Background

Clomipramine is a tricyclic antidepressant indicated for the treatment of symptoms of obsessive-compulsive disorder, as well as for the management of depression, panic disorder and certain anxiety-related conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing clomipramine 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 clomipramine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add cardiomyopathy and cardiac failure as undesirable effects with a frequency 'not known'. In addition, the product information should be updated to add a warning regarding cardiac septal defects in the offspring after in utero exposure, as well as a warning regarding *status cataplecticus* upon clomipramine withdrawal. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAHs should provide a cumulative review of cases of h*epatic disorders* in association with clomipramine, including data from literature, clinical studies and post-marketing setting. The MAHs should also closely monitor the risk of dilated cardiomyopathy in the next PSUR.

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

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. Clozapine (NAP) – EMA/PSUR/0000282232

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000836/202503)

Background

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

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing clozapine 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 clozapine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning on the risk of appendicitis related to the anticholinergic effects of clozapine and to include appendicitis as an undesirable effect with a frequency 'not known', as well as to add haematological malignancy as an undesirable effect with a frequency' not known'. In addition, the product information should be updated to add a warning on drug reaction with eosinophilia and systemic syndrome (DRESS) and to include drug-drug interaction with valproic acid and the associated increased risk of clozapine-induced myocarditis. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- In the next PSUR, the MAHs should provide cumulative reviews of cases of eosinopenia, hypogammaglobulinemia, hypothermia and related events and interactions between clozapine and tobacco smoking, including pharmacokinetic and therapeutic drug monitoring data, as well as clinical outcomes, if available.

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

6.3.3. Codeine / paracetamol (NAP) – EMA/PSUR/0000282209

Applicants: various

PRAC Lead: Veronika Macurova

[13] 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

Scope: Evaluation of a PSUSA procedure (PSUSA/00000851/202503)

Background

Codeine is a centrally acting weak narcotic analgesic and paracetamol is a non-opioid analgesic and antipyretic. Codeine/paracetamol is a fixed dose combination indicated for the use in patients older than 12 years of age for the symptomatic treatment of acute moderate pain (e.g. headache, migraine, muscle ache, dysmenorrhoea, sore throat, musculoskeletal pain, sciatica, pain associated with sinusitis, neuralgia, pain after dental procedures/ tooth extraction, toothache, pain of osteoarthritis) which cannot be relieved by other analgesics such as paracetamol or ibuprofen (alone).

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of codeine/paracetamol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing warning on the risk of drug dependency/drug abuse and to add warnings regarding central sleep apnoea (CSA) and hyperalgesia. In addition, sphincter of Oddi dysfunction should be added as undesirable effect with frequency 'not known' (unless a different frequency is already specified in the product information, in which case that should be retained). Finally, the product information should be amended to add the drug-drug interaction with gabapentinoids and to highlight the need to store the product in a safe and secure place. Therefore, the current terms of the marketing authorisation(s) should be varied[14].

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

6.3.4. Metoprolol (NAP) – EMA/PSUR/0000282258

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002039/202503)

Background

Metoprolol is a β-1-selective adrenoreceptor blocking agent indicated for the treatment of hypertension, angina pectoris, disturbances of cardiac rhythm, maintenance treatment after myocardial infarction, functional heart disorders with palpitations and migraine prophylaxis.

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

[14] 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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of metoprolol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding the risk of severe hypoglycaemia following the concomitant administration of beta-blockers and sulfonylureas. Therefore, the current terms of the marketing authorisation(s) should be varied[15].

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

6.3.5. Prazepam (NAP) – EMA/PSUR/0000282243

Applicants: various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00002502/202503)

Background

Prazepam is a benzodiazepine derivative indicated for the management of anxiety or tension states and short-term relief of anxiety symptoms, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing prazepam 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 prazepam-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning regarding the risk of falls in elderly patients due to sedation and/or musculoskeletal weakness. Therefore, the current terms of the marketing authorisation(s) should be varied[16].
- In the next PSUR, the MAHs Pfizer and Alfasigma should provide a cumulative review of cases of prolonged neurological and persistent withdrawal symptoms from all sources, including data from literature, and discuss whether the current product information and risk minimization measures adequately reflect these long-term risks.

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.

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

6.3.6. Rifampicin (NAP) – EMA/PSUR/0000282245

Applicants: various

PRAC Lead: Maria Popova-Kiradjieva

Scope: Evaluation of a PSUSA procedure (PSUSA/00002640/202503)

Background

Rifampicin is a semi-synthetic antibiotic with bactericidal activity against mycobacteria and Gram-positive microorganisms indicated for the treatment of infections caused by susceptible strains of microorganisms.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing rifampicin 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 rifampicin-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add information about the drug-drug interaction between rifampicin and antivirals for treatment of hepatitis C virus infections such as sofosbuvir, as well as between rifampicin and antiretrovirals such as cabotegravir, fostemsavir, lenacapavir, as this leads to significant decrease in their plasma concentrations and loss of therapeutic effect. Moreover, a contraindication regarding concomitant use of rifampicin with these medicinal products should be added to the product information. Finally, the product information should be updated to add a warning regarding the possibility of paradoxical drug reaction following treatment with rifampicin and the appropriate therapeutic behaviour if a paradoxical response is suspected and to include paradoxical drug reaction as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[17].
- In the next PSUR, the MAHs should closely monitor cases of carcinogenicity, congenital malformations and impaired fertility.

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

6.3.7. Rocuronium (NAP) – EMA/PSUR/0000282292

Applicants: various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00002656/202502)

Background

[17] Update of SmPC sections 4.3, 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

Rocuronium is a fast-onset, intermediate acting, non-depolarizing neuromuscular blocking agent indicated in adults and paediatric patients as an adjunct to general anaesthesia to facilitate tracheal intubation during routine sequence induction, and to provide skeletal muscle relaxation during surgery. Additionally, in adults, it is indicated during rapid sequence induction and as an adjunct in the intensive care unit (ICU) to facilitate intubation and mechanical ventilation.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing rocuronium 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 rocuronium-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding hypertensive crisis in patients with known or latent phaeochromocytoma and to include information about hypersensitivity reactions also for sugammadex-rocuronium complex. Therefore, the current terms of the marketing authorisation(s) should be varied[18].
- In the next PSUR, the MAHs should further monitor and discuss the available scientific evidence regarding the administration of rocuronium in patients with chromaffin cell tumours (pheochromocytoma or paraganglioma) and assess whether there is a need to update the product information based on the available data.

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.

6.3.8. Selegiline (NAP) – EMA/PSUR/0000282210

Applicants: various

PRAC Lead: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00002688/202503)

Background

Selegiline is a monoamine oxidase B inhibitor indicated, as monotherapy or in combination with levodopa (with or without a peripheral decarboxylase inhibitor), for the treatment of Parkinson’s disease (PD) or symptomatic parkinsonism.

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

Summary of recommendation(s) and conclusions

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of selegiline-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include information about the drug-drug interaction between selegiline and serotonin agonists. In addition, the product information should be updated to add impulse control disorders and compulsions as undesirable effects with a frequency 'not known', specifying individual examples of impulse control disorders. Therefore, the current terms of the marketing authorisation(s) should be varied[19].
- In the next PSUR, the MAHs should provide data related to the recommendation to start treatment with serotonin agonists (e.g. sumatriptan, naratriptan, zolmitriptan, rizatriptan, lasmiditan) no earlier than 24 hours after discontinuation of selegilin.

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

6.3.9. Tranexamic acid (NAP) – EMA/PSUR/0000282254

Applicants: various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00003006/202503)

Background

Tranexamic acid is an antifibrinolytic and it is indicated in adults and children from one year in prevention and treatment of haemorrhages due to general or local fibrinolysis, and more specifically, for the treatment of haemorrhage caused by general or local fibrinolysis such as menorrhagia and metrorrhagia, gastrointestinal bleeding, haemorrhagic urinary disorders, further to prostate surgery or other surgical procedures, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing tranexamic 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 tranexamic acid-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, in view of the available data on adverse reactions, including fatal outcomes, following incorrect route of product administration via the intrathecal route, the product information of products for intravenous administration of tranexamic acid should be updated to strengthen the warnings that tranexamic acid injections should only be administered intravenously, to add a new contraindication regarding epidural use of tranexamic acid, and to add warnings on the risk of medication errors associated with incorrect route of administration and that syringes containing tranexamic acid

[19] Update of SmPC sections 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

should be clearly labelled with the intravenous route of administration. Particulars to appear on the outer packaging should be updated to reinforce information on the correct route of administration.

- PRAC also agreed the distribution of a direct healthcare professional communication together with a communication plan to raise awareness of the potential for serious including fatal adverse reactions due to inadvertent intrathecal administration and the recommended actions for risk minimisation.
- In addition, the product information of products containing tranexamic acid should be updated to add acute renal cortical necrosis and fixed drug eruption as undesirable effects with a frequency 'not known' *(*unless a different frequency is already specified in the product information, in which case that should be retained). Therefore, the current terms of the marketing authorisation(s) should be varied[20].
- In the next PSUR, the MAH should continue monitoring cases of myocardial infarction, in particular acute myocardial infarction, and discuss any new information on this topic. In addition, all MAHs of intravenous tranexamic acid products should include 'medication errors due to incorrect route of administration' as an important identified risk in the safety concerns in the PSUR and present any new relevant information in the next PSUR.

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

6.3.10. Varicella vaccine (live) (NAP) – EMA/PSUR/0000282219

Applicants: various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010473/202503)

Background

Varicella vaccine (live) is a lyophilised preparation of the live attenuated Oka strain of varicella-zoster virus, intended for active immunisation against varicella in healthy individuals from the age of 9 or 12 months.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing varicella vaccine 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 varicella vaccine-containing medicinal products (except Varilrix) in the approved indication(s) remains unchanged. The current terms of the marketing authorisation(s) should be maintained.

[20] Update of SmPC sections 4.2, 4.3, 4.4, and 6.6 for intravenous formulations only, and section 4.8 for intravenous and oral formulations. The package leaflet and outer packaging are 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 Varilrix (varicella vaccine) in the approved indication(s) remains unchanged. Nevertheless, the product information should be updated to amend the existing warning regarding individuals at high risk of severe varicella, removing the recommendation of a fixed waiting period between discontinuation of immunosuppressive therapy/chemotherapy and the administration of live attenuated vaccines such as Varilrix, as it might be too short for some patients. Therefore, the current terms of the marketing authorisation(s) should be varied[21].
- In the next PSUR, the MAHs should continue to provide a review of fatal cases, regardless of whether a new signal or safety concern is identified, and should carefully monitor the amount of fatal cases involving patients under immunosuppressive therapy. Also, the MAHs should continue to monitor the literature and discuss any update on the impact of universal varicella vaccination on herpes zoster epidemiology.

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

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

See Annex I 16.5.

6.6. Expedited summary safety reviews[22]

None

7. Post-authorisation safety studies (PASS)

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

See Annex I 17.1.

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

See Annex I 17.2.

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

See Annex I 17.3.

[21] Update of SmPC section 4.4. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position
[22] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC
[23] In accordance with Article 107n of Directive 2001/83/EC
[24] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004
[25] In accordance with Article 107p-q of Directive 2001/83/EC

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

See also Annex I 17.4.

7.4.1. Abatacept – ORENCIA (CAP) – EMA/VR/0000287898

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: A grouped application consisting of:

C.I.13: Submission of the final report from study IM101803 listed as a category 3 study in the RMP. This is a nationwide post-marketing study on the safety of abatacept treatment in Denmark using the DANBIO register. The RMP version 29.0 has also been submitted.

C.I.13: Submission of the final report from study IM101816 listed as a category 3 study in the RMP. This is a nationwide post-marketing study on the safety of abatacept treatment in Sweden using the ARTIS Register. The RMP version 29.0 has also been submitted.

Background

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

As stated in the RMP of Orencia (abatacept), the MAH conducted two non-imposed non-interventional PASS (IM101803 and M101816) to assess the safety of abatacept treatment in Denmark (DANBIO register) and Sweden (ARTIS register). The Rapporteur assessed the MAH's final study reports.

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 RSI.
- PRAC agreed with the removal of malignancies from the list of safety concerns, as well as with the removal of the two completed PASSs from the RMP. However, PRAC considered that the product information should be amended to reflect the key results of PASS studies IM101803 and IM101816 regarding the risk of non-melanoma skin cancer (NMSC) (basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)) and that the MAH should provide a proposal for such update, in line with the PRAC's RSI. Finally, PRAC considered that the MAH should reassess whether infusion- and injection-related hypersensitivity reactions with abatacept are still justified to be classified as an important identified risks in the RMP and, consequently, whether continuation of additional RMM (as part of the patient card) to mitigate these risks is still needed.

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

See Annex I 17.5.

[26] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

7.6. New Scientific Advice

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

7.7. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1.

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2.

8.3. Renewals of the marketing authorisation

See Annex I 18.3.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

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. Hydrocortisone (NAP); hydrocortisone sodium succinate (NAP); methylprednisolone (NAP); methylprednisolone acetate (NAP); methylprednisolone sodium succinate (NAP); prednisolone (NAP); dexamethasone sodium phosphate (NAP) - SE/H/xxxx/WS/873

Applicant: Pfizer AB (Cortef, Solu-Cortef, Medrol, Depo-Medrol, Solu-Medrol, Prednisolon Pfizer, Dexamethasone Phosphate)

PRAC Lead: Mari Thörn

Scope: PRAC consultation on a worksharing variation procedure (SE/H/xxxx/WS/873) to update the product information of all the systemic corticosteroids (methylprednisolone, prednisolone, hydrocortisone and dexamethasone) regarding panniculitis, at request of Sweden.

Background

Methylprednisolone, prednisolone, hydrocortisone and dexamethasone are systemic corticosteroids indicated for the treatment of inflammatory and autoimmune conditions, allergic reactions, and as part of immunosuppressive therapy.

In the context of the evaluation of a worksharing variation procedure on the need to update the product information of methylprednisolone, prednisolone, hydrocortisone and dexamethasone regarding panniculitis, Sweden requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC agreed that the product information of methylprednisolone, prednisolone, hydrocortisone and dexamethasone should be updated to add panniculitis as an undesirable effect with a frequency 'not known'. Moreover, PRAC concluded that the occurrence of panniculitis is a class effect for corticosteroids and that similar updates of product information for applicable steroid-containing medicinal product might be considered in the relevant upcoming procedures.

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

12.1.2. The Chair welcomed Dirk Mentzer, as the new alternate for Germany and Stanislav Stoilov as the new alternate for Bulgaria. Chair also informed the committee about swapping of roles in Cyprus delegation - Panagiotis Psaras became member and Elena Kaisis became alternate.Vote by proxy

Julia Pallos gave a proxy to Maria Popova-Kiradjieva and Rugile Pilviniene gave a proxy to Zane Neikena, covering the entire meeting.

12.1.3. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q3 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 Q3 2025 of PRAC meetings.

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. Methodology Working Party (MWP) - Guideline on predictive biomarker assay development in the context of medicinal product lifecycle

The EMA Secretariat presented the draft guideline on predictive biomarker assay development within the medicinal product lifecycle, aiming to provide scientific and regulatory guidance for biomarker-driven therapies. The guideline addresses analytical and clinical validation requirements, regulatory considerations under the European framework, and the interface with IVDR for companion diagnostics. It covers scenarios from exploratory biomarker use to candidate CDx development, multi-marker panels, bridging studies, and

post-authorisation follow-up. PRAC members were invited to provide their comments on the draft guideline by 5 December 2025.

12.4. Cooperation within the EU regulatory network

12.4.1. Health threats and EMA Emergency Task Force (ETF) activities - update

The EMA Secretariat provided PRAC with an update on the development of vaccines for the prevention of *B. pertussis* infection, combined influenza and COVID-19 mRNA vaccines, as well as information on the spread of Rift Valley fever, including its transmission and mortality rates. PRAC noted the information.

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. PRAC workload statistics – Q3 2025

The EMA secretariat informed PRAC about the quarterly and cumulative figures to estimate the evolution of the PRAC workload for Q3 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

12.9.1. Pharmacovigilance inspections - 2025 CAP Inspection Programme Revision

The EMA Secretariat presented an outline of a revision of the CAP inspection programme, focusing on activities to help improving efficiency such as introducing a new risk assessment tool that allows flexible inspection intervals based on compliance status, better resource allocation and enhanced collaboration among Member States. The EMA Secretariat also provided an update on the Pharmacovigilance Inspectors Working Group (PhV IWG) activities, including upcoming revisions to GVP Modules, alongside training initiatives. PRAC noted the information

12.9.2. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Petar Mas

The topic was postponed for the next plenary meeting.

12.10.3. PSURs repository

None

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

In line with the criteria for plenary presentation of updates to the EURD List adopted by PRAC in December 2021, PRAC endorsed the draft revised EURD list, version November 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 November 2025, the updated EURD list was adopted by CHMP and CMDh at their November 2025 meetings and published on the EMA website, see: Home> Human Regulatory>Post-authorisation>Pharmacovigilance>Periodic safety update reports>> List of Union reference dates and frequency of submission of periodic safety update reports (PSURs)

12.11. Signal management

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

PRAC lead: The EMA Secretariat and the Co-Chair of the SMART WG on processes presented the outcome of the WG discussions on the national distribution of the DHPCs, as well as some key clarifications on the end of EudraVigilance signal detection pilot by the MAHs following the Implementing Regulation (EU) 2025/1466, amending Implementing Regulation 520/2012. PRAC noted the information.

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. Introducing the new Early Notification System (ENS) portal

The EMA Secretariat presented PRAC the new Early Notification System (ENS) portal, a secure platform for sharing emerging safety and non-safety information within the EU regulatory network. The portal is designed to streamline communication, deliver tailored notifications and provide advanced search capabilities. It is scheduled to go live in November 2025 following user acceptance testing in October. PRAC noted the information.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[27]

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[28].

[27] 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

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

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Nemolizumab – NEMLUVIO (CAP)

Applicant: Galderma International

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of erythema multiforme

EPITT 20207 – New signal

14.1.2. Selumetinib – KOSELUGO (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Signal of photosensitivity reaction

EPITT 20208 – New signal

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. Teriparatide (CAP MAA) - EMEA/H/C/006688

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

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

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

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

Applicants: 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. Ceftazidime / Avibactam – ZAVICEFTA (CAP) – EMA/VR/0000287802

Applicant: Pfizer Ireland Pharmaceuticals Unlimited Company

PRAC Rapporteur: Rugile Pilviniene

Scope: Submission of an updated RMP version 3.4 in order to propose the reclassification of the following safety concerns: Removal of 'Bacterial resistance development' as an Important potential risk and the removal of Missing Information 'Pregnancy exposure', 'Lactation exposure', and 'Immunocompromised population exposure.'

15.2.3. Denosumab – PROLIA (CAP) – EMA/VR/0000288149

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of an updated RMP version 33.0 in order to remove and reclassify important identified risks, potential risks, and to remove completed category 3 Study 20090522. Update in RMP of the information about Patient reminder cards for osteonecrosis of the jaw have been reflected in Annex II of the PI.

15.2.4. Ipilimumab - YERVOY (CAP); nivolumab – OPDIVO (CAP) – EMA/VR/0000285155

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: To extend the due date related to the PAES study CA2098Y8, listed in the Product Information (PI) Annex II and in the RMP from 26.02.2026 to 28.02.2027.

15.2.5. Mepolizumab – NUCALA (CAP) – EMA/VR/0000291438

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of an updated RMP version 15 following procedure EMA/CHMP/PRAC/525630/2024.

15.2.6. Ocrelizumab – OCREVUS (CAP) – EMA/VR/0000291534

Applicant: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of an updated RMP version 13.0 in order to add non-infectious colitis as an important potential risk along with an additional pharmacovigilance activity in the form of a voluntary Category 3 non-interventional post-authorization study to further characterize this risk.

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

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of adolescent patients (12 to less than 18 years) with severe alopecia areata for OLUMIANT, based on results from study I4V-MC-JAIO; this is a Phase 3, double-blind, randomised, placebo-controlled trial to evaluate the efficacy, safety, and pharmacokinetics of baricitinib in children from 6 years to less than 18 years of age with alopecia areata. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 26.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI and to update the list of local representatives in the Package Leaflet.

15.3.2. Bempedoic acid – NILEMDO (CAP); bempedoic acid / ezetimibe - NUSTENDI (CAP) – EMA/VR/0000284929

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

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

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

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include treatment of adults and adolescents with hypereosinophilic syndrome (HES) for FASENRA, based on interim results from study D3254C00001 (NATRON); this is a multicentre, randomised, double-blind, parallel-group, placebo-controlled, 24-week phase III study with an open-label extension to evaluate the efficacy and safety of benralizumab in patients with HES; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce editorial and administrative updates to the PI and to update the list of local representatives in the Package Leaflet. Furthermore, section 6.5 of the SmPC was updated.

15.3.4. Darunavir / Cobicistat / Emtricitabine / Tenofovir alafenamide – SYMTUZA (CAP) – EMA/X/0000248421

Applicant: Janssen Cilag International

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension application to add a new strength of 675 mg/150 mg/20mg/10 mg film-coated tablets grouped with an Extension of indication (C.I.6) to include treatment of human immunodeficiency virus type 1 (HIV 1) infection in paediatric patients (aged 6 years and older with body weight at least 25 kg) for SYMTUZA, based on the 24-week interim results from study GS-US-216-0128 (Cohort 2); this is a Phase II/III, multicenter, open-label, multicohort interventional study evaluating efficacy, safety, and pharmacokinetics of Cobicistat-boosted Atazanavir (ATV/co) or Cobicistat-boosted Darunavir (DRV/co) and Emtricitabine/Tenofovir Alafenamide (F/TAF) in HIV-1 infected children. As a consequence, sections 1, 2, 3, 4.1, 4.2, 4.8, 5.1, 5.2, 6.1, 6.3, 6.4, 6.5 and 8 of the SmPC are updated. The Annex II, Labelling and Package Leaflet are updated accordingly. Version 9.1 of the RMP has also been submitted. Furthermore, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4 and to update the list of local representatives in the Package Leaflet.

15.3.5. Dupilumab – DUPIXENT (CAP) – EMA/VR/0000248778

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of adults with bullous pemphigoid (BP) for DUPIXENT, based on final results from study R668-BP-1902 (LIBERTY-BP ADEPT); this is a phase 2/3, multicenter, randomized, double blind, placebo-controlled, parallel group study to assess the efficacy and safety of dupilumab in adult patients with bullous pemphigoid; 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 12.0 of the RMP has also been submitted.

15.3.6. Durvalumab – IMFINZI (CAP) – EMA/VR/0000289524

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication for IMFINZI in combination with Bacillus Calmette-Guérin (BCG) for the treatment of adults with BCG-naive, high-risk non-muscle-invasive bladder cancer (NMIBC), based on results from the POTOMAC study. POTOMAC is a phase 3, randomized multi-centre, open-label, global study to determine the efficacy and safety of durvalumab + BCG (induction + maintenance) combination therapy vs BCG (induction + maintenance) alone, and durvalumab + BCG (induction only) combination therapy vs BCG (induction + maintenance) alone for the treatment of patients with high-risk NMIBC. 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 with the SmPC. In addition, the Applicant took the opportunity to implement editorial changes to SmPC sections 4.2 and 5.1. Version 15 (Succession 1) of the RMP has also been submitted.

15.3.7. Efgartigimod alfa – VYVGART (CAP) – EMA/VR/0000291882

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Quality

15.3.8. Eltrombopag – REVOLADE (CAP) – EMA/VR/0000288153

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study CETB115E2201, listed as a category 3 study in the RMP. This is a paediatric phase II, open-label, uncontrolled, intra-patient dose escalation study to characterise the pharmacokinetics after oral administration of eltrombopag in paediatric patients with refractory, relapsed severe aplastic anaemia or recurrent aplastic anemia. The RMP version 57.0 has also been submitted.

15.3.9. Epinephrine – EURNEFFY (CAP) – EMA/X/0000248440

Applicant: Alk-Abello A/S

PRAC Rapporteur: Terhi Lehtinen

Scope: Extension application to introduce a new strength (1 mg nasal spray, solution). The new strength is indicated for children with a body weight of 15 kg to less than 30 kg.

15.3.10. Ganaxolone - ZTALMY (CAP) - EMEA/H/C/005825/II/0015/G, Orphan

Applicant: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

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

C.I.13: Submission of the final report from non-clinical study 1022-9241 listed as a category 3 study in the RMP. This is a 26-Week Toxicity Study of Ganaxolone Metabolite, M2, by Oral Gavage in the Sprague-Dawley rat with a 2-Week Recovery Period. The RMP version 3 has also been submitted.

C.I.13: Submission of the final report from non-clinical study 20447815 listed as a category 3 study in the RMP. This is a An Oral (Gavage) Study of the Effects of M2 (Ganaxolone Metabolite) Administration on Embryo/Fetal Development in CD (Sprague Dawley) IGS Rat. The RMP version 3 has also been submitted.

C.I.13: Submission of the final report from Weight of Evidence (WoE) assessment to evaluate the need for a 2-year carcinogenicity study in rats with GNX, listed as a category 3 study in the RMP.

C.I.13: Submission of the final report from WoE assessment to evaluate the need for a 2-year carcinogenicity study in rats with M2, listed as a category 3 study in the RMP.

C.I.13: Submission of the final report from WoE assessment to evaluate the need for a juvenile toxicity study with M2, listed as a category 3 study in the RMP.

15.3.11. Ganaxolone – ZTALMY (CAP) – EMA/VR/0000263646

Applicant: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application consisting of:

C.I.4: Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from a transgenic mouse carcinogenicity study listed as a category 3 study in the RMP; this is a 26-week Oral Gavage Carcinogenicity Study of Ganaxolone in Hemizygous CByB6F1-Tg(HRAS)2Jic Mice; The RMP version 3.2 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.

C.I.4: Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from non-clinical study for juvenile toxicity in M2 (metabolite) listed as a category 3 study in the RMP; this is an Oral (Gavage) administration juvenile toxicity study of M2 (Ganaxolone Metabolite) in CD (Sprague Dawley) IGS Rats.

15.3.12. Hydrocortisone – EFMODY (CAP) – EMA/VR/0000282500

Applicant: Neurocrine Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of adrenal insufficiency (AI) in adolescents aged 12 years and over and adults for Efmody, based on final results from study DIUR-016-AI; this is a double-blind, double-dummy, two-way cross-over, randomised, phase II study of efficacy, safety and tolerability of modified-release hydrocortisones: Chronocort (Efmody) versus Plenadren, in AI. Consequently, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, e-mail of MAH was updated. Version 2.0 of the RMP has also been submitted.

15.3.13. Idecabtagene vicleucel – ABECMA (CAP) – EMA/VR/0000293201

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Mari Thorn

Scope: Update of sections 4.2, 4.4, and 4.7 of the SmPC in order to change the post-approval safety monitoring requirements after administration of Abecma; Annex II and the Package Leaflet are updated accordingly. The RMP version 5.0 has also been submitted.

15.3.14. Imipenem / Cilastatin / Relebactam – RECARBRIO (CAP) – EMA/VR/0000265089

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to extend the approved adult indications for RECARBRIO to include treatment of paediatric population from birth to <18 years of age, based on final

results from two paediatric studies (MK-7655A-021 and MK-7655A-020); phase 2/3 study MK-7655A-021 addressed safety, tolerability, efficacy and PK, and phase 1b study MK-7655A-020 addressed PK, safety, and tolerability of MK-7655A in paediatric subjects from birth to less than 18 years of age with confirmed or suspected gram-negative infections. 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 2.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and implement minor editorial corrections.

15.3.15. Isatuximab – SARCLISA (CAP) – EMA/X/0000281242

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Extension application to introduce a new pharmaceutical form (solution for injection), a new strength (1400 mg) and a new route of administration (subcutaneous use). The RMP (version 3.0) is updated in accordance.

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

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

15.3.17. Lutetium (^{177}Lu) vipivotide tetraxetan – PLUVICTO (CAP) – EMA/VR/0000288073

Applicant: Novartis Europharm Limited

PRAC Rapporteur: John Joseph Borg

Scope: Extension of indication to include treatment of adult patients with prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC) who are asymptomatic or mildly symptomatic after having progressed on androgen receptor pathway inhibitor (ARPI) and for whom chemotherapy is not yet clinically indicated for PLUVICTO, based on interim results from study CAAA617B12302 (PSMAfore); this is a phase III, open-label, multi-center, randomized study comparing 177Lu-PSMA-617 vs. a change of androgen receptor-directed therapy in the treatment of taxane naïve men with progressive metastatic castrate resistant prostate cancer; as a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted to include clinical data from the PSMAfore study to support the addition of the new therapeutic indication.

15.3.18. Mavacamten – CAMZYOS (CAP) – EMA/VR/0000294573

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: A grouped application consisting of:

C.I.4: Update of section 4.2 of the SmPC in order to remove the Week 8 echocardiography monitoring and associated down-titration opportunity based on the modelling and simulation analyses along with safety data from two studies conducted in Japan (HORIZON-HCM; CV027004) and China (EXPLORER-CN; CV0271097/LB2001301). The updated RMP version 7.0 has also been submitted.

C.I.4: Update of sections 4.2, and 4.5 of the SmPC in order modify maximum dose requirement from 5 mg to 15 mg for CYP2C19 poor metabolisers (PM), in alignment with the requirement for non-PM based on the modelling and simulation analyses along with safety data from two studies conducted in Japan (HORIZON-HCM; CV027004) and China (EXPLORER-CN; CV0271097/LB2001301). The updated RMP version 7.0 has also been submitted.

15.3.19. Nivolumab – OPDIVO (CAP) – EMA/VR/0000288087

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Dirk Mentzer

Scope: Update of sections 4.1 and 4.2 of the SmPC following procedure EMEA/H/C/003985/X/0144. In addition, the MAH took the opportunity to update sections 4.4, 4.8, and 5.1 of the SmPC to align it with the new indications and to implement editorial changes to the PI. The Package Leaflet is updated in accordance. The RMP version 46.0 has also been submitted.

15.3.20. 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).

15.3.21. Osilodrostat – ISTURISA (CAP) – EMA/VR/0000290393

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study CLCI699C2X01B listed as a category 3 study in the RMP. This is a Phase IIb, Open-label, Multi-centre, Roll-over Study to Assess Long Term Safety in Patients with Endogenous Cushing's Syndrome who have Completed a Prior Novartis-sponsored Osilodrostat (LCI699) Study and are Judged by the Investigator to Benefit from Continued Treatment with Osilodrostat. The RMP version 3.1 has also been submitted.

15.3.22. Ozanimod – ZEPOSIA (CAP) – EMA/VR/0000291324

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Update of section 5.1 of the SmPC in order to update efficacy and safety information based on the final results from study RPC01-3102, listed as a category 3 study in RMP. This is a Phase 3, multicenter, open-label extension trial of oral RPC1063 as therapy for moderate to severe ulcerative colitis. The RMP version 11.0 has also been submitted.

15.3.23. Ponatinib – ICLUSIG (CAP) – EMA/VR/0000263550

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of adult patients with newly-diagnosed Ph+ ALL for ICLUSIG, based on interim results from study Ponatinib-3001 (PhALLCON); this is a phase 3, randomized, open-label, multicenter study comparing ponatinib versus imatinib, administered in combination with reduced intensity chemotherapy, in patients with newly diagnosed Ph+ ALL; supportive data were derived from two single-arm, open-label clinical studies (AP24534 11 001 in combination with chemotherapy and INCB 84344-201 as monotherapy). As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 23.2 of the RMP has also been submitted. In addition, earlier approved updates were incorporated to the PI.

15.3.24. Selinexor – NEXPOVIO (CAP) – EMA/VR/0000291736

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Bianca Mulder

Scope: A grouped application consisting of:

C.I.4: Update of sections 4.2, and 5.2 of the SmPC in order to include the recommended dose adjustment strategy in patients with severe hepatic impairment, and update pharmacokinetic, information based on interim results from study KCP-330-027; this is an open-label, phase 1/2, interventional study assessing the effect of hepatic impairment on selinexor pharmacokinetics; the Package Leaflet is updated accordingly. The RMP version 4.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce editorial changes to the PI.

C.I.4: Update of section 4.5 of the SmPC in order to add drug-drug interaction information with strong CYP3A4 and UGT inducer carbamazepine based on final results from study XPORT-HV-045; this is a phase 1 drug-drug interaction study in healthy volunteers to evaluate the effect of carbamazepine (a strong CYP3A4 inducer) on the pharmacokinetics of selinexor.

15.3.25. Serplulimab – HETRONIFLY (CAP) – EMA/VR/0000291455

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4 and 4.8 of SmPC in order to include myasthenia gravis and myasthenic syndrome as part of the warning section and to add them to the list of adverse drug reactions (ADRs) with frequency not known, based on a signal assessment report. The Package Leaflet is updated accordingly. The updated RMP version 1.4 has also been submitted.

15.3.26. Serplulimab – HETRONIFLY (CAP) – EMA/VR/0000290021

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include HETRONIFLY in combination with carboplatin and nab-paclitaxel is indicated for the first-line treatment of adult patients with unresectable, locally advanced or metastatic squamous non-small cell lung carcinoma based on final results from study HLX10-004-NSCLC303; this is a randomized, double-blind, multi-center, phase III pivotal study, was conducted to compare the clinical efficacy and safety of serplulimab combined with chemotherapy (carboplatin and nab-paclitaxel) versus placebo combined with chemotherapy (carboplatin and nab-paclitaxel). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP Version 1.3 has been submitted.

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

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Anna Mareková

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

15.3.28. Tasimelteon - HETLIOZ (CAP) - EMEA/H/C/003870/II/0040, Orphan

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include the treatment of nighttime sleep disturbances in adults with Smith Magenis Syndrome (SMS) for HETLIOZ, based on results from study VP-VEC-162-2401. This is a double-blind, randomized, two-period crossover study evaluating the effects of tasimelteon vs. placebo on sleep disturbances of individuals with Smith-Magenis Syndrome (SMS). As a consequence, sections 4.1, 4.5, 5.1, 5.2 and 5.3 of the

SmPC are updated. The Labelling and Package Leaflet are updated in accordance. The RMP version 5.0 has also been submitted. Furthermore, the PI is brought 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.

15.3.29. 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.

15.3.30. Tedizolid phosphate – SIVEXTRO (CAP) – EMA/X/0000282136

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension application to introduce a new pharmaceutical form (powder for oral suspension, 200 mg). The RMP (version 8.1) is updated in accordance. Additionally, the marketing authorisation holder took the opportunity to align the PI with the latest QRD template.

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

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

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

15.3.32. 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.

15.3.33. Ustekinumab – STEQEYMA (CAP) – EMA/VR/0000292238

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Quality

15.3.34. Ustekinumab – QOYVOLMA (CAP) – EMA/VR/0000292065

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Quality

15.3.35. Ustekinumab – YESINTEK (CAP) – EMA/VR/0000290373

Applicant: Biosimilar Collaborations Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Quality

15.3.36. Ustekinumab – STELARA (CAP) – EMA/VR/0000290099

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include treatment of moderately to severely active Crohn's disease in paediatric patients from the age of 2 years and older, who have had an inadequate response to, or were intolerant to either conventional or biologic therapy, for STELARA, based on final results from the Phase 3 open-label CNTO1275CRD3004 study and the supportive results from the Phase 1 PK CNTO1275CRD1001 study. Study CNTO1275CRD3004 is a Phase 3 study of the efficacy, safety, and pharmacokinetics of ustekinumab as open-label intravenous induction treatment followed by randomized double-blind subcutaneous ustekinumab maintenance in pediatric participants 2 to <18 years of age with moderately to severely active Crohn’s disease. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are being updated. The Package Leaflet is updated accordingly. The RMP version 32.1 has also been submitted. In addition, the MAH took the opportunity to introduce editorial, formatting and administrative changes to the PI, bringing it in line with the latest QRD template. In addition, the MAH updated the list of local representatives in the Package Leaflet.

15.3.37. Vonicog alfa – VEYVONDI (CAP) – EMA/VR/0000264863

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of haemorrhage in children aged less than 18 years for VEYVONDI, based on results from studies 071102 and SHP677-304. Study 071102 is a phase 3, prospective, multicenter, uncontrolled, open-label clinical study to

determine the efficacy, safety, and tolerability of the recombinant von Willebrand factor (rVWF) with or without ADVATE (octocog alfa) in the treatment and control of bleeding episodes, the efficacy and safety of rVWF in elective and emergency surgeries, and the pharmacokinetics (PK) of rVWF in children diagnosed with severe von Willebrand disease (VWD); study SHP677-304 is a phase 3B, prospective, open-label, uncontrolled, multicenter study on long term safety and efficacy of vonicog alfa in pediatric and adult subjects with severe VWD. 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 accordingly. Version 6.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.4, to update the PI in accordance with the latest EMA excipients guideline, and to implement editorial changes to the PI.

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. Atogepant – AQUIPTA (CAP) – EMA/PSUR/0000282279

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00000100/202503)

16.1.2. Avacopan – TAVNEOS (CAP) – EMA/PSUR/0000282275

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010967/202503)

16.1.3. Cangrelor – KENGREXAL (CAP) – EMA/PSUR/0000282280

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010360/202503)

16.1.4. Cinacalcet – MIMPARA (CAP) – EMA/PSUR/0000282225

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00000756/202502)

16.1.5. Concizumab – ALHEMO (CAP) – EMA/PSUR/0000282246

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011105/202503)

16.1.6. COVID-19 vaccine (recombinant, adjuvanted) – BIMERVAX (CAP) – EMA/PSUR/0000282290

Applicant: Hipra Human Health S.L.

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure (PSUSA/00011045/202503)

16.1.7. Dupilumab – DUPIXENT (CAP) – EMA/PSUR/0000282220

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010645/202503)

16.1.8. Duvelisib – COPIKTRA (CAP) – EMA/PSUR/0000282286

Applicant: Secura Bio Limited

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00010939/202503)

16.1.9. Enalapril maleate – AQUMELDI (CAP) – EMA/PSUR/0000282217

Applicant: Proveca Pharma Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00000201/202503)

16.1.10. Erdafitinib – BALVERSA (CAP) – EMA/PSUR/0000282264

Applicant: Janssen Cilag International

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011072/202504)

16.1.11. Etrasimod – VELSIPITY (CAP) – EMA/PSUR/0000282221

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00000273/202504)

16.1.12. Fingolimod – GILENYA (CAP) – EMA/PSUR/0000282248

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00001393/202502)

16.1.13. Fostamatinib – TAVLESSE (CAP) – EMA/PSUR/0000282287

Applicant: Instituto Grifols S.A.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010819/202504)

16.1.14. Futibatinib – LYTGOBI (CAP) – EMA/PSUR/0000282216

Applicant: Taiho Pharma Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00000068/202503)

16.1.15. Glofitamab – COLUMVI (CAP) – EMA/PSUR/0000282293

Applicant: Roche Registration GmbH

PRAC Rapporteur: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00000067/202503)

16.1.16. Idecabtagene vicleucel – ABECMA (CAP) – EMA/PSUR/0000282288

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010954/202503)

16.1.17. Isatuximab – SARCLISA (CAP) – EMA/PSUR/0000282274

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: Evaluation of a PSUSA procedure (PSUSA/00010851/202503)

16.1.18. Lapatinib – TYVERB (CAP) – EMA/PSUR/0000282260

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00001829/202503)

16.1.19. Lorlatinib – LORVIQUA (CAP) – EMA/PSUR/0000282241

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00010760/202503)

16.1.20. Lutetium (^{177}Lu) vipivotide tetraxetan – PLUVICTO (CAP) – EMA/PSUR/0000282271

Applicant: Novartis Europharm Limited

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00011031/202503)

16.1.21. Maralixibat – LIVMARLI (CAP) – EMA/PSUR/0000282276

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011032/202503)

16.1.22. Marstacimab – HYMPAVZI (CAP) – EMA/PSUR/0000282253

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011101/202504)

16.1.23. *Meningococcal* group a, c, w135 and y conjugate vaccine – MENVEO (CAP) – EMA/PSUR/0000282240

Applicant: Glaxosmithkline Vaccines S.r.l.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00001969/202503)

16.1.24. Methylnaltrexone bromide – RELISTOR (CAP) – EMA/PSUR/0000282262

Applicant: Bausch Health Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002023/202503)

16.1.25. Mirikizumab – OMVOH (CAP) – EMA/PSUR/0000282215

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000049/202503)

16.1.26. Nintedanib – OFEV (CAP) – EMA/PSUR/0000282233

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00010319/202504)

16.1.27. Niraparib – ZEJULA (CAP) – EMA/PSUR/0000282222

Applicant: Glaxosmithkline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010655/202503)

16.1.28. Pemigatinib – PEMAZYRE (CAP) – EMA/PSUR/0000282272

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010923/202504)

16.1.29. Rezafungin – REZZAYO (CAP) – EMA/PSUR/0000282237

Applicant: Mundipharma GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00000221/202503)

16.1.30. Risankizumab – SKYRIZI (CAP) – EMA/PSUR/0000282229

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010765/202503)

16.1.31. Selinexor – NEXPOVIO (CAP) – EMA/PSUR/0000282278

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010926/202503)

16.1.32. Selumetinib – KOSELUGO (CAP) – EMA/PSUR/0000282270

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010936/202504)

16.1.33. Serplulimab – HETRONIFLY (CAP) – EMA/PSUR/0000282289

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00011112/202503)

16.1.34. Sodium zirconium cyclosilicate – LOKELMA (CAP) – EMA/PSUR/0000282227

Applicant: AstraZeneca AB

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010675/202503)

16.1.35. Tepotinib – TEPMETKO (CAP) – EMA/PSUR/0000282273

Applicant: Merck Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010979/202503)

16.1.36. Tucatinib – TUKYSA (CAP) – EMA/PSUR/0000282281

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010918/202504)

16.1.37. Velmanase alfa – LAMZEDE (CAP) – EMA/PSUR/0000282224

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010677/202503)

16.1.38. Vibegron – OBGEMSA (CAP) – EMA/PSUR/0000282266

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00011068/202503)

16.1.39. Vilobelimab – GOHIBIC (CAP) – EMA/PSUR/0000282277

Applicant: InflaRx GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011103/202504)

16.1.40. Yttrium (90Y) chloride – YTTRIGA (CAP) – EMA/PSUR/0000282267

Applicant: Eckert & Ziegler Radiopharma GmbH

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00003137/202503)

16.1.41. Zilucoplan – ZILBRYSQ (CAP) – EMA/PSUR/0000282282

Applicant: UCB Pharma

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00000169/202503)

16.1.42. Zolbetuximab – VYLOY (CAP) – EMA/PSUR/0000282259

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011095/202503)

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

16.2.1. Germanium (^{68}Ge) chloride / Gallium (^{68}Ga) chloride – GALLIAPHARM (CAP); NAP – EMA/PSUR/0000282223

Applicants: Eckert & Ziegler Radiopharma GmbH, various

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00010364/202503)

16.2.2. Gozetotide – LOCAMETZ (CAP); NAP – EMA/PSUR/0000282269

Applicants: Novartis Europharm Limited, various

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00011030/202503)

16.2.3. Hepatitis B vaccine (rDNA) – HBVAXPRO (CAP); NAP – EMA/PSUR/0000282244

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

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00001597/202502)

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

16.3.1. Alprazolam (NAP) – EMA/PSUR/0000282218

Applicants: various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00000109/202503)

16.3.2. Cefaclor (NAP) – EMA/PSUR/0000282255

Applicants: various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00000583/202503)

16.3.3. Chlorhexidine (NAP) – EMA/PSUR/0000282226

Applicants: various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00000662/202503)

16.3.4. Clobetasol (NAP) – EMA/PSUR/0000282239

Applicants: various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00000799/202502)

16.3.5. Clotrimazole (NAP) – EMA/PSUR/0000282284

Applicants: various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00000829/202503)

16.3.6. Cyamemazine (NAP) – EMA/PSUR/0000282261

Applicants: various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00000886/202503)

16.3.7. Diazepam (NAP) – EMA/PSUR/0000282242

Applicants: various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00001029/202503)

16.3.8. Doxycycline (NAP) – EMA/PSUR/0000282238

Applicants: various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00001173/202503)

16.3.9. Erythromycin (systemic use) (NAP) – EMA/PSUR/0000282208

Applicants: various

PRAC Lead: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00010808/202503)

16.3.10. Ethinylestradiol (NAP) – EMA/PSUR/0000282265

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00001306/202503)

16.3.11. Ethyl loflazepate (NAP) – EMA/PSUR/0000282236

Applicants: various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00001317/202503)

16.3.12. Flucytosine (NAP) – EMA/PSUR/0000282257

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00001405/202503)

16.3.13. Fomepizole (NAP) – EMA/PSUR/0000282234

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00001466/202503)

16.3.14. Gentamicin (topical use) (NAP) – EMA/PSUR/0000282256

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00001522/202503)

16.3.15. Mannitol (all indications apart from cystic fibrosis) (NAP) – EMA/PSUR/0000282283

Applicants: various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00010005/202502)

16.3.16. Thiamazole (NAP) – EMA/PSUR/0000282251

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002922/202503)

16.3.17. Trandolapril / verapamil (NAP) – EMA/PSUR/0000282249

Applicants: various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00003005/202503)

16.3.18. Urokinase (NAP) – EMA/PSUR/0000282263

Applicants: various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00003083/202503)

16.4. Follow-up to PSUR/PSUSA procedures

None

16.5. Variation procedure(s) resulting from PSUSA evaluation

16.5.1. Ixekizumab – TALTZ (CAP) – EMA/PAM/0000262763

Applicant: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Response to the PRAC request for a LEG for a cumulative review on MACE using data from clinical trials, post-marketing sources and literature adopted on 31 October 2024 following an assessment of EMEA/H/C/PSUSA/00010493/202403 (ixekizumab PSUR 11 - covering period 23 March 2021 to 22 March 2024) and to be submitted within 6 months.

16.6. Expedited summary safety reviews[29]

None

17. Annex I – Post-authorisation safety studies (PASS)

Based on the assessment of the following PASS protocol(s), result(s), interim result(s) or feasibility study(ies), and following endorsement of the comments received, PRAC adopted the conclusion of the Rapporteurs on their assessment for the medicines listed below without further plenary discussion.

17.1. Protocols of PASS imposed in the marketing authorisation(s)[30]

17.1.1. Blinatumomab – BLINCYTO (CAP) – EMA/PASS/0000263976

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Veronika Macurova

Scope: PASS amendment [107o]: Substantial amendment to an observational PASS of long-term safety in paediatric patients with B-precursor acute lymphoblastic leukaemia (ALL) who have been treated with either blinatumomab or chemotherapy, followed by transplantation

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[31]

17.2.1. Delgocitinib – ANZUPGO (CAP) – EMA/PAM/0000291999

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of a revised protocol for the non-imposed non-interventional PASS "Delgocitinib cream 20 mg/g in moderate to severe chronic hand eczema and risk of non-melanoma skin cancer: a nationwide registry based long-term post-authorisation safety study", as requested as part of MEA 003.

17.2.2. Mirikizumab – OMVOH (CAP) – EMA/PAM/0000292275

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Following Omvoh line extension procedure EMEA/H/C/005122/X/0006/G to include Crohn's Disease (CD) as a new indication:

[29] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC
[30] In accordance with Article 107n of Directive 2001/83/EC
[31] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

Protocol amendment to I6T-MC-B003: Observational Study of Pregnancy and Infant Outcomes Among Women Exposed to Mirikizumab During Pregnancy in US-based Administrative Claims Data.

Protocol amendment to I6T-MC-B004: Observational Secondary Database Study to Assess the Long-Term Safety of Mirikizumab in Routine Clinical Practice Using US Administrative Claims Data.

17.2.3. Selexipag – UPTRAVI (CAP) – EMA/PAM/0000256686

Applicant: Janssen Cilag International

PRAC Rapporteur: Zoubida Amimour

Scope: Amendment of the EXPOSURE (AC-065A401) protocol (amendment 7 version 8 dated 17 February 2025). The protocol was amended to update the milestones of the study and to include OPSYNVI/YUVANCI into the list of PAH-specific marketed products from the MAH. In addition, the MAH proposes a reduction of the sample size planned for both cohorts of the study.

17.2.4. Tofacitinib – XELJANZ (CAP) – EMA/PAM/0000261850

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the third interim study reports for the four Rheumatoid Arthritis (RA) Registry Post-Authorization Safety Studies (PASSs) in line with protocol milestones for A3921312 (v3.0), A3921314 (v4.0), A3921316 (v3.0) & A3921317 (v5.0) for Xeljanz (tofacitinib).

- A3921312: UK, British Society for Rheumatology Biologics Register-Rheumatoid Arthritis (BSRBR-RA)
- A3921314: Sweden (SE), Anti Rheumatic Treatment in Sweden (ARTIS) register.
- A3921316: Spain (ES), Registry of Adverse Events of Biological Therapies and Biosimilars in Rheumatoid Diseases (BIOBADASER)
- A3921317: Germany (DE), Registry Rheumatoide Arthritis: Beobachtung der Biologika-Therapie (RABBIT)

Submission of a revised PASS protocol version 4.0 (A3921312), version 5.0 (A3921314), version 4.0 (A3921316), and version 6.0 (A3921317) for Tofacitinib (Xeljanz). Follow on from MEA 8.7+9.7+10.7+11.8.

17.2.5. Valoctocogene roxaparvovec – ROCTAVIAN (CAP) – EMA/PAM/0000292813

Applicant: Biomarin International Limited

PRAC Rapporteur: Bianca Mulder

Scope: PASS NINI: Submission of the final protocol of the survey of haematologists to assess the effectiveness of the additional risk minimisation measures (aRMMs) for Roctavian (valoctocogene roxaparvovec).

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

17.3.1. Blinatumomab – BLINCYTO (CAP) – EMA/PASS/0000262863

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Veronika Macurova

Scope: PASS results [107q]: Final study report for an observational study of blinatumomab safety and effectiveness, utilisation, and treatment practices

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

17.4.1. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/II/0051, Orphan

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Submission of the final study report for the non-interventional study KT-EU-472-5966 titled "Quantitative Testing of Health Care Professional Knowledge About Tecartus Risk Minimisation Measures'' listed as a category 3 study in the RMP.

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

17.5.1. Avapritinib – AYVAKYT (CAP) – EMA/PAM/0000292344

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Fourth progress report of study BLU-285-1406

Study BLU-285-1406: In order to further confirm the safety and efficacy of avapritinib in the treatment of adult patients with unresectable or metastatic GIST harbouring the PDGFRA D842V mutation, the MAH should submit the results of an observational safety and efficacy study in patients with unresectable or metastatic PDGFRA D842V-mutant GIST.

17.5.2. Ciltacabtagene autoleucel – CARVYKTI (CAP) – EMA/PAM/0000291466

Applicant: Janssen Cilag International

PRAC Rapporteur: Jo Robays

Scope: First Interim Report for study 68284528MMY4002 - Long-term Follow-up Study for Participants Previously Treated with Ciltacabtagene Autoleucel.

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

17.5.3. Givosiran – GIVLAARI (CAP) – EMA/PAM/0000292266

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Study ALN-AS1-006: ELEVATE, a global observational longitudinal prospective registry of patients with acute hepatic porphyria (AHP)

ALN-AS1-006, PAM Report #4.0 (4th Interim study result)

17.5.4. Pirtobrutinib – JAYPIRCA (CAP) – EMA/PAM/0000291872

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an integrated safety analysis of patients with hematologic malignancies treated with pirtobrutinib monotherapy at the 200mg daily dose in clinical trials and from post-marketing reports to further characterise the risk of second primary malignancies.

17.5.5. Venetoclax – VENCLYXTO (CAP) – EMA/PAM/0000262601

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: 7th Study Progress Report for Study P16-562: A prospective observational study to assess the long-term safety profile of venetoclax in a Swedish cohort of Chronic Lymphocytic Leukemia (CLL) Patients

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. Evinacumab – EVKEEZA (CAP) – EMA/S/0000288394

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: Annual reassessment of the marketing authorisation

18.1.2. Lomitapide – LOJUXTA (CAP) – EMA/S/0000290089

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Annual reassessment of the marketing authorisation

18.1.3. Nelarabine – ATRIANCE (CAP) – EMA/S/0000285152

Applicant: Sandoz Pharmaceuticals d.d.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Annual reassessment of the marketing authorisation

18.1.4. Odevixibat – BYLVAY (CAP) – EMA/S/0000287370

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.1.5. rADAMTS13 – ADZYNMA (CAP) – EMA/S/0000288329

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Maia Uusküla

Scope: Annual reassessment of the marketing authorisation

18.1.6. Smallpox and monkeypox vaccine (live modified vaccinia virus Ankara) – IMVANEX (CAP) – EMA/S/0000288022

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Dirk Mentzer

Scope: Annual reassessment of the marketing authorisation

18.1.7. Tafamidis – VYNDAQEL (CAP) – EMA/S/0000287643

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Zoubida Amimour

Scope: Annual reassessment of the marketing authorisation

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

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Martin Huber

Scope: Conditional renewal of the marketing authorisation

18.2.2. Delamanid – DELTYBA (CAP) – EMA/R/0000293774

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Conditional renewal of the marketing authorisation

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

Applicant: CSL Behring GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Abiraterone acetate – ABIRATERONE ACCORD (CAP) – EMA/R/0000286405

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

18.3.2. Azacitidine – ONUREG (CAP) – EMA/R/0000289529

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

18.3.3. Bevacizumab – ABEVMY (CAP) – EMA/R/0000287528

Applicant: Biosimilar Collaborations Ireland Limited

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

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Karin Erneholm

Scope: 5-year renewal of the marketing authorisation

18.3.6. Drospirenone / Estetrol – LYDISILKA (CAP) – EMA/R/0000288429

Applicant: Estetra

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

18.3.7. Drospirenone / Estetrol – DROVELIS (CAP) – EMA/R/0000288412

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

18.3.8. Hydrocortisone – EFMODY (CAP) – EMA/R/0000288092

Applicant: Neurocrine Netherlands B.V.

PRAC Rapporteur: Mari Thorn

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

18.3.11. Potassium citrate / Potassium hydrogen carbonate – SIBNAYAL (CAP) – EMA/R/0000284883

Applicant: Advicenne

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

18.3.13. Tralokinumab – ADTRALZA (CAP) – EMA/R/0000288404

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Kimmo Jaakkola

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 November 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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Jan Neuhauser	Member	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	
Stanislav Stoilov	Alternate	Bulgaria	No interests declared	
Petar Mas	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi	Alternate	Croatia	No interests declared	
Panagiotis Psaras	Member	Cyprus	No interests declared	
Elena Kaisis	Alternate	Cyprus	No interests declared	
Eva Jirsová	Member	Czechia	No interests declared	
Marie Louise Schougaard Christiansen	Member	Denmark	No interests declared	
Karin Erneholm	Alternate	Denmark	No interests declared	
Maia Uusküla	Member	Estonia	No interests declared	
Krõõt Aab	Alternate	Estonia	No interests declared	
Terhi Lehtinen	Member	Finland	No interests declared	
Kimmo Jaakkola	Alternate	Finland	No interests declared	
Tiphaine Vaillant	Member	France	No interests declared	
Zoubida Amimour	Alternate	France	No participation in discussion, final	7.4.1. EMA/VR/00002 87898 15.2.4. EMA/VR/00002 85155

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			deliberations and voting on:	15.3.13. EMA/VR/000029320 1 15.3.18. EMA/VR/000029457 3 15.3.19. EMA/VR/000028808 7 15.3.22. EMA/VR/000029132 4 16.1.16. EMA/PSUR/0000282288 18.3.2. EMA/R/0000289529
Martin Huber	Member	Germany	No interests declared	
Georgia Gkegka	Member	Greece	No interests declared	
Maria Poulianiti	Alternate	Greece	No restrictions applicable to this meeting	
Melinda Palfi	Alternate	Hungary	No interests declared	
Guðrún Stefánsdóttir	Member	Iceland	No participation in discussion, final deliberations and voting on:	15.2.3. EMA/VR/000028814 9 16.1.4. EMA/PSUR/0000282225 17.1.1. EMA/PASS/0000263976 17.3.1. EMA/PASS/0000262863

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
				4.2.1. Adalimumab – AMGEVITA (CAP); AMSPARITY (CAP); HEFIYA (CAP); HUMIRA (CAP) - EMEA/H/C/000481/SDA/128; HUKYNDRA (CAP); HULIO(CAP); HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP); LIBMYRIS (CAP); YUFLYMA (CAP) 6.1.1. EMA/PSUR/0000282235
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	
Anne-Cecile Vuillemin	Member	Luxembourg	No interests declared	
Magdalena Wielowieyska	Alternate	Luxembourg	No participation in discussion, final deliberations and voting on:	18.1.5 EMA/S/000028 8329
John Joseph Borg	Member	Malta	No restrictions	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			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 deliberations and voting on:	5.3.1. EMA/X/0000248026 16.3.3. EMA/PSUR/0000282226 16.3.5. EMA/PSUR/0000282284
Pernille Harg	Alternate	Norway	No interests declared	
Katarzyna Ziolkowska	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins	Member	Portugal	No interests declared	
Carla Torre	Alternate	Portugal	No restrictions applicable to this meeting	
Roxana Dondera	Member	Romania	No interests declared	
Anna Mareková	Member	Slovakia	No interests declared	
Miroslava Gocova	Alternate	Slovakia	No interests declared	
Marjetka Plementas	Alternate	Slovenia	No interests declared	
Maria del Pilar Rayon	Member	Spain	No interests declared	
Maria Martinez Gonzalez	Alternate	Spain	No interests declared	
Mari Thorn	Member	Sweden	No restrictions	

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	
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:	18.1.5 EMA/S/0000288329
Martin Votava	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Yiannoula Koulla	Member	Patients' Organisation Representative	No interests declared	
Christelle Bizimungu	Expert	Belgium	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Evelien De Clercq	Expert	Belgium	No interests declared	
Olga Kholmanskikh Van Criekingen	Expert	Belgium	No interests declared	
Gabriela Burianová	Expert	Czech Republic	No interests declared	
Lucie Skálová	Expert	Czech Republic	No interests declared	
Marian Hjortlund Allon	Expert	Denmark	No interests declared	
Mette Hjorslev Knudgaard	Expert	Denmark	No interests declared	
Elina Rönnemaa	Expert	Finland	No interests declared	
Benjamin Burrus	Expert	France	No interests declared	
Elsa Grangier	Expert	France	No interests declared	
Youssef Shaim	Expert	France	No restrictions applicable to this meeting	
Jorg Engelbergs	Expert	Germany	No interests declared	
Dennis Lex	Expert	Germany	No interests declared	
Sara Rieke	Expert	Germany	No restrictions applicable to this meeting	
Laura Zein	Expert	Germany	No interests declared	
Risteard Prendergast	Expert	Ireland	No interests declared	
Virginia Cuconato	Expert	Italy	No interests declared	
Federico De Angelis	Expert	Italy	No interests declared	
Pasquale Marchione	Expert	Italy	No interests declared	
Maria Cristina Piattella	Expert	Italy	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Laura Sottosanti	Expert	Italy	No interests declared	
Talip Eroglu	Expert	Netherlands	No restrictions applicable to this meeting	
Serena Marchetti	Expert	Netherlands	No restrictions applicable to this meeting	
Joao Fernandes	Expert	Portugal	No restrictions applicable to this meeting	
Consuelo Argumánez	Expert	Spain	No interests declared	
Luz Medrano	Expert	Spain	No interests declared	
Charlotte Backman	Expert	Sweden	No interests declared	
Annika Ekbom Schnell	Expert	Sweden	No interests declared	
Rolf Gedeborg	Expert	Sweden	No restrictions applicable to this meeting	
Sissela Liljeqvist	Expert	Sweden	No restrictions applicable to this meeting	
Asa Lindh	Expert	Sweden	No interests declared	
Paulina Werner Nosrati	Expert	Sweden	No interests declared	
Asimina Zisi	Expert	Sweden	No interests declared	
Elina Rönnemaa	Expert	Finland	No interests declared	
A representative from the European Commission attended the meeting				
Observers from Health Canada and FDA 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