03 November 2025
EMA/PRAC/238878/2025 Revision[1]
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes for PRAC meeting on 02-05 June 2025

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

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

[1] As the outcome for this procedure EMA/VR/0000262308 was adopted following a plenary discussion, the minutes are now included under the section 7.4.2 (instead of section 17)

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1. Introduction

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

The Chairperson opened the 02-05 June 2025 meeting by welcoming all participants. The meeting was held in-person.

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

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

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

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

1.2. Agenda of the meeting on 02-05 June 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 05-08 May 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 05-08 May 2025 were published on the EMA website on 04 July 2025 (EMA/PRAC/199835/2025).

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[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

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

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

See also Annex I 14.1.

4.1.1. Varicella vaccine (live) (NAP)

Applicant: various

PRAC Rapporteur: Jean-Michel Dogné

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

Scope: Signal of new aspect of the known risk of encephalitis

EPITT 20180 – New signal

Background

This varicella vaccine is a lyophilised live virus vaccine containing as the active ingredient the attenuated Varicella Zoster Virus (VZV) Oka strain. It is indicated for active immunisation against varicella in healthy individuals from 9 to 11 months of age, under special circumstances, in healthy individuals from the age of 12 months, for post-exposure prophylaxis if administered to healthy, susceptible individuals exposed to varicella within 72 hours of contact and in individuals at high risk of severe varicella.

The Office of Registration Medicinal Products, Medical Devices and Biocidal Products (Poland) has received 1 fatal case of encephalitis in a child following administration of Varilrix. A EudraVigilance search retrieved 31 cases of encephalitis in association with Varilrix, as well as 20 cases of encephalitis with Varicella vaccine [live, attenuated] and 50 cases of encephalitis with Varivax. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence, PRAC agreed that further evaluation of the signal is warranted.

PRAC appointed Jean-Michel Dogné as Rapporteur for the signal.

Summary of recommendation(s)

- The MAHs market leaders for Varilrix (GlaxoSmithKline Biologicals S.A.) and Varivax (Merck Sharp & Dohme B.V.) should submit by 18 June 2025 a cumulative review of all cases of encephalitis from all sources, including pre-clinical data, available data from clinical trials, scientific literature and post marketing exposure, including data from the MAH's safety database and EudraVigilance and discuss whether an update of the PI and/or RMP is warranted.
- PRAC will assess the cumulative review within an accelerated timetable, which would allow for the following PRAC recommendation to be adopted during the July 2025 PRAC plenary meeting.

4.2. Signals follow-up and prioritisation

4.2.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/SDA/017; Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/SDA/014; Ciltacabtagene autoleucel – CARVYKTI (CAP) - EMEA/H/C/005095/SDA/020; Idecabtagene vicleucel - ABECMA (CAP) - EMEA/H/C/004662/SDA/023; Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/SDA/024; Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/SDA/025;

Applicant: Bristol-Myers Squibb Pharma EEIG (Abecma, Breyanzi), Janssen-Cilag International NV (Carvykti), Kite Pharma EU B.V. (Yescarta, Tecartus), Novartis Europharm Limited (Kymriah)

PRAC Rapporteur: Jo Robays

Scope: Signal of immune-mediated enterocolitis / immune effector cell-associated enteritis

with CAR T-cell products

EPITT 20133 – Follow-up to January 2025

Background

For background information, see PRAC minutes January 2025.

The MAHs replied to the request for information on the signal of immune-mediated enterocolitis / immune effector cell-associated enteritis with CAR T-cell products and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence from case reports in EudraVigilance, literature and the responses submitted by the MAHs, PRAC agreed that there is sufficient evidence to establish a causal association between immune-mediated enterocolitis and Carvykti (ciltacabtagene autoleucel). Therefore, the product information should be updated to add immune-mediated enterocolitis as a warning and as an undesirable effect with a frequency 'common'.

In addition, PRAC concluded that the current evidence is insufficient to establish a causal relationship between Abecma (idecabtagene vicleucel), Breyanzi (lisocabtagene maraleucel), Kymriah (tisagenlecleucel), Tecartus (brexucabtagene autoleucel) and Yescarta (axicabtagene ciloleucel) and immune-mediated enterocolitis to further warrant an update to the product information and/or risk management plan at present.

Summary of recommendation(s)

- The MAH of Carvykti (ciltacabtagene autoleucel) should submit to EMA, within 60 days, a variation to update the product information[4]. The MAHs of Abecma (idecabtagene vicleucel), Breyanzi (lisocabtagene maraleucel), Kymriah (tisagenlecleucel), Tecartus (brexucabtagene autoleucel) and Yescarta (axicabtagene ciloleucel) should continue to monitor these events as part of routine pharmacovigilance.

4.2.2. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/SDA/006

Applicant: LEO Pharma A/S

PRAC Rapporteur: Monica Martinez Redondo

Scope: Signal of pyoderma gangrenosum

EPITT 20162 – Follow-up to April 2025

Background

For background information, see PRAC minutes April 2025.

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

Discussion

Having considered the available evidence in EudraVigilance and in the literature, including the responses submitted by the MAH, PRAC considered there is sufficient evidence to establish a causal association between Kyntheum (brodalumab) and pyoderma

[4] Update of sections 4.4 and 4.8 of the SmPC.

gangrenosum. Therefore, the product information should be updated to add pyoderma gangrenosum as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAH for Kyntheum (brodalumab) should submit to EMA, within 60 days, a variation to update the product information[5].

4.2.3. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/SDA/016; ENZALUTAMIDE VIATRIS (CAP), NAP; Digoxin (NAP)

Applicants: Astellas Pharma Europe B.V. (Xtandi), Viatris Limited (Enzalutamide Viatris), various

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Signal of laboratory test interference leading to falsely elevated digoxin plasma levels with enzalutamide

EPITT 20134 – Follow-up to January 2025

Background

For background information, see PRAC minutes January 2025.

The MAHs of Xtandi (enzalutamide) and the MAH Aspen Pharma Trading Limited of digoxin-containing product, replied to the request for information on the signal of laboratory test interference leading to falsely elevated digoxin plasma levels with enzalutamide and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance and in the literature, including the responses submitted by the MAHs, PRAC agreed that the enzalutamide-induced laboratory interference leading to falsely elevated digoxin levels should be reflected in the product information of both enzalutamide and digoxin-containing products.

Summary of recommendation(s)

- The MAHs for enzalutamide- and digoxin-containing medicinal products should submit to EMA and/or to national competent authorities, within 60 days, a variation to amend the product information[6]. PRAC has noted that the digoxin product information does not contain information on the inhibition of the efflux transporter P-gp by enzalutamide, potentially leading to increased digoxin plasma levels. The MAHs for digoxin-containing medicinal products should consider addressing this topic through an appropriate regulatory procedure.

4.2.4. Omalizumab – XOLAIR (CAP) - EMEA/H/C/000606/SDA/076; OMLYCLO (CAP)

Applicant: Celltrion Healthcare Hungary Kft. (Omlyclo), Novartis Europharm Limited (Xolair)

PRAC Rapporteur: Mari Thorn

Scope: Signal of hearing losses

[5] Update of section 4.8 of the SmPC. The package leaflet is updated accordingly.
[6] Update of section 4.5 of the enzalutamide SmPC. Update of sections 4.4 and 4.5 of the digoxin SmPC and update of the package leaflet.

EPITT 20128 – Follow-up to January 2025

Background

For background information, see PRAC minutes January 2025.

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

Discussion

Having considered the available evidence in EudraVigilance, the literature and the responses of the MAH of Xolair (omalizumab), PRAC has concluded that the current evidence is insufficient to establish a causal relationship between omalizumab and hearing losses to further warrant an update to the product information and/or risk management plan at present.

Summary of recommendation(s)

- The MAHs of omalizumab-containing medicinal products Xolair and Omlyclo should monitor cases of hearing losses in the next PSUR.

4.2.5. Vortioxetine - BRINTELLIX (CAP) - EMEA/H/C/002717/SDA/010

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Jo Robays

Scope: Signal of hallucinations, not related to serotoninergic syndrome

EPITT 20152 – Follow-up to February 2025

Background

For background information, see PRAC minutes February 2025.

The MAH replied to the request for information on the signal of hallucinations, not related to serotoninergic syndrome and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence, including data from EudraVigilance, literature and the cumulative review submitted by the MAH, PRAC concluded that there is sufficient evidence to establish a causal association between vortioxetine and hallucinations. Therefore, the product information should be updated to add hallucinations as an undesirable effect with a frequency 'uncommon'.

Summary of recommendation(s)

- The MAH for Brintellix (vortioxetine) should submit to EMA, within 60 days, a variation to update the product information[7].

4.3. Variation procedure(s) resulting from signal evaluation

See Annex I 14.3.

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

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

5.1.1. Belumosudil - (CAP MAA) - EMEA/H/C/006421, Orphan

Applicant: Sanofi Winthrop Industrie

Scope (pre D-180 phase): Treatment of chronic graft-versus host disease (cGVHD) after failure of at least two prior lines of systemic therapy

5.1.2. Hydrocortisone - (CAP MAA) - EMEA/H/C/005201, PUMA[8]

Scope (pre D-180 phase): Prevention of bronchopulmonary dysplasia in preterm infants born less than 28 weeks of gestation

5.1.3. Mozafancogene autotemcel - (CAP MAA) - EMEA/H/C/005537, PRIME, Orphan

Applicant: Rocket Pharmaceuticals B.V., ATMP

Scope (pre D-180 phase): Treatment of paediatric patients with Fanconi Anaemia Type A

5.1.4. Nipocalimab - (CAP MAA) - EMEA/H/C/006379

Scope (pre D-180 phase): Treatment of generalised myasthenia gravis

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

Applicant: Arrowhead Pharmaceuticals Ireland Limited

Scope (pre D-120 phase, accelerated assessment): Treatment of familial chylomicronaemia syndrome (FCS)

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

See also Annex I 0

5.2.1. Apixaban – ELIQUIS (CAP) – EMA/VR/0000262422

Applicant: Bristol-Myers Squibb Pfizer EEIG

[8] Paediatric-use marketing authorisation(s)

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an updated RMP version 22.0 and updated Annex II of the PI in order to discontinue the apixaban Prescriber Guide (PG) and Patient Alert Card (PAC) as an additional risk minimization measure (aRMM) for healthcare professionals (HCPs) and patients. Accordingly, information about PG and PAC is removed from Annexes III of the PI

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 Eliquis, a centrally authorised medicine containing apixaban, to update the RMP to discontinue the apixaban Prescriber Guide (PG) and Patient Alert Card (PAC) as an additional risk minimization measure (aRMM) 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 for Eliquis (apixaban) in the context of the variation procedure under evaluation by PRAC and CHMP could be considered acceptable provided that an update to RMP version 22.0 is submitted.
- PRAC supported the MAH's proposal to remove the prescriber guide as aRMM from the RMP and product information. However, PRAC emphasized that the patient card includes information on specific signs and symptoms—such as bruising, bleeding under the skin, blood in the stool, and blood in the urine—related to the risk of bleeding. Given the seriousness of this risk, PRAC considered it essential to retain the patient card as an aRMM in the RMP.

5.2.2. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0028, Orphan

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: Submission of a revised protocol for study EP0218 listed as an obligation in the Annex II of the Product Information. This is a Long-term Registry in approved indications for fenfluramine, with a specific focus on cardiovascular events and growth retardation. The RMP version 4.0 is updated accordingly. In addition, the MAH introduced minor amendments in the targeted follow-up questionnaire for cardiovascular 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 Fintepla, a centrally authorised medicine containing fenfluramine, to update the RMP as a consequence of a revised protocol for study EP0218 listed as an obligation in the Annex II of the Product Information. PRAC is

responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation. For further background, see PRAC minutes January 2025, April 2025.

Summary of advice

- The RMP version 4.3 for Fintepla (fenfluramine) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.
- PRAC supported the Rapporteur's assessment and conclusions and agreed that a reduction of the sample size may only be considered when the potential for recruitment in EP0218 has become clearer. Further, the MAH should re-discuss and re-evaluate the inclusion of additional European countries in the study at a later stage, in case the agreed sample size could not be achieved in chosen study countries.
- As there is currently another RMP (version 4.1) under assessment in the Renewal of the marketing authorisation procedure EMA/R/0000256601, the MAH committed on integrating all approved RMP changes of this type II variation procedure into the final RMP version of the Renewal procedure EMA/R/0000256601.

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

See also Annex I 0

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

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

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

Background

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

CHMP is evaluating a type II variation for Lutathera, a centrally authorised product containing lutetium (177Lu) oxodotreotide, to include an indication as per the scope. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure. For further background, see PRAC minutes March 2025.

Summary of advice

- The RMP for Lutathera (lutetium (177Lu) oxodotreotide) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP is submitted.
- PRAC agreed that long-term safety data collection for the adolescent population should be explored via the means of a study in existing EU registries. PRAC also supported the addition of safety concerns 'hyposplenism' and 'hypopituitarism' as missing information with additional pharmacovigilance activities proposed.

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. Amivantamab – RYBREVANT (CAP) – EMA/PSUR/0000248975

Applicant: Janssen Cilag International

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010977/202411)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Rybrevant, a centrally authorised medicine containing amivantamab 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 Rybrevant (amivantamab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add skin ulcer as a warning and an undesirable effect with a frequency 'uncommon' for amivantamab monotherapy, and 'common' for amivantamab in combination with carboplatin and pemetrexed, and amivantamab in combination with lazertinib. Therefore, the current terms of the marketing authorisation(s) should be varied[9].
- In the next PSUR, the MAH should analyse, summarise and discuss new emerging cardiovascular events, new cases of anaphylactic reaction and of systemic

[9] 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.

administration related reactions differentiated between intravenous and subcutaneous administration if information on the route of administration is available.

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. Andexanet alfa – ONDEXXYA (CAP) – EMA/PSUR/0000248508

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010764/202410)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Ondexxya, a centrally authorised medicine containing andexanet 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 Ondexxya (andexanet alfa) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the interaction regarding heparin. Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAH should discuss the results of the study REVERXaL (NCT06147830) .

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

6.1.3. Ceftaroline fosamil – ZINFORO (CAP) – EMA/PSUR/0000248505

Applicant: Pfizer Ireland Pharmaceuticals Unlimited Company

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00010013/202410)

Background

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

[10] Update of SmPC sections 4.4 and 4.5. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Zinforo (ceftaroline fosamil) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning regarding severe cutaneous adverse reactions (SCARs) and to add drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) as undesirable effects 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 provide a cumulative review on drug-induced liver injury (DILI) cases and on the risk of acute renal failure (SMQ narrow), and discuss the need to update the product information, as warranted.

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

6.1.4. Darifenacin – EMSELEX (CAP) – EMA/PSUR/0000248469

Applicant: pharmaand GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00000933/202410)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Emselex, a centrally authorised medicine containing darifenacin 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 Emselex (darifenacin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add confusional state and muscle spasms as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR(s), the MAH should closely monitor cases of dementia. Relevant publications about darifenacin and other antimuscarinic medicines used for overactive bladder (OAB) should be presented, as well as on the additive effects of different anticholinergic medicines along with darifenacin or other antimuscarinic medicines used for OAB. Cases of dementia with darifenacin should be cumulatively reviewed in the next PSUR with detailed information on concomitant medications. The MAH should also continue to closely monitor diabetes mellitus (new onset or impairment of pre-existing diabetes), muscular weakness and myalgia.

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

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.

6.1.5. Pegcetacoplan – ASPAVELI (CAP) – EMA/PSUR/0000248510

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010974/202411)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Aspaveli, a centrally authorised medicine containing pegcetacoplan 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 Aspaveli (pegcetacoplan) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide a cumulative review of cases of meningococcal infection during pegcetacoplan treatment, including information on type of *Neisseria meningitides* causing the infection (A, C, W, Y, B), vaccination status of the patient for different types of *Neisseria meningitides*, medical history of the patient, as well as discuss whether risk minimisation activities are properly functioning to minimise risk of meningococcal infections. The MAH should also present available data on vaccination status of patients experiencing serious infections caused by other encapsulated bacteria, *Streptococcus pneumoniae* and *Haemophilus influenzae*, including whether these infections occurred in patients vaccinated according to established recommendation. In addition, the MAH should discuss whether the additional risk minimisation measures in place, including controlled distribution programme, for the important identified risk of serious infections and meningococcal infections in particular, are still considered necessary. Moreover, the MAH should discuss and re-assess the aeducational materials and consider whether some of the other safety concerns addressed by the educational materials should be removed, given that some of these risks are well known by healthcare professionals. Finally, the MAH should monitor the ongoing evaluation of the signal of anaphylactic reaction (EMEA/H/C/005553/II/0028).

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

6.1.6. Recombinant respiratory syncytial virus pre-fusion f protein, adjuvanted with as01e – AREXVY (CAP) – EMA/PSUR/0000248473

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00000031/202411)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Arexvy, a centrally authorised medicine containing recombinant respiratory syncytial virus pre-fusion f protein, adjuvanted with as01e 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 Arexvy (recombinant respiratory syncytial virus pre-fusion f protein, adjuvanted with as01e) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add Guillain-Barré syndrome as an undesirable effect with a frequency 'very rare'. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- In the next PSUR, the MAH should provide a cumulative review of cases of syncope with a time to onset >7 days. In addition, the MAH should continue to closely monitor cases of atrial fibrillation, seizures, new cases of injection site necrosis, the important potential risks for other regions (pIMD -neurological other than GBS and non neurological- and risk of shock and anaphylaxis), as well as the missing information use in immunocompromised adults aged 60 years and older. Fatal cases should continue to be analysed in the next PSUR. Finally, the MAH should explain how cases of use in pregnancy not considered vaccination errors were identified and how are managed.

The frequency of PSUR submission should be revised from 6-monthly to yearly and the next PSUR should be submitted to EMA within 90 days of the data lock point[14]. The EURD list provided for under Article 107c(7) of Directive 2001/83/EC is updated accordingly.

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

See also Annex I 0

6.2.1. Stiripentol – DIACOMIT (CAP); NAP – EMA/PSUR/0000248464

Applicant(s): Biocodex, various

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00002789/202411)

Background

[13] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[14] Since the MAH wants to align the data lock point (DLP) to the international birth date (IBD), the next PSUR should cover the reporting period from 3 November 2024 to 3 May 2026.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Diacomit, (a) centrally authorised medicine(s) containing stiripentol, and nationally authorised medicines containing stiripentol 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 stiripentol-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add pneumonia, aspiration pneumonia as undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisations 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. PSUR single assessment (PSUSA) procedures including nationally authorised products (NAPs) only

See also Annex I 16.2.1.

6.3.1. Benzydamine (NAP) - EMA/PSUR/0000248448

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000375/202410)

Background

Benzydamine is a non-steroidal anti-inflammatory active substance with analgesic and antiexudative properties. At topical concentrations, benzydamine also acts as a slight disinfectant and superficial anaesthetic. It is indicated for the symptomatic treatment of inflammatory, painful and swelling conditions of the mouth and throat (e.g. gingivitis, stomatitis, pharyngitis, aphthous ulcers and oral ulceration due to radiation therapy), vulvovaginitis of any origin and nature featuring small vaginal discharges, itching, irritation, burning and vulvar pain, personal hygiene after giving birth, relief of symptoms associated with painful inflammatory conditions of the musculo-skeletal system including traumatic conditions and acute inflammatory disorders, as well as for traumatic conditions: pharyngitis following tonsillectomy or the use of a naso-gastric tube, dental operations, as warranted.

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

Summary of recommendation(s) and conclusions

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of benzydamine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning on new information with regards to the risk(s) of the product when used during pregnancy. Therefore, the current terms of the marketing authorisation(s) should be varied[16]. The text is to be adapted, at a national level, to the existing wordings in the product information, while an already existing similar or stricter advice remains valid and should remain. In case the product information contains statements indicating no teratogenic effects or no relevant systemic exposure, this text should be deleted.

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.

6.3.2. Dexketoprofen (NAP) - EMA/PSUR/0000248453

Applicant(s): various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure (PSUSA/00000997/202410)

Background

Dexketoprofen is a non-steroidal anti-inflammatory group of drugs and used as an analgesic, anti-inflammatory and antipyretic.

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of dexketoprofen-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information for the systemic formulations should be updated to add a warning on Kounis syndrome, as well as Kounis syndrome and fixed drug eruption as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) for the systemic formulations should be varied[17].
- The product information for topical formulations should be also updated to add contraindication and recommendation about the use in pregnancy. Therefore, the

[16] Update of SmPC section 4.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.
[17] 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.

current terms of the marketing authorisation(s) for topical formulations should be varied[18].

- In the next PSUR, the MAHs should closely monitor cases of hypertensive crisis, DRESS, Generalised Bullous Fixed Drug Eruption (GBFDE) and cases related to cardiovascular and cerebrovascular events. The MAHs should also closely monitor cases of serious skin reaction including fixed drug eruption only for topical formulations.

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.

6.3.3. Isoniazid (NAP) - EMA/PSUR/0000248454

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00001789/202411)

Background

Isoniazid is a chemotherapeutic active substance against strains of *Mycobacterium tuberculosis* and is indicated for the treatment of tuberculosis caused by *Mycobacterium tuberculosis*.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing isoniazid 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 isoniazid-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding severe cutaneous adverse reactions (SCAR) and to add acute generalised exanthematous pustulosis (AGEP) and lupus-like syndrome as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[19].
- In the next PSUR, the MAHs should provide a cumulative review of cases of life-threatening and fatal hepatocellular damage and hepatitis related to isoniazid treatment, and discuss the need to update the product information as warranted.

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

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

6.3.4. Methylphenidate hydrochloride (NAP) - EMA/PSUR/0000248487

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002024/202410)

Background

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

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing methylphenidate hydrochloride 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 methylphenidate hydrochloride-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add obsessive-compulsive disorder (including trichotillomania and dermatillomania) as an undesirable effect with a frequency 'rare', increased intraocular pressure and glaucoma as warnings and undesirable effects with a frequency 'not known', and dry eye as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[20].
- In the next PSUR, the MAHs should include the risk 'Cardiac malformation risk following maternal first trimester methylphenidate use' as an important potential risk in the list of safety concerns. The MAHs should also provide cumulative reviews on cases of increased cortisol levels, testicular hypofunction, hypopigmentation disorders, (acute) angle closure glaucoma, decreased visual acuity and aggravated myopia, as well as colour blindness (including acquired colour blindness) and visual field disorders. The MAHs should continue to closely monitor the risk of pulmonary hypertension and discuss any need to update the product information as warranted. In addition, the MAHs are requested to analyse and discuss the results of Ayme-Dietrich et al., 2024 and to assess all relevant cases available on valvular heart diseases. Finally, the MAHs should remove the following risks from the list of safety concerns and the RMP: psychosis/mania, verbal or motoric tics, depression, aggression, drug abuse/drug dependence, withdrawal syndrome, seizures, cerebrovascular disorders, neonatal toxicity, priapism, drug induced liver failure/injury, suicidality, self-injury and self-injurious ideation, off label use, carcinogenicity, serious cardiovascular events, reduced weight gain (paediatric indication only), decreased rate of growth (paediatric indication only), sexual maturation delayed (paediatric indication only), and long-term effects.

[20] 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.

- The MAHs should submit a variation to the relevant national competent authorities to remove monitoring of publications from ADDUCE studies from Part III of the RMP along with related safety concerns.

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

6.3.5. Miconazole, hydrocortisone / miconazole nitrate, miconazole nitrate / zinc oxide (NAP) - EMA/PSUR/0000248459

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00002052/202410)

Background

Miconazole is an antifungal and antibacterial indicated (as monocomponent and/or in combination) for the treatment of candidiasis of the oropharynx and gastrointestinal tract and of digestive tract mycoses, local treatment of vulvovaginal candidiasis (VVC) and superinfections due to gram positive bacteria, and treatment of mycotic infections of skin or skin appendages, as warranted.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing miconazole, hydrocortisone/miconazole nitrate and miconazole nitrate/zinc oxide 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 miconazole-, hydrocortisone/miconazole nitrate- and miconazole nitrate/zinc oxide-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information of all topical formulations (dermatological and gynaecological) should be updated to add a warning regarding potential bleeding events with concomitant use of miconazole and warfarin, as well as a drug-drug interaction regarding miconazole and warfarin or other vitamin k antagonists. Therefore, the current terms of the marketing authorisation(s) should be varied[21].
- The product information of the oral formulations should be updated to add fixed drug eruption as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[22].

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

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

6.3.6. Timolol[23] (NAP) - EMA/PSUR/0000249788

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure (PSUSA/00010432/202410)

Background

Timolol is a nonselective beta blocking agent, indicated for the treatment of angina pectoris (due to ischaemic heart disease), hypertension, reduction of mortality and reinfarction in patients surviving acute myocardial infarction, as well as migraine (prophylactic treatment) in order to reduce the number of attacks, as warranted.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing timolol 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 timolol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing warning and the information regarding the drug-drug interaction to add the risk of severe hypoglycaemia with the concomitant use of beta-blockers and sulfonylureas. Therefore, the current terms of the marketing authorisation(s) should be varied[24].
- In the next PSUR, the MAHs should provide a cumulative review of the cases of Parkinson´s disease, including cases from the safety database, data from clinical trials and literature search and to discuss the publication by *Wei et al, 2023*[25].

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

6.4. Follow-up to PSUR/PSUSA procedures

See also Annex I 0

6.4.1. Azacitidine – ONUREG (CAP) – EMA/PAM/0000262249

Applicant(s): various

PRAC Rapporteur: Bianca Mulder

[23] For systemic use only
[24] 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.
[25] Wei, Cheng-Yu et al. The risk of beta blockers and the benefit of beta2 agonists in Parkinson's disease. Journal of the Neurological Sciences, Volume 455, 121813. https://www.jns-journal.com/article/S0022-510X(23)01274-1/fulltext

Scope: Clinical safety review: provision of a thorough causality assessment of all cumulative cases of differentiation syndrome and provision of a review of any cases of pericardial effusion and pericarditis with oral azacitidine and discuss the need for an update of the product information (LEG from EMEA/H/C/PSUSA/00010935/202405)

Background

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

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit further data on differentiation syndrome and of any cases of pericardial effusion and pericarditis with oral azacitidine. The responses were assessed by the Rapporteur for further PRAC advice. For further background, see PRAC minutes January 2025.

Summary of advice/conclusion(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed that there is sufficient evidence to establish a causal relationship between azacitidine oral formulation and differentiation syndrome. On the other hand, in light of the current knowledge there is insufficient evidence to establish a causal association between oral azacitidine and pericardial effusion; thus, the MAH should continue monitoring events of pericarditis and pericardial effusion in upcoming PSURs.
- The MAH should submit to EMA, within 60 days, a variation[26] to update the product information to add differentiation syndrome as a warning and an undesirable effect with a frequency 'not known'.

6.4.2. Semaglutide – OZEMPIC (CAP) – EMA/PAM/0000262468

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Clinical Safety Review: To assess the potential association between semaglutide exposure and non-arteritic anterior ischemic optic neuropathy (NAION)

Background

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

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit further data on NAION. The responses were assessed by the Rapporteur for further PRAC advice. For further background, see PRAC minutes January 2025.

Summary of advice/conclusion(s)

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

- Based on the available data and the Rapporteur's assessment, as well as the explanations provided during the oral explanation, PRAC agreed that there is sufficient evidence to establish a causal relationship between semaglutide and NAOIN.
- The MAH should submit to EMA, within 60 days, a variation[27] to update the product information to add a warning on NAION, and add NAION as an undesirable effect with a frequency 'very rare'.

6.4.3. Semaglutide – RYBELSUS (CAP) – EMA/PAM/0000262449

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Clinical Safety Review: To assess the potential association between semaglutide exposure and non-arteritic anterior ischemic optic neuropathy (NAION)

Background

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

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit further data on NAION. The responses were assessed by the Rapporteur for further PRAC advice. For further background, see PRAC minutes January 2025.

Summary of advice/conclusion(s)

- Based on the available data and the Rapporteur's assessment, as well as the explanations provided during the oral explanation, PRAC agreed that there is sufficient evidence to establish a causal relationship between semaglutide and NAOIN.
- The MAH should submit to EMA, within 60 days, a variation[28] to update the product information to add a warning on NAION and add NAION as an undesirable effect with a frequency 'very rare'.

6.4.4. Semaglutide – WEGOVY (CAP) – EMA/PAM/0000262475

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Mari Thorn

Scope: Clinical Safety Review: To assess the potential association between semaglutide exposure and non-arteritic anterior ischemic optic neuropathy (NAION)

Background

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

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

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit further data on NAION. The responses were assessed by the Rapporteur for further PRAC advice. For further background, see PRAC minutes January 2025.

Summary of advice/conclusion(s)

- Based on the available data and the Rapporteur's assessment, as well as the explanations provided during the oral explanation, PRAC agreed that there is sufficient evidence to establish a causal relationship between semaglutide and NAOIN.
- The MAH should submit to EMA, within 60 days, a variation[29] to update the product information to add a warning on NAION and add NAION as an undesirable effect with a frequency 'very rare'.

6.5. Variation procedure(s) resulting from PSUSA evaluation

See Annex I 16.4.1.

6.6. Expedited summary safety reviews[30]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[31]

See also Annex I 17.2.

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

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

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

Background

[29] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly.
[30] 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
[31] In accordance with Article 107n of Directive 2001/83/EC

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

In order to fulfil the specific obligation to conduct a PASS (Annex II-E) imposed as conditions to the marketing authorisation, the MAH Biogen Netherlands B.V. submitted to EMA an amended PASS protocol version 2.0 for a study entitled: 'An observational registry-based study to evaluate the long-term safety of tofersen in people with SOD1-ALS', for review by PRAC. PRAC is responsible for evaluating the PASS protocol.

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 2.0 in accordance with Article 107n of Directive 2001/83/EC, PRAC objected to the draft protocol for the above listed medicinal product(s), as the Committee considered that that the design of the study did not fulfil the study at this stage.
- PRAC therefore recommended that the MAH should include in the study milestones of the protocol that the study report planned to be submitted within 12 months of end of proposed data extraction may not be 'final report of study results' and that the continuation of the study is determined based on the data available at that stage. In addition, PRAC recommended that potential continuation of the study should be determined based on the results obtained from this study as well as all other information gathered from other SOBs at that stage.
- The MAH should submit a revised PASS protocol within 30 days to EMA. A 30 days-assessment timetable will be followed.

7.1.2. Volanesorsen – WAYLIVRA (CAP) – EMA/PASS/0000262889

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: PASS amendment [107o]: Substantial amendment to a PASS to characterise the safety and effectiveness of WAYLIVRA in patients with Familial Chylomicronaemia Syndrome (FCS) under real-world conditions

Background

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

In order to fulfil the specific obligation to conduct a PASS (Annex II-E) imposed as conditions to the marketing authorisation, the MAH Akcea Therapeutics Ireland Limited submitted to EMA an amended PASS protocol version 5.0 for a study entitled 'WAYLIVRA Post-Authorisation Safety Study (PASS) and Product Registry', for review by PRAC. PRAC is responsible for evaluating the PASS protocol.

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 5.0 in accordance with Article 107o of Directive 2001/83/EC, PRAC considered that the study is non-interventional and the

substantial amendments to the imposed category 2 PASS protocol for Waylivra (volanesorsen sodium) can be endorsed.

- PRAC therefore recommended that the MAH should submit a variation to amend the RMP and Annex II.E to reflect the updated milestones.

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

See also Annex I 17.2. 17.2.1.

7.2.1. Rozanolixizumab – RYSTIGGO (CAP) – EMA/PAM/0000262838

Applicant: UCB Pharma

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Revised protocol for PASS No. MG0027 Real-world observational secondary data study: A Multi-National Cohort Study to evaluate the safety of rozanolixizumab in generalized myasthenia gravis patients

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 part of the RMP for Rystiggo (rozanolixizumab), the MAH was required to conduct a PASS in order to assess the risks of aseptic meningitis, serious infections and the missing information on long term safety and use in pregnancy. The MAH submitted a protocol for a study (as part of the RMP but outside the scope of Article 107n of Directive 2001/83/EC) which was assessed by the Rapporteur. PRAC was requested to provide advice to CHMP on the protocol submitted by the MAH.

Summary of advice

- The study protocol for Rystiggo (rozanolixizumab) version 2.0 is not considered acceptable. Due to the questionable feasibility of the study, PRAC recommended that the PASS should be removed from the pharmacovigilance plan of the RMP and the safety concerns (serious infections, use during pregnancy, aseptic meningitis and long-term safety) should be further characterised by routine pharmacovigilance activities.
- The MAH is requested to remove the study from the RMP and updated it in the next regulatory opportunity.

7.3. Results of PASS imposed in the marketing authorisation(s)[33]

See also Annex I 17.3.

[32] 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
[33] In accordance with Article 107p-q of Directive 2001/83/EC

7.3.1. Pomalidomide – IMNOVID (CAP) – EMA/PASS/0000262876

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: PASS results [107q]: Final study report for a non-interventional post authorization registry of patients treated with pomalidomide for relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on the last therapy

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 a condition to the marketing authorisation(s) (Annex-IID), the MAH was required to conduct a non-interventional post-authorisation registry of patients treated with pomalidomide for relapsed and refractory multiple myeloma to monitor the incidence of adverse drug reactions and to monitor the implementation and compliance of risk minimisation measures (CC-4047-MM-015).

The final study report was submitted to EMA by the MAH on 21 March 2025. PRAC discussed the final study results in addition to the MAH's responses.

Summary of recommendation(s) and conclusions

- Based on the review of the final report of the non-interventional PASS CC-4047-MM-015, PRAC considered that the benefit-risk balance of Imnovid (pomalidomide) remains unchanged.
- As a consequence, PRAC recommended that the terms of the marketing authorisation(s) for Imnovid (pomalidomide) should be varied to remove the PASS from Annex II-D on the 'conditions or restrictions with regard to the safe and effective use of the medicinal product'. In addition, PRAC supported the removal of the pregnancy reporting form included in the educational healthcare professional brochure and consequently the black triangle and additional monitoring statements from the product information.

7.4. Results of PASS non-imposed in the marketing authorisation(s)[34]

See also Annex I 17.4.

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

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Mari Thorn

Scope: Update of section 4.6 based on final results from the Icatibant Outcome Survey (IOS) registry listed as a category 3 study in the RMP; this is a prospective, observational disease

[34] 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

registry. The RMP version 8 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI and to bring the PI in line with the latest QRD template version 10.4

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 Firazyr (icatibant), the MAH conducted a non-imposed non-interventional PASS registry IOS to assess the important potential risks and the missing information. The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI). For further background, see PRAC minutes February 2025.

Summary of advice

- Based on the available data, the MAH's responses to the RSI and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be considered acceptable provided that the MAH submits satisfactory responses to a RSI.
- PRAC considered that no further additional pharmacovigilance activities are warranted that, in light of the current knowledge, can characterise the risks. Therefore, the risks and missing information included in the safety specification of the RMP can be removed apart from the missing information 'Use in in Pregnant and Lactating Women' which PRAC suggested to be kept since the data are still very scarce.

7.4.2. Covid-19 vaccine (recombinant, adjuvanted) – BIMERVAX (CAP) – EMA/VR/0000262308

Applicant: Hipra Human Health S.L.

PRAC Rapporteur: Zane Neikena

Scope: Submission of an updated RMP version 2.0 in order to remove one category 3 study (C-VIPER PASS), to include changes to the due date for the provision of the final study report for two category 3 studies (VAC4EU PASS, VAC4EU PAES) and to add BIMERVAX XBB.1.16 (Omicron XBB.1.16-adapted BIMERVAX)

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 Bimervax, the MAH planned to conduct a non-imposed non-interventional PASS to assess obstetric, neonatal and infant outcomes among women vaccinated during pregnancy with a COVID-19 vaccine. The Rapporteur assessed the MAH's justification for removing this study from the RMP as well as other changes proposed by the MAH as stated in the scope of this variation.

Summary of advice

- Based on the available data and the Rapporteur's review, PRAC agreed with the removal of the category 3 PASS of the COVID-19 Vaccines International Pregnancy Exposure Registry (C-VIPER) based on the MAH's justification and considered that the RMP version 2.0 is acceptable.

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

See also Annex I 17.5.

7.5.1. Talimogene laherparepvec – IMLYGIC (CAP) – EMA/PAM/0000262826

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: 7th interim report: PASS 20130193: A post-marketing, prospective cohort study of patients treated with talimogene laherparepvec in clinical practice to characterize the risk of herpetic infection among patients, close contacts, and healthcare providers; and long term safety in treated patients

Background

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

The MAH had committed to perform a PASS (20130193) according to the RMP (Annex II-D). Interim results of study 20130193 examining the risk of herpetic illness among patients, close contacts, and healthcare providers and the long-term safety in treated patients, were assessed by the Rapporteur for PRAC review.

Summary of advice

- PRAC discussed the request of the MAH to remove the PASS from the pharmacovigilance plan of the RMP. PRAC supported the MAH's request to finalise the study earlier and, in principal, the removal of the study after the final assessment of the final study report, which should be submitted via an appropriate procedure.

7.6. Others

See Annex I 17.6.

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1.

8.2. Conditional renewals of the marketing authorisation

None

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. Buprenorphine (transdermal patches) (NAP) - DE/H/4394/001-003/II/016

Applicant: Glenmark Arzneimittel GmbH

PRAC Lead: Martin Huber

Scope: PRAC consultation on type II variations to update the product information of buprenorphine-containing products (transdermal patches) regarding the risks of persistent post-operative opioid use (PPOU) and opioid-induced ventilatory impairment (OIVI) based on MHRA safety reviews, at the request of Germany

Background

Buprenorphine is an opioid used for the treatment of pain of moderate intensity when an opioid is necessary for obtaining adequate analgesia (transdermal patches formulation).

In the context of the evaluation of a type II variation procedure on type II variations to update the product information of buprenorphine-containing products (transdermal patches) regarding the risks of persistent post-operative opioid use (PPOU) and opioid-induced ventilatory impairment (OIVI) based on MHRA safety reviews, Germany requested PRAC advice on its assessment.

Summary of advice

- Considering that opioid use disorder and CNS/respiratory depression are already addressed in detail in the SmPC, and that buprenorphine-containing transdermal patches are not to be used in the treatment of acute pain, PRAC agreed with the Reference Member State position that the proposed changes for the medicinal products under review in the variations DE/H/4394/001-003/II/016 and DE/H/5080/001-003/II/013 should not be implemented.

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The Chair welcomed Martin Votava, as the new alternate representing Healthcare Professionals (HCP) and Yiannoula Koulla as the new member representing Patients' Organisation nominated by the European Commission (EC) for a 3 year-mandate (01/05/2025 to 30/04/2028).

12.1.2. The Chair thanked Salvatore Messana for his contribution as an alternate representing HCPs nominated by the EC, as well as Marko Korenjak and Michal Rataj for their contribution as a member and alternate, respectively, representing Patients' Organisations nominated by the EC.Vote by proxy

Annalisa Capuano gave a proxy to Maria Teresa Herdeiro, Georgia Gkegka gave a proxy to Elena Kaisis and Anette Stark gave a proxy to Hedvig Nordeng, covering the entire meeting.

12.1.3. Scientific Committee Meetings – alternating face-to-face and virtual meetings schedule for 2026

The topic was postponed.

12.1.4. Oral Explanations for face-to-face meetings

At the organisational, regulatory and methodological matters (ORGAM) meeting on 23 June 2025, the EMA Secretariat presented to PRAC a proposal for a 1-year pilot to reintroduce the possibility for MAHs/Applicants to hold face-to-face oral explanations during in-person PRAC plenary meetings. PRAC agreed with the proposal.

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

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

The topic was postponed.

12.4.2. Explanatory note on the withdrawal of the 'Interim guidance of seasonal influenza vaccines enhanced safety surveillance systems'

PRAC leads: Jean Michel Dogné

The PRAC Lead together with the EMA Secretariat presented PRAC with the proposal to withdraw the *Interim guidance on enhanced safety surveillance for seasonal influenza vaccines in the EU - Scientific guideline ' (EMA/PRAC/222346/2014)*. PRAC was also presented with the explanatory note with the justification for such decision to be published on EMA website. PRAC endorsed both the proposal and the explanatory note.

12.4.3. The Incident Management Plan - overview and guidance update

At the organisational, regulatory and methodological matters (ORGAM) meeting on 23 June 2025, the EMA Secretariat presented PRAC with an overview of the EU-Incident Management Plan, summarizing the changes introduced in the revised guidance. PRAC expressed its support for the proposed revision.

12.5. Cooperation with International Regulators

12.5.1. EMA/FDA Collaboration and the Liaison Program

The topic was postponed.

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

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits - Working Group of Quality Managers (WGQM) - report to PRAC

PRAC lead: Jan Neuhauser; Klaus Stuewe (WGQM Chair)

The WGQM Chair presented to PRAC the revision 3 of the *Guide to Pharmacovigilance Audit Strategies and Risk Ratings,* focusing on the update of the network risk ratings of core pharmacovigilance process areas. PRAC endorsed the proposed changes.

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

None

12.10.3. PSURs repository

None

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

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

12.11. Signal management

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

PRAC lead: Martin Huber

The Chair of the SMART working group – Processes presented to PRAC a proposal for further streamlining the current process for managing class signals, including the identification of the Lead Rapporteur, defining the responsibilities of each Rapporteur, as well as the timelines for

circulating the consolidated assessment report. PRAC welcomed the initiative and endorsed the proposal.

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. Necessity and proportionality of assessment of the retention pseudonymised Individual Case Safety Reports (ICSRs) in EudraVigilance – European Data Protection Supervisor (EDPS) Audit recommendation

The EMA Secretariat presented to PRAC a recommendation resulting from an EDPS EudraVigilance audit which refers to the re-assessment of the necessity and proportionality of maintaining pseudonymised ICSR data in EudraVigilance, taking into account that data that are no longer necessary should be erased or anonymised. The EMA Secretariat further presented a summary of the EMA's assessment performed together with the conclusion that no changes to the established retention period are considered necessary. PRAC endorsed the conclusions of the assessment.

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

12.18.3. Webpage dedicated to risk minimisation measures on EMA website - new initiative

At the organisational, regulatory and methodological matters (ORGAM) meeting on 23 June 2025, the EMA Secretariat presented to PRAC the draft risk minimisation measures (RMM) webpage text and draft communication strategy, as agreed by the PRISMA group. The aim of this initiative is to provide a central virtual space in the EU to link to the webpages of NCAs providing access to additional RMM materials. PRAC members were invited to send their comments on the proposed text by 04 July 2025.

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. Association of venous thromboembolism with non-steroidal anti-inflammatory drug use in women 15-49 years using hormonal contraceptives (P3-C3-008) DARWIN EU® - PRAC Sponsor's critical appraisal

PRAC lead: Karin ErneholmPRAC discussed the PRAC Sponsor's appraisal of the DARWIN EU® Study 'Association of venous thromboembolism with non-steroidal anti-inflammatory drug use in women 15-49 years using hormonal contraceptives' (EUPAS1000000443).

The study was requested to investigate this association after prior studies suggested an increased risk of VTE among NSAIDs users and in women with concomitant use of high/medium risk hormonal contraception (including the recent study by Meaidi et al.). The DARWIN EU study used self-controlled case analysis to assess the association in risk windows of 14 days prior to, on the day of, and within 7 days after the use of NSAIDs; and within 30 days after their cessation. The study also used paracetamol, which is not known to be the cause of VTE, as a negative control, in order to detect unmeasured/residual confounding. The results showed that the risk of VTE was increased in the period before NSAID initiation, increasing further on the day of NSAID start and later decreasing to the previous levels. The results were consistent across the four databases and for the individual NSAIDs and hormonal contraceptive classes. The results for paracetamol showed a similar pattern to the NSAIDs, which suggested the presence of unmeasured/residual confounding.

In conclusion, the temporal association between the initiation of NSAIDs and VTE, in women using hormonal contraceptives who had a VTE, was most likely explained by confounding by indication.

PRAC agreed with the PRAC Sponsor's appraisal and considered that the study findings did not warrant regulatory action at this stage.

12.21.2. The MAHs of the products in scope of the study are reminded as part of their routine pharmacovigilance requirements, to include the study findings (EUPAS1000000443) and any other relevant published data, as part of their upcoming PSUR submissions, together with their comments.Fitness-for-use of Real-world data (RWD) sources on Duchenne Muscular Dystrophy (DMD)

At the organisational, regulatory and methodological matters (ORGAM) meeting on 23 June 2025, the EMA Secretariat provided PRAC with an update on real-world evidence activities, with particular emphasis on the project addressing the description and assessment of the fitness-for-purpose of real-world data (RWD) sources related to Duchenne Muscular Dystrophy for regulatory decision-making, including the project's objectives and its deliverables planned for 2026. PRAC members were invited to indicate their interest in participating in this initiative . PRAC was also notified about the upcoming multi-stakeholder workshop on patient registries for Alzheimer's disease (Joint Heads of Medicines Agencies (HMA)/European Medicines Agency (EMA) multistakeholder workshop on Patient Registries for Alzheimer's disease | European Medicines Agency (EMA).

12.21.3. Good Pharmacovigilance Practice (GVP) – mid-year update 2025

PRAC lead: Ulla Wändel Liminga

The EMA Secretariat presented to PRAC the regular update of the activities regarding GVP

update development in line with PRAC and EMA work plans for 2025. PRAC noted the information.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[35]

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[36].

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Epcoritamab – TEPKINLY (CAP)

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Signal of hypogammaglobulinaemia

EPITT 20174 – New signal

14.2. New signals detected from other sources

None

14.3. Variation procedure(s) resulting from signal evaluation

14.3.1. Telmisartan / hydrochlorothiazide – TOLUCOMBI (CAP); NAP – EMA/VR/0000242380

Applicant(s): KRKA tovarna zdravil d.d. Novo mesto, various

PRAC Rapporteur: Amelia Cupelli

Scope: C.I.z: Update section 4.4 and 4.8 of the SmPC to added new safety information regarding intestinal angioedema. The package leaflet was update accordingly.

C.I.2.a: Update of sections 4.2, 4.3 (anuria), 4.4 (hyponatremia), 4.5 (iodinated contrast products), 4.6 (fertility), 4.7 (syncope, vertigo), 4.8 (combined table of ADR) and 5.2 (renal impairment) of the SmPC in order to align with reference labels for both active substances. The Package Leaflet is updated accordingly.

[35] 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

[36] 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

In addition, the MAH has taken to opportunity to update the annexes in line with QRD version 10.4 and to update the list of local representatives

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

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

15.1.1. Denosumab - (CAP MAA) - EMEA/H/C/006490

Scope (pre D-180 phase): Treatment of osteoporosis and bone loss in postmenopausal women and in men

15.1.2. Denosumab - (CAP MAA) - EMEA/H/C/006722

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

15.1.3. Denosumab - (CAP MAA) - EMEA/H/C/006734

Scope : Treatment of osteoporosis and bone loss

15.1.4. Denosumab - (CAP MAA) - EMEA/H/C/006238

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

15.1.5. Denosumab - (CAP MAA) - EMEA/H/C/006552

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

15.1.6. Golimumab - (CAP MAA) - EMEA/H/C/006560

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

15.1.7. Pegfilgrastim - (CAP MAA) - EMEA/H/C/006739

Scope : Treatment of neutropenia

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. Adalimumab – IDACIO (CAP) – EMA/VR/0000246858

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Karin Bolin

Scope: Submission of an updated RMP version 6.2 in order to remove the Observational registry RABBIT listed as a category 3 study in the RMP

15.2.2. Alemtuzumab – LEMTRADA (CAP) – EMA/VR/0000259153

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: Submission of an updated RMP version 13.0 following the completion of the two non-interventional PASS category 1 Drug Utilization Study (dut0008) and Mortality study (csa0002). The risks table was updated with new DLP 12 September 2024 without new safety concerns

15.2.3. Covid-19 mRNA vaccine – COMIRNATY (CAP) – EMA/VR/0000262269

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of:

C.I.11.b: Submission of an updated RMP version 14.1 in order to revise key objectives, design and study population of study C4591048 according to protocol amendment 6.

C.I.11.b: Submission of an updated RMP version 14.1 in order to propose the removal of the missing information 'Use in pregnancy and while breast feeding' from the list of the safety concerns with consequential removal of study C4591022 (US Pregnancy Postmarketing Requirement) study). In addition, the MAH took the opportunity to implement minor administrative changes to the RMP

15.2.4. Covid-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP) – EMA/VR/0000257347

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of an updated RMP version 7.1 in order to align with the latest information in the SmPC, recently completed clinical study reports, and PSUR

15.2.5. Linagliptin – TRAJENTA (CAP); JENTADUETO (CAP); GLYXAMBI (CAP) – EMA/VR/0000248932

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Submission of an updated RMP version 15.0 for Trajenta and Jentadueto and updated RMP version 12.0 for Glyxambi in order to review the list of safety concerns in line with GVP Module V, Rev 2

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. Afamelanotide – SCENESSE (CAP) – EMA/VR/0000247271

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to include the risk of "anaphylactic reactions" based on post-marketing data and literature. The Package Leaflet is updated accordingly. The RMP version 9.15 has also been submitted

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

Applicant: Formycon AG
PRAC Rapporteur: Zoubida Amimour

Scope: Quality

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15.3.3. Aflibercept – YESAFILI (CAP) – EMA/VR/0000245097

Applicant: Biosimilar Collaborations Ireland Limited

PRAC Rapporteur: Zoubida Amimour

Scope: Quality

15.3.4. Atezolizumab – TECENTRIQ (CAP) – EMA/VR/0000262253

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Update of section 4.4 of the SmPC in order to amend an existing warning on infusion-related reactions with anaphylaxis based on Drug safety report No. 1135433; the Package Leaflet is updated accordingly. The RMP version 32.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version

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

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

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

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

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

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

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

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: A grouped application consisting of:

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

clinical experience, (2) to introduce editorial changes to the PI, (3) to bring the PI in line with the latest QRD template, current guidelines, and Paul-Ehrlich-Institut (PEI) requests.

C.I.4: Update of section 4.8 of the SmPC in order to add urticaria to the list of adverse drug reactions (ADRs) with frequency common based on data from clinical trials and post-authorisation data sources; the Package Leaflet is updated accordingly. The RMP version 9.0 has also been submitted

15.3.8. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0084

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report from study CRZ-NBALCL listed as a category 3 study in the RMP. This is a phase I/II study to evaluate the adverse effects of ocular toxicity and bone toxicity and impaired bone growth associated with crizotinib in paediatric and young adult patients with recurrent/refractory anaplastic lymphoma kinase-positive anaplastic large cell lymphoma or neuroblastoma. The RMP version 9.2 is updated accordingly

15.3.9. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58[37]) - EMEA/H/W/002168/II/0027

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include reducing the risk of HIV-1 infection via vaginal intercourse in HIV-uninfected women 16 years and older for Dapivirine Vaginal Ring 25 mg, based on final results from study MTN-034 (REACH) listed as a category 3 study in the RMP; this is a Phase 2a crossover trial evaluating the safety of and adherence to a vaginal matrix ring containing dapivirine and oral emtricitabine/tenofovir disoproxil fumarate in an adolescent and young adult female population. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 1.5 of the RMP has also been submitted

15.3.10. 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

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

from study GS-US-216-0128 (Cohort 2); this is a Phase II/III, multicentere, 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 product information (PI) in line with the latest QRD template version 10.4 and to update the list of local representatives in the Package Leaflet

15.3.11. Defatted powder of *Arachis hypogaea l.,* semen (peanuts) – PALFORZIA (CAP) – EMA/VR/0000256580

Applicant: Stallergenes

PRAC Rapporteur: Terhi Lehtinen

Scope: Update of section 4.8 of the SmPC in order update the description of Eosinophilic esophagitis cases occurring in Palforzia clinical trials following CHMP request in EMEA/H/C/004917/P46/011 concerning report from study ARC008. The RMP version 1.3 has also been submitted. In addition, the MAH took the opportunity to bring minor updates to the SmPC following the Paul-Ehrlich-Institut (PEI) linguistic review

15.3.12. Dupilumab – DUPIXENT (CAP) – EMA/VR/0000257461

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of moderate to severe chronic spontaneous urticaria in adults and adolescents 12 years and older, whose disease is inadequately controlled by H1 antihistamines and who are naive to anti-IgE therapy for chronic spontaneous urticaria (CSU) for Dupixent, based on final results from 2 studies: EFC16461 (CUPID) study A and study C; both of them were phase 3, randomised, double-blind, placebo-controlled, multi-center, parallel-group study of dupilumab in patients with CSU who remain symptomatic despite the use of H1 antihistamine treatment in patients naïve to omalizumab. 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 13.0 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce editorial changes to the PI

15.3.13. 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

15.3.14. 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, packed in blisters of 14 tablets, 28 tablets, 98 tablets and 100 x 1 tablets (unit dose) 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

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

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

Applicant: Janssen Cilag International

PRAC Rapporteur: Gabriele Maurer

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

15.3.16. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) – EMA/VR/0000235389

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Sonja Radowan

Scope: Update of sections 4.4 and 5.1 of the SmPC to include the final results of study ZOSTER-062, listed as a category 3 study in the RMP. This is a phase III, randomized, observer-blind, placebo controlled, multicenter clinical trial to assess Herpes Zoster recurrence and the reactogenicity, safety and immunogenicity of Shingrix when administered intramuscularly on a 0 and 2 month schedule to adults ≥ 50 years of age with a prior episode of Herpes Zoster. The RMP version 9.0 has also been submitted. In addition, the MAH took the opportunity to implement a minor editorial change to Annex II of the PI

15.3.17. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0092

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Extension of indication to include IMBRUVICA in combination with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP) for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are eligible for autologous stem cell transplantation (ASCT), based on results from study MCL3003. This is a randomised, 3-arm, parallel-group, open-label, international, multicenter Phase 3 study. The purpose of Study MCL3003 is to compare 3 alternating courses of R CHOP/R-DHAP followed by ASCT (control Arm A), versus the combination with ibrutinib in induction and maintenance (experimental Arm A+I), or the experimental arm without ASCT (experimental Arm I) in participants with previously untreated MCL who are eligible for ASCT. Consequently, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Version 23.1 of the RMP has also been submitted

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

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

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

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Liana Martirosyan

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

15.3.20. Ponesimod - PONVORY (CAP) - EMEA/H/C/005163/II/0018/G

Applicant: Laboratoires Juvise Pharmaceuticals

PRAC Rapporteur: Karin Erneholm

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

C.I.13: Submission of the final report from study AC-058B202; this is a Multicenter, Randomized, Double-blind, Parallel-group Extension to Study AC-058B201 to Investigate the Long-term Safety, Tolerability, and Efficacy of 10, 20, and 40 mg/day Ponesimod, an Oral S1P1 Receptor Agonist, in Patients with Relapsing-remitting Multiple Sclerosis.

C.I.13: Submission of the final report from study AC-058B303 (OPTIMUM-LT); this is a Multicenter, Non-Comparative Extension to Study AC-058B301, to Investigate the Long-Term Safety, Tolerability, and Control of Disease of Ponesimod 20 mg in Subjects with Relapsing Multiple Sclerosis.

The RMP version 4.1 has also been submitted

15.3.21. Pyronaridine / Artesunate - PYRAMAX (Art 58[38]) - EMEA/H/W/002319/II/0036

Applicant: Shin Poong Pharmaceutical Co., Ltd.

PRAC Rapporteur: Zoubida Amimour

Scope: Update of sections 4.4 and 4.6 of the SmPC with revised recommendations for treatment during pregnancy. The Package Leaflet has been updated accordingly. An updated RMP version 18 was provided as part of the application

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

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Zoubida Amimour

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

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

both 450 mg concentrate for solution for infusion and 150 mg and 300 mg solution for injection in line with the new excipient guideline

15.3.23. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/X/0023

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (160 mg film-coated tablets)

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: A grouped application consisting of:

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

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

15.3.25. Mepolizumab – NUCALA (CAP) – EMA/VR/0000257645

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication for NUCALA to include treatment of Chronic Obstructive Pulmonary Disease (COPD) based on final results from study 208657 (MATINEE). This is a randomized, double-blind, parallel-group, placebo-controlled study of mepolizumab 100 mg SC as add-on treatment in participants with COPD experiencing frequent exacerbations and characterized by eosinophil levels. 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 14.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, 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

15.3.26. Mirikizumab – OMVOH (CAP) – EMA/VR/0000264533

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Grouped application of a Type II and a Type IB Variation, as follows:

Type II (C.I.4): Update of section 4.2 of the SmPC in order to modify administration instructions to include an alternative option for the maintenance dose administration for the treatment of ulcerative colitis (UC) changing from two injections of Omvoh 100 mg to a single injection of Omvoh 200 mg, based on results from study I6T-MC-AMCB; this is a bioequivalence study of subcutaneous injections of citrate-free mirikizumab solution using a 1-ml autoinjector and an investigational 2-ml autoinjector in healthy participants. The RMP version 2.1 has also been submitted.

The Labelling and Package Leaflet have been updated accordingly

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

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with two new strengths (790 mg and 395 mg) and new route of administration (subcutaneous use).

The RMP (version 49.1) is updated in accordance

15.3.28. Ponatinib – ICLUSIG (CAP) – EMA/VR/0000261199

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Update of sections 4.2, 4.4, 4.8, and 5.1 of the SmPC based on final results from study OPTIC (AP24534-14-203) listed as a category 3 study in the Annex II; this is a Randomised, Open-label, Phase 2 Trial of Ponatinib in Patients with Resistant Chronic Phase Myeloid Leukaemia to Characterize the Efficacy and Safety of a Range of Doses. The Package Leaflet is updated accordingly. The RMP version 23.1 has also been submitted. In addition, the MAH took the opportunity to update Annex II

15.3.29. Semaglutide – RYBELSUS (CAP) – EMA/VR/0000244874

Applicant: Novo Nordisk A/S
PRAC Rapporteur: Mari Thorn

Scope: A grouped application consisting of:

C.I.4: Update of sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC in order to update clinical efficacy and safety information based on the final results from study EX9924-4473 (SOUL); this is a phase 3b study comparing oral semaglutide versus placebo and added to standard of care in patients with type 2 diabetes at high risk of cardiovascular events; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes to the PI.

C.I.4: Update of sections 4.2, and 5.1 of the SmPC in order to introduce chronic kidney disease outcomes based on final results from study NN9535-4321 (FLOW); this is a phase 3b study evaluating the effect of semaglutide versus placebo on the progression of renal impairment in subjects with type 2 diabetes and chronic kidney disease; the Package Leaflet is updated accordingly.

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

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include in combination with lenalidomide and rituximab treatment of adult patients with relapsed or refractory follicular lymphoma (FL) after at least one line of systemic therapy for MINJUVI, based on interim results from study INCMOR 0208-301 (inMIND); this is a phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the efficacy and safety of tafasitamab plus lenalidomide and rituximab vs lenalidomide and rituximab in patients with relapsed/refractory (R/R) follicular lymphoma grade 1 to 3a or R/R marginal zone lymphoma. As a consequence, sections 4.1, 4.2, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce minor changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection

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

Applicant: Janssen Cilag International

PRAC Rapporteur: Barbara Kovacic Bytyqi

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

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. Abaloparatide – ELADYNOS (CAP) – EMA/PSUR/0000248500

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00011029/202410)

16.1.2. Acalabrutinib – CALQUENCE (CAP) – EMA/PSUR/0000248483

Applicant: AstraZeneca AB

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00010887/202410)

16.1.3. Aminosalicylic acid – GRANUPAS (CAP) – EMA/PSUR/0000248493

Applicant: Eurocept International B.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010171/202410)

16.1.4. Bazedoxifene – CONBRIZA (CAP) – EMA/PSUR/0000248443

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000302/202410)

16.1.5. Bupivacaine – EXPAREL LIPOSOMAL (CAP) – EMA/PSUR/0000248494

Applicant: Pacira Ireland Limited

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00010889/202410)

16.1.6. Capivasertib – TRUQAP (CAP) – EMA/PSUR/0000248507

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011061/202411)

16.1.7. Cariprazine – REAGILA (CAP) – EMA/PSUR/0000248475

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010623/202410)

16.1.8. Cefiderocol – FETCROJA (CAP) – EMA/PSUR/0000248460

Applicant: Shionogi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010849/202411)

16.1.9. Chikungunya vaccine (live) – IXCHIQ (CAP) – EMA/PSUR/0000248502

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011058/202411)

16.1.10. Conestat alfa – RUCONEST (CAP) – EMA/PSUR/0000248470

Applicant: Pharming Group N.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000873/202410)

16.1.11. Delamanid – DELTYBA (CAP) – EMA/PSUR/0000248476

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00010213/202410)

16.1.12. Dinutuximab beta – QARZIBA (CAP) – EMA/PSUR/0000248495

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010597/202411)

16.1.13. Efbemalenograstim alfa – RYZNEUTA (CAP) – EMA/PSUR/0000248467

Applicant: Evive Biotechnology Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000286/202411)

16.1.14. Elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide – GENVOYA (CAP) – EMA/PSUR/0000248490

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010449/202411)

16.1.15. Emicizumab – HEMLIBRA (CAP) – EMA/PSUR/0000248515

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010668/202411)

16.1.16. Etranacogene dezaparvovec – HEMGENIX (CAP) – EMA/PSUR/0000248978

Applicant: CSL Behring GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011037/202411)

16.1.17. Exagamglogene autotemcel – CASGEVY (CAP) – EMA/PSUR/0000248449

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000244/202411)

16.1.18. Fezolinetant – VEOZA (CAP) – EMA/PSUR/0000248472

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000231/202411)

16.1.19. Flutemetamol (18f) – VIZAMYL (CAP) – EMA/PSUR/0000248481

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010293/202410)

16.1.20. Follitropin alfa – GONAL-F (CAP); OVALEAP (CAP); BEMFOLA (CAP) – EMA/PSUR/0000248456

Applicant: Merck Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001463/202410)

16.1.21. Follitropin alfa / lutropin alfa – PERGOVERIS (CAP) – EMA/PSUR/0000248455

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00001464/202410)

16.1.22. Fosnetupitant / netupitant / palonosetron – AKYNZEO (CAP) – EMA/PSUR/0000248514

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010393/202410)

16.1.23. Glasdegib – DAURISMO (CAP) – EMA/PSUR/0000248492

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010859/202411)

16.1.24. Hepatitis b surface antigen – HEPLISAV B (CAP) – EMA/PSUR/0000248489

Applicant: Dynavax GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010919/202411)

16.1.25. Idarucizumab – PRAXBIND (CAP) – EMA/PSUR/0000248479

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010435/202410)

16.1.26. Insulin detemir – LEVEMIR (CAP) – EMA/PSUR/0000248485

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00001750/202410)

16.1.27. Insulin icodec – AWIQLI (CAP) – EMA/PSUR/0000248499

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011053/202411)

16.1.28. Ivosidenib – TIBSOVO (CAP) – EMA/PSUR/0000248512

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011048/202411)

16.1.29. Latanoprost – CATIOLANZE (CAP) – EMA/PSUR/0000248447

Applicant: Santen Oy

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00000202/202411)

16.1.30. Lebrikizumab – EBGLYSS (CAP) – EMA/PSUR/0000248530

Applicant: Almirall S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000175/202411)

16.1.31. Ledipasvir / sofosbuvir – HARVONI (CAP) – EMA/PSUR/0000248480

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010306/202410)

16.1.32. Letermovir – PREVYMIS (CAP) – EMA/PSUR/0000248461

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010660/202411)

16.1.33. Linzagolix choline – YSELTY (CAP) – EMA/PSUR/0000248513

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010998/202411)

16.1.34. Lonafarnib – ZOKINVY (CAP) – EMA/PSUR/0000248976

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011005/202411)

16.1.35. Lumasiran – OXLUMO (CAP) – EMA/PSUR/0000248463

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010884/202411)

16.1.36. Mavacamten – CAMZYOS (CAP) – EMA/PSUR/0000248442

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00000074/202410)

16.1.37. Meningococcal group b vaccine (recombinant, adsorbed) – TRUMENBA (CAP) – EMA/PSUR/0000248484

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010607/202410)

16.1.38. Micafungin – MYCAMINE (CAP) – EMA/PSUR/0000248462

Applicant: Sandoz Pharmaceuticals d.d.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002051/202410)

16.1.39. Midostaurin – RYDAPT (CAP) – EMA/PSUR/0000248529

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010638/202410)

16.1.40. Miglustat – ZAVESCA (CAP) – EMA/PSUR/0000248450

Applicant: Janssen Cilag International

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00002062/202410)

16.1.41. Nirsevimab – BEYFORTUS (CAP) – EMA/PSUR/0000248497

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00011026/202410)

16.1.42. Palopegteriparatide – YORVIPATH (CAP) – EMA/PSUR/0000248444

Applicant: Ascendis Pharma Bone Diseases A/S

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure (PSUSA/00000173/202411)

16.1.43. Pandemic influenza vaccine (h5n1) (live attenuated, nasal) – PANDEMIC INFLUENZA VACCINE H5N1 ASTRAZENECA (CAP) – EMA/PSUR/0000248977

Applicant: AstraZeneca AB

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010501/202411)

16.1.44. Pazopanib – VOTRIENT (CAP) – EMA/PSUR/0000248488

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00002321/202410)

16.1.45. Pegunigalsidase alfa – ELFABRIO (CAP) – EMA/PSUR/0000248528

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011049/202411)

16.1.46. Radamts13 – ADZYNMA (CAP) – EMA/PSUR/0000248509

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00011077/202411)

16.1.47. Rurioctocog alfa pegol – ADYNOVI (CAP) – EMA/PSUR/0000248511

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010663/202411)

16.1.48. Selpercatinib – RETSEVMO (CAP) – EMA/PSUR/0000248503

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010917/202411)

16.1.49. Sirolimus – HYFTOR (CAP) – EMA/PSUR/0000248441

Applicant: Plusultra Pharma GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00000025/202411)

16.1.50. Somatrogon – NGENLA (CAP) – EMA/PSUR/0000248527

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010982/202410)

16.1.51. Tirzepatide – MOUNJARO (CAP) – EMA/PSUR/0000248506

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011019/202411)

16.1.52. Tixagevimab / cilgavimab – EVUSHELD (CAP) – EMA/PSUR/0000248482

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010992/202411)

16.1.53. Tofacitinib – XELJANZ (CAP) – EMA/PSUR/0000248531

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010588/202411)

16.1.54. Vamorolone – AGAMREE (CAP) – EMA/PSUR/0000248446

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00000223/202410)

16.1.55. Volanesorsen – WAYLIVRA (CAP) – EMA/PSUR/0000248465

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010762/202411)

16.1.56. Zanubrutinib – BRUKINSA (CAP) – EMA/PSUR/0000248496

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010960/202411)

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

16.2.1. Levodopa / carbidopa / entacapone – CORBILTA (CAP); LEVODOPA/CARBIDOPA/ENTACAPONE ORION (CAP); STALEVO (CAP); NAP – EMA/PSUR/0000248477

Applicant(s): Orion Corporation, various

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000547/202410)

16.2.2. Sevelamer – RENAGEL (CAP); RENVELA (CAP); SEVELAMER CARBONATE WINTHROP (CAP); NAP – EMA/PSUR/0000248474

Applicant(s): Sanofi Winthrop Industrie, various

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00002697/202410)

16.2.3. Thalidomide – THALIDOMIDE BMS (CAP); THALIDOMIDE LIPOMED (CAP); NAP – EMA/PSUR/0000248471

Applicant(s): Bristol-Myers Squibb Pharma EEIG; Lipomed GmbH, various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00002919/202410)

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

16.3.1. Acitretin (NAP) - EMA/PSUR/0000248445

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000051/202410)

16.3.2. Ascorbic acid / magnesium aspartate / leucine L / lysine L / phenylalanine L / valine L (NAP) - EMA/PSUR/0000248498

Applicant(s): various

PRAC Lead: Guðrún Stefánsdóttir

Scope: Evaluation of a PSUSA procedure (PSUSA/00010988/202410)

16.3.3. Azelastine / fluticasone (NAP) - EMA/PSUR/0000248486

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010067/202410)

16.3.4. Clindamycin (NAP) - EMA/PSUR/0000248466

Applicant(s): various

PRAC Lead: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000795/202410)

16.3.5. Colecalciferol, colecalciferol / calcium, ergocalciferol, ergocalciferol / calcium (NAP) - EMA/PSUR/0000248516

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010386/202410)

16.3.6. Corticorelin (NAP) - EMA/PSUR/0000248451

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00000876/202410)

16.3.7. Drospirenone (NAP) - EMA/PSUR/0000248478

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010853/202411)

16.3.8. Fluticasone / salmeterol[39] (NAP) - EMA/PSUR/0000248452

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00001455/202410)

[39] For nationally authorised products only

16.3.9. Letrozole (NAP) - EMA/PSUR/0000248457

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00001842/202410)

16.3.10. Meningococcal group c polysaccharide conjugate vaccine (NAP) - EMA/PSUR/0000248458

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00001971/202410)

16.3.11. Milrinone (NAP) - EMA/PSUR/0000248468

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00002064/202410)

16.4. Follow-up to PSUR/PSUSA procedures

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

Applicant(s): various

PRAC Rapporteur: Gabriele Maurer

Scope: PAM/0000262763 - Response to the PRAC request for a LEG on Taltz for a cumulative review on major adverse cardiovascular events (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

16.5. Variation procedure(s) resulting from PSUSA evaluation

16.5.1. Burosumab – CRYSVITA (CAP) – EMA/VR/0000246754

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 4.6 of the SmPC in order to add a statement on how long contraception should be continued after burosumab treatment has been discontinued, as requested in procedure PSUSA/00010669/202402. The Package Leaflet is updated accordingly

16.5.2. Rituximab – BLITZIMA (CAP); TRUXIMA (CAP) - EMA/VR/0000244743

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Karin Erneholm

Scope: C.I.2.a: To update sections 4.1, 4.2, 4.3, 4.8, 5.1, 6.2, 6.4 and 6.5 of the SmPC in order to introduce several structural and editorial changes to align with the current SmPC guideline and to remove the educational materials for HCPs and patients, following the request by the PRAC in the AR for the PSUSA procedure EMA/PRAC/257005/2023. The Annex II, Labelling and Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI in line with the same changes to the reference product.

C.I.11.z: To update the RMP following the assessment of PSUR EMEA/H/C/PSUSA/00002652/202311

16.6. Expedited summary safety reviews[40]

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)[41]

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Lukacisinova

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

[40] 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

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

17.1.2. Ciltacabtagene autoleucel – CARVYKTI (CAP) – EMA/PASS/0000264227

Applicant: Janssen Cilag International

PRAC Rapporteur: Jo Robays

Scope: PASS amendment [107o]: Substantial amendment to Study 68284528MMY4004: An Observational Post-authorization Safety Study to Evaluate the Safety of Multiple Myeloma Patients Treated with Ciltacabtagene Autoleucel [MAH's response to EMEA/H/C/PSA/S/0116]

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

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

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

17.1.4. Pitolisant – WAKIX (CAP) – EMA/PASS/0000264232

Applicant: Bioprojet Pharma

PRAC Rapporteur: Terhi Lehtinen

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

17.1.5. Voretigene neparvovec – LUXTURNA (CAP) – EMA/PASS/0000263977

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: PASS amendment [107o]: Substantial amendment to a post-authorization observational study to collect long-term safety information (i.e., for 5 years after treatment) associated with voretigene neparvovec (vector and/or transgene), its subretinal injection procedure, the concomitant use of corticosteroids, or a combination of these procedures and products [MAH's response to EMEA/H/C/PSA/S/0114.1]

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[42]

17.2.1. Fremanezumab – AJOVY (CAP) – EMA/PAM/0000262615

Applicant: TEVA GmbH

PRAC Rapporteur: Terhi Lehtinen

Scope: Revised protocol for Study TV48125-MH-50038 "Assessment of Pregnancy Outcomes in Patients Treated with AJOVY (fremanezumab) in the Pregnancy Database Study (Non-Interventional Phase IV Study)"

17.2.2. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) – EMA/PAM/0000262632

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Sonja Radowan

Scope: From Initial MAA: previously MEA 009

Study EPI-ZOSTER-030 VS (Targeted Safety Study):

Non-interventional (observational) prospective cohort study to evaluate the safety of Shingrix in older adults (⩾ 50 YOA) in the US.

protocol amendment for Study No. EPI-ZOSTER-030**

17.2.3. Interferon beta-1a – AVONEX (CAP) – EMA/PAM/0000262800

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Joint PASS see EMA/PAM/0000262645 (Betaferon) Revised protocol PASS INFORM 2600153: Observational Study regarding Interferon-Beta Exposure in the 2nd and 3rd Trimester of Pregnancy - a Register-Based Drug Utilisation Study in Finland and Sweden

17.2.4. Interferon beta-1a – REBIF (CAP) – EMA/PAM/0000264549

Applicant: Merck Europe B.V.

PRAC Rapporteur: Maria del Pilar Rayon

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

Scope: Joint PASS see EMA/PAM/0000262645 (Betaferon) Revised protocol PASS INFORM 2600153: Observational Study regarding Interferon-Beta Exposure in the 2nd and 3rd Trimester of Pregnancy - a Register-Based Drug Utilisation Study in Finland and Sweden

17.2.5. Interferon beta-1b – BETAFERON (CAP) – EMA/PAM/0000262645

Applicant: Bayer AG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Joint PASS see EMA/PAM/0000262645 (Betaferon) Revised protocol PASS INFORM 2600153: Observational Study regarding Interferon-Beta Exposure in the 2nd and 3rd Trimester of Pregnancy - a Register-Based Drug Utilisation Study in Finland and Sweden

17.2.6. Maribavir – LIVTENCITY (CAP) – EMA/PAM/0000262637

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of an amendment to the protocol version 1.0 for the Retrospective Chart Review Study (TAK-620-4007, a category 3Retrospective chart review study) as initially endorsed on September 14, 2023.

17.2.7. Peginterferon beta-1a – PLEGRIDY (CAP) – EMA/PAM/0000263236

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Joint PASS see EMA/PAM/0000262645 (Betaferon) Revised protocol PASS INFORM 2600153: Observational Study regarding Interferon-Beta Exposure in the 2nd and 3rd Trimester of Pregnancy - a Register-Based Drug Utilisation Study in Finland and Sweden

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

Applicant: UCB Pharma

PRAC Rapporteur: Tiphaine Vaillant

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

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

Applicant: UCB Pharma

PRAC Rapporteur: Tiphaine Vaillant

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

17.2.10. Setmelanotide – IMCIVREE (CAP) – EMA/PAM/0000262795

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Anna Mareková

Scope: Protocol Amendment for the registry of patients with Biallelic Pro Opiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) Deficiency Obesity, or Bardet-Biedl Syndrome (BBS), Treated with Setmelanotide (RM-IMC-901) following CHMP recommendation on the extension of indications in paediatric population from 2 to less than 6 years of age (EMEA/H/C/5089/II/18). The registry is included as category 3 study in the RMP

17.2.11. Tirzepatide – MOUNJARO (CAP) – EMA/PAM/0000262771

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Protocol amendment for PASS No I8F-MC-B013: A database linkage study to evaluate the important potential risk of medullary thyroid cancer

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

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

17.2.13. 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

17.2.14. Zilucoplan – ZILBRYSQ (CAP) – EMA/PAM/0000262862

Applicant: UCB Pharma

PRAC Rapporteur: Karin Erneholm

Scope: Revised protocol for PASS MG0026: A Multi-National Cohort Study to Assess the Implementation of the Risk Minimization Measures to Prevent Meningococcal Infection in Patients with Generalized Myasthenia Gravis Initiating Zilucoplan, and Zilucoplan Safety in Real-World Settings

17.3. Results of PASS imposed in the marketing authorisation(s)[43]

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Lukacisinova

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

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

17.4. Results of PASS non-imposed in the marketing authorisation(s)[44]

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

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

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansens

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

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: A grouped application consisting of:

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

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

17.4.4. Filgrastim – FILGRASTIM HEXAL (CAP); ZARZIO (CAP) – EMA/VR/0000249070

Applicant: Sandoz GmbH

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

PRAC Rapporteur: Bianca Mulder

Scope: Submission of the final report from study EP06-501 listed as a category 3 study in the RMP. This is a non-interventional, prospective, long-term observational PASS to assess the safety and effectiveness of Zarzio / Filgrastim HEXAL (EP2006) administered to healthy unrelated stem cell donors for peripheral blood progenitor cell mobilization. The RMP version 14.0 has also been submitted

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

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

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

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: A grouped application consisting of:

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

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

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report for study ML28664 (RABBIT), listed as a category 3 study in the RMP. This was a non-interventional post-authorisation safety study aimed at collecting and analysing safety data related to the use of tocilizumab in rheumatoid arthritis

patients in Germany. The RMP version 30.0 has also been submitted. In addition, the MAH removed the education materials from the RMP and PI as agreed by PRAC during procedure PSUSA/00002980/202204. Furthermore, the MAH took the opportunity to introduce editorial and formatting changes to the PI and to align the wording used for the pre-filled syringe and the pre-filled pen, as well as to update the list of local representatives in the Package Leaflet

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

17.5.1. Cabotegravir – VOCABRIA (CAP) – EMA/PAM/0000262608

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: 3rd interim study report from EuroSIDA-hepatotoxicity study (study 215162, cat. 3 study). A Prospective Observational Cohort Study to Monitor for Hepatotoxicity and Regimen Discontinuation due to Liver Related Adverse Events among People with HIV, initiating Cabotegravir + Rilpivirine Regimens

17.5.2. Efgartigimod alfa – VYVGART (CAP) – EMA/PAM/0000263274

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: 2nd interim report for PASS category 3 study (ARGX-113-PAC-2206): This is a multi-country, prospective safety study of pregnant women exposed to efgartigimod during pregnancy and/or breastfeeding or any time within 25 days prior to conception in order to assess maternal, fetal, and infant outcomes

17.5.3. Filgotinib – JYSELECA (CAP) – EMA/PAM/0000261394

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: Interim study report for GLPG0634-CL-408: Evalutation of the effectiveness of the additional risk minimization measures for filgotinib use in patients with moderate to severe active rheumatoid arthritis within European registries

17.5.4. Ketoconazole – KETOCONAZOLE ESTEVE (CAP) – EMA/PAM/0000256150

Applicant: Esteve Pharmaceuticals S.A.

PRAC Rapporteur: Petar Mas

Scope: Response to RSI from seventh interim report on PASS study EUPAS21731

17.5.5. Ofatumumab – KESIMPTA (CAP) – EMA/PAM/0000261333

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Interim study results for PASS COMB157G2399 (ALITHIOS): An open-label, single arm, multi-center extension study evaluating long-term safety, tolerability and effectiveness of ofatumumab in subjects with relapsing multiple sclerosis

17.5.6. Selexipag – UPTRAVI (CAP) – EMA/PAM/0000263266

Applicant: Janssen Cilag International

PRAC Rapporteur: Zoubida Amimour

Scope: The 8th annual interim report of study AC-065A401 (EXPOSURE) with data cut-off date of 30 November 2024 is submitted as per agreed study milestones

17.6. Others

17.6.1. Atogepant – AQUIPTA (CAP) – EMA/PAM/0000256967

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Second annual progress report dated 31 January 2025 for non-interventional, category 3 PASS P22-419 observational cohort study using administrative healthcare claims data to assess the risk of pregnancy and infant outcomes among pregnant women using atogepant

17.6.2. Atogepant – AQUIPTA (CAP) – EMA/PAM/0000256954

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Second interim annual progress report for non-interventional, category 3 PASS P22-392 observational prospective study

17.6.3. Daratumumab – DARZALEX (CAP) – EMA/PAM/0000262246

Applicant: Janssen Cilag International

PRAC Rapporteur: Carla Torre

Scope: Provision of the final Statistical Analysis Plan (SAP) for Study AMY2009: a multicentre, multicohort, open-label, Phase 2 study in participants with newly diagnosed systemic AL amyloidosis. The primary objective of the study is to further characterise cardiac adverse events in patients with newly diagnosed AL amyloidosis treated with subcutaneous daratumumab-based therapy in terms of the incidence, severity, clinical presentation, management, and outcome

17.6.4. Mavacamten – CAMZYOS (CAP) – EMA/PAM/0000262744

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: PASS No CV027-1148: First progress report for meta-analysis of Phase 3 placebo controlled, double-blind randomized studies of mavacamten in patients with symptomatic hypertrophic cardiomyopathy (HCM) to evaluate the cardiovascular (CV) safety profile. The major adverse cardiovascular events (MACE) meta-analysis will assess CV safety based on a composite endpoint of time to first occurrence of MACE meta-analysis event. It will include three clinical trials in symptomatic oHCM population (EXPLORER-HCM, VALOR-HCM, China oHCM Phase 3 trial) and one clinical trial in symptomatic nHCM population (ODYSSEY-HCM). The meta-analysis is listed as cat 3 study in the approved RMP (v. 4.1)

17.6.5. Risankizumab – SKYRIZI (CAP) – EMA/PAM/0000262752

Applicant(s): Abbvie Deutschland GmbH & Co. KGn
PRAC Rapporteur: Liana Martirosyan

Scope: Study Progress Report PASS Study P16-751: Pregnancy Exposures and Outcomes in Psoriasis Patients Treated with Risankizumab: A Cohort Study Utilising Large Healthcare Databases with Mother-Baby Linkage in the United States

17.6.6. Venetoclax – VENCLYXTO (CAP) – EMA/PAM/0000261396

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Annual update report for study P22-905: A cross-sectional study evaluating the effectiveness of the venetoclax patient card among adult patients in Europe

17.6.7. 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

17.7. New Sientific Advice

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

17.8. Ongoing Scientific Advice

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

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

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. Amifampridine – FIRDAPSE (CAP) – EMA/S/0000257410

Applicant: Serb

PRAC Rapporteur: Karin Bolin

Scope: Annual reassessment of the marketing authorisation

18.1.2. Clofarabine – EVOLTRA (CAP) – EMA/S/0000257017

Applicant: Sanofi B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual reassessment of the marketing authorisation

18.1.3. Velmanase alfa – LAMZEDE (CAP) – EMA/S/0000257415

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Annual reassessment of the marketing authorisation

18.1.4. Tabelecleucel – EBVALLO (CAP) - EMA/S/0000249324

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

None

18.3. Renewals of the marketing authorisation

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

Applicant: Orchard Therapeutics (Netherlands) B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: 5-year renewal of the marketing authorisation

18.3.2. Cabotegravir – VOCABRIA (CAP) – EMA/R/0000256925

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

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

Applicant: UCB Pharma

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

18.3.4. Formoterol / glycopyrronium bromide / budesonide – TRIXEO AEROSPHERE (CAP) – EMA/R/0000245136

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

18.3.5. Latanoprost / netarsudil – ROCLANDA (CAP) – EMA/R/0000255956

Applicant: Santen Oy

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

18.3.6. Lenalidomide – LENALIDOMIDE MYLAN (CAP) – EMA/R/0000257483

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.7. Rilpivirine – REKAMBYS (CAP) – EMA/R/0000257069

Applicant: Janssen Cilag International

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

18.3.8. Rivaroxaban – RIVAROXABAN ACCORD (CAP) – EMA/R/0000249659

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.9. Susoctocog alfa – OBIZUR (CAP) - EMA/R/0000248614

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Gabriele Maurer

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 02-05 June 2025 PRAC meeting, which was held in-person. Participants marked with "a" attended the plenary session while those marked with "b" attended the ORGAM.

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

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ulla Wändel Liminga [a,b]	Chair	Sweden	No interests declared	
Jan Neuhauser [a]	Member*	Austria	No interests declared	
Jean-Michel Dogné [a,b]	Member	Belgium	No restrictions applicable to this meeting	
Jo Robays [a]	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva [a,b]	Member	Bulgaria	No interests declared	
Petar Mas [a,b]	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi [a,b]	Alternate	Croatia	No interests declared	
Elena Kaisis [a,b]	Member	Cyprus	No interests declared	
Panagiotis Psaras[b]	Alternate*	Cyprus	No interests declared	
Eva Jirsová	Member*	Czechia	No interests declared	
Jana Lukacisinova [a]	Alternate	Czechia	No interests declared	
Marie Louise Schougaard Christiansen [a,b]	Member	Denmark	No interests declared	
Karin Erneholm [a,b]	Alternate*	Denmark	No interests declared	
Maia Uusküla [a]	Member	Estonia	No interests declared	
Krõõt Aab [a]	Alternate*	Estonia	No interests declared	
Terhi Lehtinen [a,b]	Member	Finland	No interests declared	
Kimmo Jaakkola [a,b]	Alternate	Finland	No interests declared	
Tiphaine Vaillant [a,b]	Member	France	No interests declared	
Zoubida Amimour [a,b]	Alternate*	France	No participation in discussion, final	4.2.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/00

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
			deliberations and voting on:	4480/SDA/017; Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/SDA/014; Ciltacabtagene autoleucel – CARVYKTI (CAP) - EMEA/H/C/005095/SDA/020; Idecabtagene vicleucel - ABECMA (CAP) - EMEA/H/C/004662/SDA/023; Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/SDA/024; Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/SDA/025; 5.2.1. Apixaban – ELIQUIS (CAP) – EMA/VR/0000262422 6.4.1. Azacitidine – ONUREG (CAP) – EMA/PAM/0000262249 7.3.1. Pomalidomide – IMNOVID (CAP) –

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				EMA/PASS/00 00262876 16.1.36. Mavacamten – CAMZYOS (CAP) – EMA/PSUR/0 000248442 16.2.3. Thalidomide – THALIDOMID E BMS (CAP); THALIDOMID E LIPOMED (CAP); NAP – EMA/PSUR/0 000248471 17.4.6. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/00 0717/II/0130 17.6.4. Mavacamten – CAMZYOS (CAP) – EMA/PAM/00 00262744
Martin Huber [a,b]	Member*	Germany	No interests declared	
Gabriele Maurer [a,b]	Alternate	Germany	No interests declared	
Georgia Gkegka [a,b]	Member*	Greece	No interests declared	
Maria Poulianiti [a,b]	Alternate*	Greece	No participation in discussion, final deliberations and voting on:	16.2.2. Sevelamer – RENAGEL (CAP); RENVELA (CAP); SEVELAMER CARBONATE WINTHROP (CAP); NAP – EMA/PSUR/0 000248474

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Julia Pallos	Member	Hungary	No participation in discussion, final deliberations and voting on:	4.2.1. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/SDA/017; Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/SDA/014; Ciltacabtagene autoleucel – CARVYKTI (CAP) - EMEA/H/C/005095/SDA/020; Idecabtagene vicleucel - ABECMA (CAP) - EMEA/H/C/004662/SDA/023; Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/SDA/024; Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/SDA/025; 5.2.1. Apixaban – ELIQUIS (CAP) – EMA/VR/0000262422 6.4.1. Azacitidine – ONUREG (CAP) – EMA/PAM/000262249

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				7.3.1. Pomalidomide – IMNOVID (CAP) – EMA/PASS/00000262876 16.1.36. Mavacamten – CAMZYOS (CAP) – EMA/PSUR/0000248442 16.2.3. Thalidomide – THALIDOMIDE BMS (CAP); THALIDOMIDE LIPOMED (CAP); NAP – EMA/PSUR/0000248471 17.4.6. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/000717/II/0130 17.6.4. Mavacamten – CAMZYOS (CAP) – EMA/PAM/00000262744
Melinda Palfi [a]	Alternate*	Hungary	No interests declared	
Guðrún Stefánsdóttir	Member	Iceland	No restrictions applicable to this meeting	
Rhea Fitzgerald [a]	Member	Ireland	No interests declared	
Eamon O Murchu [a,b]	Alternate	Ireland	No interests declared	
Amelia Cupelli [a,b]	Member	Italy	No interests declared	
Zane Neikena [a,b]	Member	Latvia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Diana Litenboka [a,b]	Alternate*	Latvia	No interests declared	
Rugile Pilviniene [a]	Member	Lithuania	No restrictions applicable to this meeting	
Lina Seibokiene [a]	Alternate	Lithuania	No interests declared	
Anne-Cecile Vuillemin [a]	Member	Luxembourg	No interests declared	
Magdalena Wielowieyska [a]	Alternate*	Luxembourg	No participation in discussion, final deliberations and voting on:	6.3.4. Methylphenidate hydrochloride (NAP) - EMA/PSUR/0000248487 7.4.1. Icatibant - FIRAZYR (CAP) - EMEA/H/C/000899/II/0061 16.1.46. Radamts13 – ADZYNMA (CAP) – EMA/PSUR/0000248509 17.2.6. Maribavir – LIVTENCITY (CAP) – EMA/PAM/000262637
John Joseph Borg	Member	Malta	No interests declared	
Liana Martirosyan [a,b]	Member (Vice-Chair)	Netherlands	No interests declared	
Bianca Mulder [a,b]	Alternate	Netherlands	No interests declared	
David Olsen [a,b]	Member	Norway	No participation in discussion, final deliberations and voting on:	6.3.1. Benzydamine (NAP) - EMA/PSUR/0000248448 15.3.14. Finerenone –

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				KERENDIA (CAP) – EMA/X/0000248026 16.3.5. Colecalciferol, colecalciferol / calcium, ergocalciferol , ergocalciferol / calcium (NAP) - EMA/PSUR/0000248516 17.2.3. Interferon beta-1a – AVONEX (CAP) – EMA/PAM/000262800 17.2.4. Interferon beta-1a – REBIF (CAP) – EMA/PAM/000264549 17.2.5. Interferon beta-1b – BETAFERON (CAP) – EMA/PAM/000262645 17.2.7. Peginterferon beta-1a – PLEGRIDY (CAP) – EMA/PAM/000263236
Pernille Harg [a,b]	Alternate	Norway	No interests declared	
Adam Przybylkowski [a]	Member	Poland	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Katarzyna Ziolkowska[b]	Alternate*	Poland	No interests declared	
Ana Sofia Diniz Martins [a]	Member	Portugal	No interests declared	
Carla Torre [a]	Alternate	Portugal	No restrictions applicable to this meeting	
Roxana Dondera[b]	Member*	Romania	No interests declared	
Irina Sandu [a]	Alternate	Romania	No interests declared	
Anna Mareková [a,b]	Member	Slovakia	No interests declared	
Miroslava Gocova [a,b]	Alternate*	Slovakia	No interests declared	
Marjetka Plementas [a,b]	Alternate	Slovenia	No interests declared	
Maria del Pilar Rayon [a,b]	Member	Spain	No interests declared	
Monica Martinez Redondo [a,b]	Alternate	Spain	No interests declared	
Mari Thorn [a,b]	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin [a]	Alternate	Sweden	No restrictions applicable to this meeting	
Milou-Daniel Drici [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Maria Teresa Herdeiro [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Patricia McGettigan [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Hedvig Marie Egeland Nordeng [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Roberto Frontini [a,b]	Member	Healthcare Professionals' Representative	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Martin Votava [a,b]	Alternate	Healthcare Professionals' Representative	No participation in discussion, final deliberations and voting on:	4.2.3. Enzalutamide - XTANDI (CAP) - EMEA/H/C/002639/SDA/016; ENZALUTAMIDE VIATRIS (CAP), NAP; Digoxin (NAP)
Yiannoula Koulla [a,b]	Member*	Patients' Organisation Representative	No interests declared	
Klaus Stüwe [a]		Austria	No restrictions applicable to this meeting	
Christelle Bizimungu[b]		Belgium	No interests declared	
Laurence de Fays[b]		Belgium	No interests declared	
Sophie Goethals [a]		Belgium	No restrictions applicable to this meeting	
Piyush Jain [a]		Belgium	No interests declared	
Martine Sabbe[b]		Belgium	No interests declared	
Chloé Wyndham-Thomas[b]		Belgium	No restrictions applicable to this meeting	
Nicklas Hasselblad Lundstrøm [a]		Denmark	No interests declared	
Moritz Sander [a]		Denmark	No restrictions applicable to this meeting	
Per Sindahl [a]		Denmark	No interests declared	
Hicham Ait-Lbacha		France	No restrictions applicable to this meeting	
Nathalie Morgensztejn[b]		France	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Samuel Crommelynck[b]		France	No restrictions applicable to this meeting	
Dennis Lex[b]		Germany	No interests declared	
Nerina Pflanz [a]		Germany	No interests declared	
Anne-Catherine Redeker [a]		Germany	No interests declared	
Jens Rotthauwe [a]		Germany	No interests declared	
Christopher Schulze[b]		Germany	No interests declared	
Birthe Sumpf [a]		Germany	No interests declared	
Natalie Welter [a]		Germany	No interests declared	
Maxime Cuijpers [a]		Netherlands	No restrictions applicable to this meeting	
Talip Eroglu [a]		Netherlands	No restrictions applicable to this meeting	
Margje Monster-Simons		Netherlands	No restrictions applicable to this meeting	
David Boyarizo García [a]		Spain	No interests declared	
Natividad Galiana Llorca [a]		Spain	No restrictions applicable to this meeting	
Maria Martinez Gonzalez [a]		Spain	No interests declared	
Charlotte Backman [a]		Sweden	No interests declared	
Annie George Chandy [a]		Sweden	No interests declared	
Laila Eriksson [a]		Sweden	No interests declared	
Rolf Gedeborg [a]		Sweden	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jenny Jönsson [a]		Sweden	No restrictions applicable to this meeting	
Eva Lander Persson [a]		Sweden	No interests declared	
Kristina Magnusson-Lundqvist [a]		Sweden	No interests declared	
A representative from the European Commission attended the meeting				
Observers from Health Canada and WHO attended the meeting.				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation. Signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. The evaluation of safety signals is a routine part of pharmacovigilance and is essential to ensuring that regulatory authorities have a

comprehensive knowledge of a medicine's benefits and risks.
The presence of a safety signal does not mean that a medicine has caused the reported adverse event. The adverse event could be a symptom of another illness or caused by another medicine taken by the patient. The evaluation of safety signals is required to establish whether or not there is a causal relationship between the medicine and the reported adverse event.
The evaluation of safety signals may not necessarily conclude that the medicine caused the adverse event in question. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)
(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)
(Item 6 of the PRAC minutes)

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

Post-authorisation Safety Studies (PASS)
(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections
(Item 9 of the PRAC minutes)

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

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