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Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes for PRAC meeting on 05-08 May 2025

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

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

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

Note on access to documents

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

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1. Introduction

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

The Chairperson opened the 05-08 May 2025 meeting by welcoming all participants. The meeting was held remotely.

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

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

The 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 05-08 May 2025

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

1.3. Minutes of the previous meeting on 07-10 April 2025

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

Post-meeting note: the PRAC minutes of the meeting held on 07-10 April 2025 were published on the EMA website on 29 May 2025 (EMA/PRAC/169632/2025).

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

3.1.1. Chikungunya virus (CHIKV) Δ5nsP3 strain (live, attenuated) – IXCHIQ (CAP) – EMA/REF/0000269473

Applicant: Valneva Austria GmbH

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

Scope: Review of the benefit-risk balance following notification by the European Commission (EC) of a referral under Article 20 of Regulation (EC) No 726/2004, based on pharmacovigilance data

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 European Commission (EC) sent a letter of notification dated 5 May 2025 triggering a procedure under Article 20 of Directive 2001/83/EC for the review of Ixchiq (Chikungunya virus (CHIKV) Δ5nsP3 strain (live, attenuated)) following reports of serious adverse events in elderly people, including two cases resulting in death.

Considering the above, the EC referred the matter to PRAC in the interest of the Union for further evaluation, requesting the Committee to assess the impact of the above concerns on the benefit-risk balance of Ixchiq (Chikungunya virus (CHIKV) Δ5nsP3 strain (live, attenuated)) and to give its recommendation as to whether the marketing authorisation for this product should be maintained, varied, suspended or revoked across the EU. In addition, the EC requested the Agency/PRAC to give its opinion, as to whether temporary measures were necessary to protect public health.

Discussion

PRAC noted the notification letter from the EC.

PRAC appointed Gabriele Maurer as Rapporteur and Jean-Michel Dogné as Co-Rapporteur for the procedure.

PRAC considered the need for temporary measures for Ixchiq in accordance with Article 20(3) of Regulation (EC) No 726/2004. PRAC reviewed the available data including data provided by the MAH in writing and at an oral explanation, as well as from EudraVigilance. PRAC discussed potential temporary measures and recommended, as a precaution, that Ixchiq should be contraindicated in individuals aged 65 years and older while the review is ongoing, and a thorough assessment of all available data is performed.

In view of the above, PRAC considered that the benefit-risk balance of Ixchiq remains favourable subject to the agreed temporary amendments to the product information. This recommendation is without prejudice to the final conclusions of the ongoing procedure under Article 20 of Directive 2001/83/EC.

PRAC adopted the wording of a direct healthcare professional communication (DHPC) to communicate temporary restrictions described above to healthcare professionals. PRAC also agreed on a communication plan.

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

Summary of recommendation(s)/conclusions

- PRAC adopted temporary measures (EMA/166857/2025), by consensus, to vary[1] the terms of the marketing authorisation(s) for Ixchiq, while an in-depth review is ongoing. PRAC also agreed the distribution of a DHPC together with a communication plan.
- PRAC adopted a LoQ to the MAH (EMA/PRAC/158050/2025) and a timetable for the procedure (EMA/PRAC/157937/2025).
- PRAC discussed the option to conduct a public hearing in the context of the current procedure according to the pre-defined criteria set out in the rules of procedure (EMA/11523/2023 Rev.2). It was agreed by PRAC that at this stage in the assessment, in light of the currently available data and the need to determine the suitable approach to stakeholder engagement, a public hearing would not be appropriate. PRAC can reconsider this at a later stage of the procedure as needed.

See the EMA press release (EMA/170564/2025) entitled 'EMA starts review of Ixchiq (live attenuated chikungunya vaccine)'.

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.3.1. Dutasteride (NAP); dutasteride, tamsulosin (NAP); finasteride (NAP); finasteride, tadalafil (NAP); finasteride, tamsulosin (NAP) – EMEA/H/A-31/1539

Applicant(s): various

PRAC Rapporteur: Jana Lukačišinová; PRAC Co-rapporteur: Martin Huber

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

Background

A referral procedure under Article 31 of Directive 2001/83/EC for finasteride- and dutasteride-containing product(s) following concerns regarding suicidal ideation and suicide

[1] Update of sections 4.1 and 4.3 of the SmPC. The package leaflet is updated accordingly.

is to be concluded. A final assessment of the data submitted was produced by the Rapporteurs according to the agreed timetable. For further background, see PRAC minutes October 2024[2] and PRAC minutes February 2025.

Discussion

PRAC reviewed the available data in relation to suicidal ideation and behaviours associated with the use of finasteride- and dutasteride-containing products. The data included the responses submitted by the MAHs in writing, data from clinical trials, spontaneous reporting and literature, non-clinical data as well as interventions by third parties.

Based on the evaluated cases of suicidal ideation or suicidal behaviours reported with oral finasteride, PRAC confirmed a causal association between oral finasteride and suicidal ideation. Therefore, suicidal ideation should be reflected as an undesirable effect in the product information of all medicinal products containing finasteride 1 mg or finasteride 5 mg for oral use with a frequency 'not known'. PRAC noted that the product information of all medicinal products containing finasteride 1 mg or finasteride 5 mg for oral use already includes a warning on mood alterations, including suicidal ideation.

PRAC also concluded that sexual dysfunction, a known adverse drug reaction of finasteride, may have a contributory role in suicidal ideation in some patients being treated with finasteride 1 mg for oral use and recommended this to be reflected as a warning in the product information of these products.

PRAC noted that most cases of suicidal ideation were reported following treatment with finasteride for androgenetic alopecia, despite a considerably larger exposure from treatment of benign prostate hyperplasia. Therefore, PRAC recommended a patient card for medicinal products containing finasteride 1 mg for oral use, to be provided inside the package to inform patients on the risks of mood alterations as well as of sexual dysfunction that may contribute to these reactions and provide instructions on the appropriate course of action should these occur. This additional risk minimisation measure should be reflected in a RMP, constituting a condition to the marketing authorisations.

In addition, PRAC concluded that there is insufficient evidence to link suicidal ideation to dutasteride-containing medicinal products. However, based on the common mechanism of action for the class of 5-alpha reductase inhibitors, PRAC agreed that a warning referring to a potential risk of mood alterations, including depressed mood, depression and, less frequently, suicidal ideation should be reflected in the product information of dutasteride-containing medicinal products for oral use as a precautionary measure.

As a consequence, PRAC considered that the benefit-risk balance of finasteride- and dutasteride containing products for oral use remains favourable subject to the agreed amendments to the product information, risk minimisation measures and condition mentioned above, as applicable.

Regarding finasteride-containing medicinal products for cutaneous use, PRAC did not identify sufficient evidence linking suicidal ideation to such products that would prompt an update of the existing warning on mood alterations. Thus, PRAC considered that the benefit-risk balance of medicinal products containing finasteride for cutaneous use remains favourable and recommended the maintenance of their marketing authorisations.

[2] Held 30 September - 03 October 2024

Summary of recommendation(s)/conclusions

- PRAC adopted a recommendation, by majority, to vary[3] the terms of the marketing authorisations for finasteride- and dutasteride-containing products for oral use and to maintain the marketing authorisations for medicinal products containing finasteride for cutaneous use. This recommendation will be further considered by CMDh for adoption of a position.
- PRAC agreed on the distribution of a direct healthcare professional communication (DHPC) together with a communication plan.

Twenty-nine members voted in favour of the recommendation whilst two[4] members had a divergent view. The Icelandic and Norwegian PRAC members agreed with the recommendation

Post-meeting note 1: On 08 May 2025, the public health communication entitled 'Measures to minimise risk of suicidal thoughts with finasteride and dutasteride medicines' (EMA/142716/2025) was published on the EMA website.

Post-meeting note 2: On 20 June 2025, the public health communication (EMA/202053/2025) as published on the EMA website following the adoption of the CMDh position.

3.4. Re-examination procedures[5]

None

3.5. Others

None

4. Signals assessment and prioritisation[6]

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. Adalimumab – AMGEVITA, AMSPARITY, HEFIYA, HUMIRA, HUKYNDRA, HULIO, HYRIMOZ, IDACIO, IMRALDI, LIBMYRIS, YUFLYMA (CAP)

Applicant: AbbVie Deutschland GmbH & Co. KG (Humira), Amgen Europe B.V. (Amgevita),

[3] Medicinal products containing finasteride 1 mg, for oral use: Update of SmPC sections 4.4, and 4.8. The labelling is updated accordingly; Medicinal products containing finasteride 5 mg, for oral use: Update of SmPC section 4.8; Medicinal products containing dutasteride, for oral use: Update of SmPC section 4.4. The package leaflets are updated accordingly.
[4] Jean-Michel Dogné, Tiphaine Vaillant
[5] Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC
[6] 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

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

PRAC Rapporteur: Karin Bolin

Scope: Signal of morphoea

EPITT 20166 – New signal

Background

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

During routine signal detection activities, a signal of morpheoea was identified by EMA, based on 5 cases retrieved from literature[7] and EudraVigilance. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from case reports in EudraVigilance and the literature, PRAC agreed that further evaluation on the signal of morphoea following administration of adalimumab is warranted.

Summary of recommendation(s)

- The MAH of Humira, AbbVie Deutschland GmbH & Co. KG should submit, within 60 days, a cumulative review of all cases of morphoea associated with adalimumab, including a review of the published literature, data from mechanistic studies, spontaneous reports and reports from studies including all cases in EudraVigilance database, as well as a discussion on possible biological plausibility and mechanism of this association. The MAH should also discuss the need for any potential amendment to the product information and/or the RMP, as warranted.
- A 60-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.2. Chikungunya virus (CHIKV) Δ5nsP3 strain (live, attenuated) – IXCHIQ (CAP)

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of adverse events (AEs) requiring hospitalisation in elderly patients

EPITT 20178 – New signal

Background

[7] Venetsanopoulou AI, Mavridou K, Pelechas E, Voulgari PV, Drosos AA. Development of Morphea Following Treatment with an ADA Biosimilar: A Case Report. Curr Rheumatol Rev. 2024;20(4):451-454. doi: 10.2174/0115733971266803231117072453. PMID: 38243962

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 signal validated by EMA concerns adverse events (AEs) requiring hospitalisation in elderly patients after active immunisation with the live attenuated Chikungunya virus vaccine IXCHIQ (CHIKV Δ5nsP3 strain). The procedure was prompted by two serious Individual Case Safety Reports (ICSRs). The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence, PRAC agreed that a thorough review at EU level should be performed with regard to adverse events requiring hospitalisation in elderly individuals after active immunisation with the live attenuated vaccine IXCHIQ (Chikungunya virus (CHIKV) Δ5nsP3 strain [live, attenuated]). Whilst the PRAC acknowledges that uncertainties remain, the data raise serious concerns that need to be further addressed.

Summary of recommendation(s)

- PRAC notes the newly initiated referral under Article 20 of Regulation (EC) No 726/2004 where this matter will be further evaluated in depth (see section 3.1).

4.1.3. Desogestrel (NAP), etonogestrel (NAP)

Applicant(s): various

PRAC Rapporteur: Karin Bolin

Scope: Signal of meningioma

EPITT 20167 – New signal

Background

Etonogestrel is a progestogen indicated for use as a hormonal contraceptive. Desogestrel is biologically inactive and is metabolised to the pharmacologically active compound, etonogestrel.

During routine signal detection activities, a signal of meningioma was identified by France, based on the results of an epidemiologic study using the French national health data system (SNDS).The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from the epidemiological study and the case reports in EudraVigilance, PRAC agreed that further evaluation on the signal of meningioma following administration of etonogestrel and/or desogestrel- containing medicinal products is warranted.

PRAC appointed Karin Bolin as Rapporteur for the signal.

Summary of recommendation(s)

- The MAH Organon for the innovator products containing desogestrel 75 µg, desogestrel 150 µg/ethinyl oestradiol, etonogestrel implant and etonogestrel/ethinyl oestradiol

vaginal ring should submit to EMA, within 90 days, a cumulative review of all cases of meningioma associated with desogestrel and etonogestrel, including a review of the published literature, data from spontaneous reports and reports from studies, as well as a discussion on possible biological plausibility and mechanism of this association. Within this proposal the MAH should consider the need for separate proposals across the different indications and context for use. The MAH should also provide a discussion on the systemic exposure to etonogestrel for their product in relation to desogestrel 75 µg and summarise for all cases the time to onset and prior treatment with other hormonal products. The MAH should also discuss the need for any potential amendment to the product information and/or RMP as warranted. The MAH is also requested to discuss the need for a DHPC and send a draft proposal, as warranted.

- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.2. Signals follow-up and prioritisation

4.2.1. Adalimumab - AMGEVITA (CAP); AMSPARITY (CAP); HEFIYA (CAP); HUKYNDRA (CAP); HULIO (CAP); HUMIRA (CAP) - EMEA/H/C/000481/SDA/127; HYRIMOZ (CAP); IDACIO (CAP); IMRALDI (CAP); LIBMYRIS (CAP); YUFLYMA (CAP)

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

PRAC Rapporteur: Karin Bolin

Scope: Signal of paradoxical hidradenitis

EPITT 20126 – Follow-up to December 2024

Background

For background information, see PRAC minutes December 2024.

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

Discussion

Having considered the available evidence in EudraVigilance and the literature, as well as the responses of the MAH for Humira, PRAC concluded that the current evidence is insufficient to establish a causal relationship between adalimumab and paradoxical hidradenitis suppurativa to further warrant an update to the product information and/or RMP.

Summary of recommendation(s)

- In the next PSUR[8], the MAHs for adalimumab-containing medicinal products should monitor paradoxical hidradenitis suppurativa.

[8] Data lock point: 31 December 2025

4.2.2. Sertraline (NAP)

Applicant(s): various

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of multiple acyl-coenzyme A dehydrogenase deficiency (MADD)

EPITT 20125 – Follow-up to January 2025

Background

For background information, see PRAC minutes January 2025.

The MAH Viatris for Zoloft (sertraline) replied to the request for information on the signal of MADD and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence from literature and the EudraVigilance database, as well as the responses of the MAH, PRAC agreed that there is sufficient evidence to establish a causal association between sertraline and MADD. Therefore, the product information for all sertraline-containing medicinal products should be updated to add MADD-like disorder as an undesirable effect with frequency 'not known'.

Summary of recommendation(s)

- The MAHs for sertraline-containing medicinal products should submit to Member States, within 60 days, a variation to amend the product information[9] (depending on the already existing wording in some nationally authorised products, the text needs to be adapted by MAHs to individual products).

4.2.3. Sulfamethoxazole, trimethoprim (co-trimoxazole) (NAP)

Applicant: various

PRAC Rapporteur: Barbara Kovačić Bytyqi

Scope: Signal of circulatory shock

EPITT 20135 – Follow-up to January 2025

Background

For background information, see PRAC minutes January 2025.

The MAH Eumedica Pharmaceuticals GMBH as the market lead for trimethoprim/sulfamethoxazole (co-trimoxazole) replied to the request for information on the signal of circulatory shock and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence from literature and the EudraVigilance database, as well as the response by the MAH, PRAC concluded that there is sufficient evidence to establish a causal association between sulfamethoxazole/trimethoprim (co-trimoxazole) and circulatory shock. Therefore, the product information of all sulfamethoxazole/trimethoprim

[9] Update of SmPC section 4.8. The package leaflet is to be updated accordingly

(co-trimoxazole)-containing medicinal products should be updated to add circulatory shock as an undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAHs for trimethoprim-sulfamethoxazole (co-trimoxazole)-containing medicinal products should submit to Member States, within 60 days, a variation to amend the product information[10] (depending on the already existing wording in some nationally authorised products, the text needs to be adapted by MAHs to individual products).

4.3. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

5.1.1. Bifikafusp alfa, onfekafusp alfa - (CAP MAA) - EMEA/H/C/005651

Scope (pre D-180 phase): Neoadjuvant treatment of adult patients with locally advanced fully resectable melanoma.

5.1.2. Lenacapavir - (CAP MAA) - EMEA/H/C/006658

Scope (pre D-90 phase, accelerated assessment): Pre-exposure prophylaxis to prevent HIV-1

5.1.3. Lenacapavir - EMEA/H/W/006659

Scope (pre D-90 phase, accelerated assessment): Pre-exposure prophylaxis to prevent HIV-1

5.1.4. Lifileucel - (CAP MAA) - EMEA/H/C/004741

ATMP

Scope (pre D-180 phase): Treatment of unresectable or metastatic melanoma

[10] Update of SmPC section 4.8. The package leaflet is to be updated accordingly

5.1.5. Olezarsen - CAP MAA) - EMEA/H/C/006477, Orphan

Applicant: Ionis Ireland Limited

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

5.1.6. Pridopidine - (CAP MAA) - EMEA/H/C/006261, Orphan

Applicant: Prilenia Therapeutics B.V.

Scope (pre D-180 phase): Treatment of Huntington's disease

5.1.7. Sebetralstat - (CAP MAA) - EMEA/H/C/006211, Orphan

Applicant: Kalvista Pharmaceuticals (Ireland) Limited

Scope (pre D-180 phase): Treatment of hereditary angioedema (HAE) attacks in adult and adolescents aged 12 years and older

5.1.8. Zuranolone - (CAP MAA) - EMEA/H/C/006488

Scope (pre D-180 phase): Treatment of postpartum depression (PPD) in adults

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

See also Annex I 15.2.

5.2.1. Agalsidase beta – FABRAZYME (CAP) - EMA/VR/0000254249

Applicant: Sanofi B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of an updated RMP version 3.0 in order to remove the PASS category 3 study "Fabrazyme home infusion educational materials effectiveness evaluation" from the pharmacovigilance plan in the RMP and to consider the routine pharmacovigilance monitoring with submission of safety assessment in PSURs to cover this commitment instead. In addition, the MAH introduced RMP updates agreed in previous procedures

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 Fabrazyme, a centrally authorised medicine containing agalsidase beta, to update the RMP to reflect the removal of PASS for the evaluation of the home infusion educational materials effectiveness. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

S**ummary of advice**

- The RMP version 3.0 for Fabrazyme (agalsidase beta) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.

- PRAC agreed that the PASS 'Fabrazyme home infusion educational materials effectiveness evaluation' can be removed from the RMP. However, PRAC highlighted that hypersensitivity reactions and medication errors occurring in the home setting should continue to be monitored within the PSUR. In addition, the MAH is requested to maximise their effort to identify the setting in which hypersensitivity reactions, medication errors, or other adverse events reported, have taken place.

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

See also Annex I 15.3.

5.3.1. Pegcetacoplan – ASPAVELI (CAP) - EMA/VR/0000248937

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

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

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 Aspaveli, a centrally authorised product containing pegcetacoplan, to extend the indication to include treatment of adults and adolescents aged 12 to 17 years with C3G or primary IC-MPGN. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

Summary of advice

- The RMP for Aspaveli (pegcetacoplan) in the context of this variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 3.2 is submitted.
- PRAC considered that the proposed new category 3 PASS long-term extension of study APL2-C3G-314 in patients with C3G or IC-MPGN in the pharmacovigilance plan to assess the long-term safety can be considered agreeable.

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. Abemaciclib - VERZENIOS (CAP) - PSUSA/00010724/202409

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Verzenios, a centrally authorised medicine containing abemaciclib 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 Verzenios (abemaciclib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include keratitis as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[11].

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

6.1.2. Aliskiren - RASILEZ (CAP); aliskiren, hydrochlorothiazide - RASILEZ HCT[12] - PSUSA/00000089/202409

Applicant: Noden Pharma DAC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Background

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

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

[12] European Commission (EC) decision on the marketing authorisation (MA) withdrawal for Rasilez HCT dated 20 December 2021

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Rasilez (aliskiren) 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 monitor the issue regarding the potential interaction between cisplatin and aliskiren in inducing acute kidney injury. In addition, the MAH should monitor cases of abdominal pain, asthenia, fatigue, malaise, aphasia, cerebrovascular accident, dysarthria, anxiety and confusional state, including a causality assessment and discuss the need for any potential amendments to the product information.

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. Axicabtagene ciloleucel - YESCARTA (CAP) - PSUSA/00010703/202410

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Yescarta, a centrally authorised medicine containing axicabtagene ciloleucel 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 Yescarta (axicabtagene ciloleucel) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add haemorrhage as an undesirable effect with a frequency 'common'. In addition, the product information should be updated to add a warning regarding secondary malignancy of myeloid origin. Moreover, the frequency of the undesirable effect 'secondary malignancy of T-cell origin' should be changed to 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[13].

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. Cemiplimab - LIBTAYO (CAP) - PSUSA/00010780/202409

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Bianca Mulder

[13] 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

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Libtayo, a centrally authorised medicine containing cemiplimab 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 Libtayo (cemiplimab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning regarding immune-mediated adverse reactions in patients with pre-existing autoimmune disease. Therefore, the current terms of the marketing authorisation(s) should be varied[14].
- In the next PSUR, the MAH should provide cumulative reviews of cases of optic neuritis and of autoimmune haemolytic anaemia.

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

6.1.5. Chenodeoxycholic acid[15] [16] - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - PSUSA/00010590/202410

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Chenodeoxycholic acid Leadiant, a centrally authorised medicine containing chenodeoxycholic acid 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 Chenodeoxycholic acid Leadiant (chenodeoxycholic acid) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add jaundice and transaminases increased as undesirable effects with frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[17].

[14] Update of SmPC section 4.4. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[15] Indicated for the treatment of inborn errors of primary bile acid synthesis due to sterol 27 hydroxylase deficiency (presenting as cerebrotendinous xanthomatosis (CTX))
[16] Centrally authorised product(s) only
[17] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

The 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. Dapagliflozin - EDISTRIDE (CAP); FORXIGA (CAP) - PSUSA/00010029/202410

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Edistride and Forxiga, centrally authorised medicines containing dapagliflozin 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 the dapagliflozin-containing medicinal products Edistride and Forxiga 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 (groin) abscesses on different locations and discuss whether an update of the product information is warranted.
- The MAH should submit to EMA, by 30 May 2025 a review of all cases related to the potential association between dapagliflozin exposure and drug reaction with eosinophilia and systemic symptoms (DRESS) as part of a post-authorisation measure (LEG). In addition, the MAH should submit to EMA, within 3 months, a review of all cases related to the potential association between dapagliflozin exposure and prolonged ketoacidosis and prolonged glucosuria as part of a post-authorisation measure (LEG).

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

6.1.7. Denosumab[18] - JUBBONTI (CAP); PROLIA (CAP) - PSUSA/00000954/202409

Applicant: Sandoz GmbH (Jubbonti), Amgen Europe B.V. (Prolia)

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Jubbonti and Prolia, centrally authorised medicines containing denosumab and issued a recommendation on their marketing authorisation(s).

[18] Indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of the denosumab-containing medicinal products Jubbonti and Prolia in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding a reduction in bone mineral density following denosumab discontinuation. Therefore, the current terms of the marketing authorisation(s) should be varied[19].
- In the next PSUR, the MAH for Prolia should submit a cumulative review of cases of preferred terms 'injection site pain' and 'injection site reaction' associated with denosumab (indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer), including cases from clinical trials and an overview of the post-marketing data and propose an update to the product information as warranted.
- The MAHs should address the completed category 3 study 20090522 in the RMP, to be submitted within an upcoming regulatory procedure affecting the RMP or at the latest by the next PSUR. The possible removal of some of the safety concerns should also be discussed.

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

6.1.8. Dulaglutide - TRULICITY (CAP) - PSUSA/00010311/202409

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Trulicity, a centrally authorised medicine containing dulaglutide 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 Trulicity (dulaglutide) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add dysgeusia 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 MAH should submit reviews of cases of nephrolithiasis and hair loss and discuss the need to update the product information as warranted. In addition, the MAH should provide a cumulative review of cases of euglycemic diabetic ketoacidosis and discuss separately the cases where dulaglutide may represent a precipitating factor. The MAH should also provide a discussion of the new literature articles about self-

[19] Update of SmPC section 4.4. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion
[20] 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

injurious ideation and suicidal ideation published in the interval period, encompassing also the articles collected between 19 September 2021 and 18 September 2024.

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.

6.1.9. Eltrombopag - REVOLADE (CAP) - PSUSA/00001205/202409

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Revolade, a centrally authorised medicine containing eltrombopag 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 Revolade (eltrombopag) 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 all cases of sepsis, in both adult and paediatric patients, as well as a cumulative review of the risk of thromboembolic events (including all potential thrombosis localisations; venous and arterial) and to discuss whether an update of the product information is warranted.

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

6.1.10. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - PSUSA/00010868/202410

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Kaftrio, a centrally authorised medicine containing ivacaftor/tezacaftor/elexacaftor 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 Kaftrio (ivacaftor/tezacaftor/elexacaftor) in the approved indication(s) remains unchanged.

- Nevertheless, the product information should be updated to amend the warning regarding depression, to add a warning regarding behavioural changes in paediatric patients and to add behavioural changes as an undesirable effect with a frequency 'not known'. In addition, the product information should be updated to amend the warning regarding elevated transaminases and hepatic injury and to amend the explanation regarding liver injury under the table of adverse reactions. Therefore, the current terms of the marketing authorisation(s) should be varied[21].
- In the next PSUR, the MAH should continue to monitor cases of idiopathic intracranial hypertension (IIH). The MAH should provide a cumulative review of cases of medication errors, differentiate them by country, and discuss whether updates to the RMP are necessary to include medication errors as a safety concern as well as on need for further risk minimization measures. The MAH should also provide a cumulative review of cases of eyelid disorders. Moreover, the MAH should monitor cases of pregnant and breastfeeding women exposed to ivacaftor/tezacaftor/elexacaftor, closely monitor pregnancy outcomes and discuss whether amendments to the product information are warranted. Additionally, the MAH should discuss whether the current measures for the identification of unplanned pregnancies are sufficient and consider amending the existing follow-up questionnaires if necessary.

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

6.1.11. Loncastuximab tesirine - ZYNLONTA (CAP) - PSUSA/00011027/202410

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Zynlonta, a centrally authorised medicine containing loncastuximab tesirine 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 Zynlonta (loncastuximab tesirine) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add sepsis as a warning and as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[22].
- In the next PSUR, the MAH should monitor all cases suggestive of capillary leak syndrome and provide a thorough discussion on all data on increased vascular

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

permeability with loncastuximab retrieved from pre-clinical studies, clinical trials, post-marketing data and literature. The MAH should discuss whether capillary leak syndrome should be classified as a new identified risk of loncastuximab and also whether dexamethasone should be considered by physicians in treatment of oedema and effusion occurring with loncastuximab therapy.

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.

6.1.12. Pitolisant - OZAWADE (CAP); WAKIX (CAP) - PSUSA/00010490/202409

Applicant: Bioprojet Pharma

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Ozawade and Wakix, centrally authorised medicines containing pitosilant 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 the pitosilant-containing medicinal products Ozawade and Wakix in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.

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

6.1.13. Tremelimumab - IMJUDO (CAP) - PSUSA/00011038/202410

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Imjudo, a centrally authorised medicine containing tremelimumab 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 Imjudo (tremelimumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add polymyalgia rheumatica as part of a warning and as an undesirable effect under the SOC Musculoskeletal and connective tissue disorders with a frequency 'uncommon' for tremelimumab in

combination with durvalumab and a frequency 'not known' for tremelimumab in combination with durvalumab and platinum-based chemotherapy. Therefore, the current terms of the marketing authorisation(s) should be varied[23].

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

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

See Annex I 16.2.

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

See also Annex I 16.3.

6.3.1. Diclofenac[24] (NAP) - PSUSA/00001048/202409

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Background

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) and is indicated in arthritic conditions, acute musculoskeletal disorders and trauma, acute pain conditions, painful and inflammatory conditions in gynaecology and fever reduction (systemic formulations).

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing diclofenac 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 diclofenac-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing warning regarding skin reactions to also include generalised bullous fixed drug eruption and to add generalised bullous fixed drug eruption and fixed drug eruption as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[25].

[23] 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
[24] Systemic formulations only
[25] 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 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. Levosimendan (NAP) - PSUSA/00001858/202409

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure

Background

Levosimendan is a pyridazinone derivative indicated for the short-term treatment of acutely decompensated severe chronic heart failure in situations where conventional therapy is not sufficient, and in cases where inotropic support is considered appropriate.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing levosimendan 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 levosimendan-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add 'hypersensitivity' as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[26].
- In the next PSUR, the MAH should provide a review of cases of angioedema, including data from clinical trials, post-marketing reports and literature, as well as a causality assessment and discuss whether an update of the product information is warranted.

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

6.3.3. Sumatriptan (NAP); Naproxen, sumatriptan (NAP) - PSUSA/00002832/202409

Applicant(s): various

PRAC Lead: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Background

Sumatriptan is a selective vascular 5-hydroxytryptamine 1B/D (5-HT1B/D) receptor agonist and it is indicated for the acute relief of migraine attacks, with or without aura and for the acute treatment of cluster headache. Naproxen/sumatriptan combination is indicated for the

[26] 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

acute treatment of the headache phase of migraine attacks with or without aura in adults where treatment with a mono-entity product has been insufficient.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing sumatriptan and naproxen/sumatriptan 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 sumatriptan and naproxen/sumatriptan-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated regarding breastfeeding to include safety information about relative infant dose, and to add information regarding breast pain and nipple pain in breastfeeding women. In addition, the product information should be updated to add breast pain as undesirable effect with a frequency 'rare'. Therefore, the current terms of the marketing authorisation(s) should be varied[27].
- In the next PSUR, the MAH Orion for naproxen/sumatriptan should review and discuss whether the two current recommendations in the product information for naproxen/sumatriptan regarding breastfeeding (avoiding use in nursing mothers and discarding breast milk for 12 hours after treatment) are scientifically and clinically appropriate and compatible, considering both drug components, and propose updates to the product information if needed.

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

6.4. Follow-up to PSUR/PSUSA procedures

See Annex I 16.4.

6.5. Variation procedure(s) resulting from PSUSA evaluation

See also Annex I 16.5.

6.5.1. Doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO (CAP) - EMA/VR/0000247253

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.4, and 4.8 of the SmPC in order amend an existing warning on bone effects and add 'bone mineral density decreased' to the list of adverse drug reactions (ADRs) with frequency 'common' following PRAC recommendation for Viread PSUSA 00002892-202303; the Package Leaflet (PL) is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the PL

Background

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

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 a variation to update the product information regarding the existing warning on bone effects. 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 recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed with the proposed update of the product information[28] to amend the existing warning on bone effects and to add 'bone mineral density decreased' to the list of adverse drug reactions (ADRs) with frequency 'common'.

6.5.2. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0055, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.6 of the SmPC in order to amend the existing wording on exposure during pregnancy following PSUR procedure (EMEA/H/C/PSUSA/00010868/202310)

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 a variation to amend the existing wording on exposure during pregnancy. 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 recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed with the proposed update of the product information[29] to amend the existing wording on exposure during pregnancy.

6.6. Expedited summary safety reviews[30]

None

[28] Update of SmPC sections 4.4 and 4.8. The package leaflet is updated accordingly.
[29] Update of SmPC sections 4.6.
[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

7. Post-authorisation safety studies (PASS)

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

See also Annex I 17.1.

7.1.1. Pegzilarginase - LOARGYS (CAP) - EMA/PASS/0000258458

Applicant: Immedica Pharma AB

PRAC Rapporteur: Martin Huber

Scope: PASS 107n (protocol): MAH's response to PSP/0105.2 [A European, non-interventional, multicentre, registry-based post-authorisation safety study to evaluate the long-term safety of Loargys treatment in arginase 1 deficiency patients in standard clinical care] as per the request for supplementary information (RSI) adopted in January 2025

Background

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

In order to fulfil the obligation to conduct a PASS imposed in accordance with Article 107n(3) of Directive 2001/83/EC, the Marketing Authorisation Holder Immedica Pharma AB submitted on 22 February 2024 a PASS protocol version 0.4 to the European Medicines Agency (E MA) for Pegzilarginase (Loargys). PRAC is responsible for evaluating the PASS protocol.

Endorsement/Refusal of the protocol

- Based on the PRAC review of the PASS protocol version 0.8 dated 15 April 2025 and in accordance with Article 107n(2)(a) of Directive 2001/83/EC, PRAC considered that the study is non-interventional and that the study design fulfils the study objectives. The PASS protocol version 0.8 dated 15 April 2025 for Pegzilarginase (loargys) can be endorsed.

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

See Annex I 17.2. .

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

See Annex I 17.3. .

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

See Annex I 17.4. .

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

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

See Annex I 17.5. .

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

See Annex I 18.2.

8.3. Renewals of the marketing authorisation

See Annex I 18.3.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

11.1.1. Levofloxacin[35] (NAP) - DE/H/5119/001-003/II/113

Applicant(s): Sanofi-Aventis Deutschland GmbH

PRAC Lead: Martin Huber

Scope: PRAC consultation on a variation procedure (DE/H/5119/001-003/II/113) to update the product information based on submitted cumulative data including causality assessment of all cases of acute generalised exanthematous pustulosis (AGEP) associated with levofloxacin, following the conclusion of the PSUSA procedure on levofloxacin (PSUSA/00010767/202310) in May 2024, at request of Germany

Background

Levofloxacin is a fluoroquinolone antibacterial agent indicated in adults for the treatment of several infections especially severe bacterial infections.

In the context of the evaluation of the variation procedure on update of the product information related to AGEP cases associated with levofloxacin, Germany requested PRAC advice on its assessment. For further background, see PRAC minutes May 2024.

[35] For intravenous and oral use only

Summary of advice

- Based on the review of the data on AGEP from the literature and spontaneous reports, PRAC supported the update of the product information[36] to reflect AGEP as a warning and as an undesirable effect for the levofloxacin-containing medicinal products (intravenous and oral use). PRAC noted that the MAH has not provided sufficient evidence to support the proposed frequency 'rare', thus the MAH should justify the frequency accordingly in the ongoing procedure. It was also noted the repetition of information in the description of adverse reactions in the section 2 and section 4 of the product leaflet ; however, it was acknowledged that this repetition is also present for other severe cutaneous adverse drug reactions already labelled, which are not in scope of the current procedure. Finally, PRAC supported that the above recommendation should apply to all levofloxacin-containing medicinal products for intravenous and oral use addressed within the PSUSA/00010767/202310.

11.1.2. Mycophenolate mofetil (NAP) - DE/H/xxxx/WS/1997

Applicant: Hexal Aktiengesellschaft, 1 A Pharma GmbH

PRAC Lead: Martin Huber

Scope: PRAC consultation on a worksharing variation procedure (DE/H/xxxx/WS/1997) regarding the need to align RMP requirements for reporting on long term safety of generic products containing mycophenolate mofetil or mycophenolic acid with the originator, and the need to reconsider whether long term safety is still considered as missing information in the RMP, at request of Germany

Background

Mycophenolate mofetil is an immunosuppressant indicated in combination with ciclosporin and corticosteroids for the prophylaxis of acute transplant rejection in adult and paediatric patients receiving allogeneic renal, cardiac or hepatic transplants.

In the context of the evaluation of a worksharing variation procedure regarding the need to align RMP requirements for reporting on long term safety of generic products with the originator, Germany requested PRAC advice on its assessment.

Summary of advice

- Based on the review of the available information, PRAC considered that relevant information regarding the risk of 'long term safety (growth retardation, pubertal maturation and fertility, bone health, metabolic problems and neurocognitive development)' will be identified by the originator. Considering the substantial post-marketing experience with mycophenolate, PRAC agreed with the member state (MS) position that the MAHs of generic products containing mycophenolate mofetil should report on long term safety in PSURs instead of annual reports to be submitted as post-authorisation measures (PAMs), to minimise redundancy and ensure that all available evidence is assessed in a single procedure. Consequently, long term safety would qualify for the generics as missing information in the PSUR, but not for the RMP. PRAC also agreed with the MS proposition to reconsider in the forthcoming PSUSA procedure whether 'long term safety (growth retardation, pubertal maturation and fertility, bone

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

health, metabolic problems and neurocognitive development)' continues to qualify as missing information in the RMP of the originator CellCept.

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

None

12.1.2. Vote by proxy

Annalisa Capuano gave a proxy to Milou Drici to vote on her behalf for the period 06 to 08 May 2025.

12.1.3. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q1 2025

In line with the adopted PRAC best practice guidance (BPG) on Committee efficiency (see PRAC minutes May 2016 and PRAC minutes June 2018) and the adopted implementation plan for the BPG including goals to measure compliance with the recommendations (see PRAC minutes June 2016 and PRAC minutes June 2018), PRAC was informed on the quantitative measures collected for Q1 2025 of PRAC meetings during the organisational, regulatory and methodological matters (ORGAM) meeting on 22 May 2025. For previous update, see PRAC minutes February 2025.

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 EMA Secretariat provided to PRAC an update on the COVID-19 vaccines including data on the dominant strains and the effectiveness of the vaccines for both COVID-19 and influenza vaccines. An update was also given on the cases of Dengue, Chikungunya and Zika viruses. PRAC noted the information.

12.5. Cooperation with International Regulators

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

The Pharmacovigilance Business Team presented to PRAC the updates in the ICH E2D(R1) guideline that were implemented in the post-public consultation phase. For background information see PRAC Minutes February 2024. PRAC was invited to provide any comments by 23 May 2025 on any potential major issues that would need to be addressed before progressing to Step 4.

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

12.8.1. Medicinal Products and Technology Pipeline: 3-Year Outlook Report

At the organisational, regulatory and methodological matters (ORGAM) meeting on 22 May 2025, the EMA Secretariat presented the 3-year outlook report for 2025-2027, including post-authorisation activities (line extensions and type II variations) and medicinal products pipeline. PRAC noted the information.

12.8.2. PRAC workload statistics – Q1 2025

At the organisational, regulatory and methodological matters (ORGAM) meeting on 22 May 2025, the EMA secretariat informed PRAC about the quarterly and cumulative figures to estimate the evolution of the PRAC workload for Q1 2025, by reflecting on the number of procedures and agenda items covered at each PRAC plenary meeting. For previous update, see PRAC minutes February 2025.

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Jana Lukacisinova

The EMA Secretariat and the GPAG Chair presented to PRAC an update on the GPAG activities, as well as the review exercise regarding the PSUR requirements for products referred to in Articles 10(1), 10a, 16a of Directive 2001/83/EC for active substances for which there is a CAP available. PRAC was informed that the outcome of this exercise will be transferred to the drafting group working on the 'Drafting group on best practices for PSUR assessment' to align and develop potential criteria to switch on generics/well-established use when CAPs are available. PRAC noted the information.

12.10.3. PSURs repository

None

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

In line with the criteria for plenary presentation of updates to the EURD List adopted by PRAC in December 2021, PRAC endorsed the draft revised EURD list, version May 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 May 2025, the updated EURD list was adopted by CHMP and CMDh at their May 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

None

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact - review of feasibility assessment outcomes

The PRAC IG Impact 2025 workplan foresees the review of feasibility assessment outcomes of studies conducted in DARWIN EU® with the aim to develop stakeholder guidance, including requirements for standard feasibility assessment, data source-specific recommendations, mitigation strategies or other aspects relevant for regulatory decision-making. PRAC was informed on the draft outline including scope, research question and objectives, and invited to provide comments until 20 May 2025.

Post-meeting note: The draft outline v1.4 for the review of feasibility assessments of studies conducted in DARWIN EU® was adopted by PRAC with no further comments.

12.21. Others

12.21.1. Good Pharmacovigilance Practices (GVP) module XVI – Addendum on pregnancy - update

PRAC lead: Ulla Wändel Liminga

At the organisational, regulatory and methodological matters (ORGAM) meeting on 22 May 2025, the EMA Secretariat updated PRAC on the activities of the author team and outlined the actions taken following the public consultation to revise Addendum I. This included presenting a proposed new title, an updated scope, a revised structure in accordance with GVP Module XVI, and clarification of the main guiding principle. The EMA Secretariat also detailed the upcoming steps required to complete the revision of the guidance. PRAC will continue to be informed as the finalisation process moves forward.

12.21.2. Onboarding experience of Committee/CMD members and alternates

The EMA Secretariat presented to PRAC the new onboarding programme for the new Committee members and alternates to enhance the onboarding experience and to ensure a smoother transition aiming to increase the new members capacity to contribute to the

Committee's activities. PRAC welcomed the initiative and was encouraged to provide any further recommendation.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[37]

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[38].

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Dabigatran – PRADAXA (CAP); NAP

Applicant(s): Boehringer Ingelheim International, various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of splenic rupture

EPITT 20164 – New signal

14.1.2. Dinutuximab beta – QARZIBA (CAP)

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of atypical haemolytic uraemic syndrome

EPITT 20169 – New signal

14.1.3. Osimertinib – TAGRISSO (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: Signal of hepatitis B reactivation

EPITT 20172 – New signal

14.1.4. Polatuzumab vedotin - POLIVY (CAP)

Applicant: Roche Registration GmbH

[37] 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

[38] 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

PRAC Rapporteur: Mari Thorn

Scope: Signal of infusion site extravasation

Action: For adoption of PRAC recommendation

EPITT 20171 – New signal

14.1.5. Somatrogon - NGENLA (CAP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of lipoatrophy

EPITT 20173 – New signal

14.2. New signals detected from other sources

None

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

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

15.1.1. Denosumab - (CAP MAA) - EMEA/H/C/006507

Scope (pre D-46 phase): Treatment of osteoporosis in postmenopausal women and in men at increased risk of fractures; treatment of bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures; treatment of bone loss associated with long-term systemic glucocorticoid therapy in adult patients at increased risk of fracture

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

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Karin Erneholm

Scope: Submission of an updated RMP version 4.3 for Tecartus and version 11.1 for

Yescarta following the PRAC recommendation for the Secondary malignancy of T-cell origin signal (EPITT no: 20040), and of a PASS protocol for a framework for the sampling and testing of secondary malignancies of T-cell origin.

15.2.2. Fezolinetant – VEOZA (CAP) - EMA/VR/0000255134

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

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

15.2.3. Rituximab - RIXATHON (CAP); RIXIMYO (CAP) - EMA/VR/0000249103

Applicant: Sandoz GmbH

PRAC Rapporteur: Karin Erneholm

Scope: To align the RMP with that of the reference product by updating the ATC code, removing the important identified risks `Hepatitis B (HBV) reactivation (all indications)', `Hypogammaglobulinemia (non-oncology indications)' and missing information `Long-term use in Granulomatosis with polyangiitis (GPA)/ microscopic polyangiitis (MPA) patients (GPA/MPA)' `Relapses' (for GPA/MPA) from the list of safety concerns. To remove the targeted follow-up questionnaire (TFUQ) details and the additional risk minimization measures HCP educational leaflet and Patient educational leaflet

15.2.4. Zoledronic acid - ZOMETA (CAP) - EMEA/H/C/000336/II/0104

Applicant: Phoenix Labs Unlimited Company

PRAC Rapporteur: Karin Erneholm

Scope: Submission of an updated RMP version 12.1 in order to update the list of safety concerns and missing information as per the guidance provided in the GVP V–Rev.2 and PSUSA/3149/202308

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) - EMEA/H/C/002548/II/0052

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

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

took the opportunity to introduce a minor editorial change to the Product Information

15.3.2. Aflibercept – YESAFILI (CAP) - EMA/VR/0000245097

Applicant: Biosimilar Collaborations Ireland Limited

PRAC Rapporteur: Zoubida Amimour

Scope: Quality variations

An updated Product Information (PI) and revised Risk Management Plan (RMP version 1.1) are being submitted

15.3.3. Anakinra – KINERET (CAP) - EMA/VR/0000249038

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Karin Erneholm

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

15.3.4. Anifrolumab - SAPHNELO (CAP) - EMEA/H/C/004975/X/0023

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Martirosyan

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with a new route of administration (subcutaneous use) and a new strength (120 mg)

15.3.5. Azacitidine - AZACITIDINE ACCORD (CAP) - EMEA/H/C/005147/X/0021

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to introduce a new pharmaceutical form (film-coated tablet) associated with new strengths (200 and 300 mg) and new route of administration (oral use). The RMP (version 2.0) is updated in accordance

15.3.6. Bedaquiline – SIRTURO (CAP) - EMA/VR/0000249065

Applicant: Janssen Cilag International

PRAC Rapporteur: Karin Bolin

Scope: Extension of indication to include treatment of paediatric patients (2 years to less than 5 years of age and weighing at least 7 kg) with pulmonary tuberculosis (TB) due to Mycobacterium tuberculosis resistant to at least rifampicin and isoniazid, for SIRTURO, based on the Week 24 primary analysis from Cohort 3 (⩾2 to <5 years of age) of Study

TMC207-C211; this is an open-label, multicentre, single-arm study to evaluate pharmacokinetics, safety/tolerability, antimycobacterial activity and dose selection of bedaquiline in children (birth to <18 years) with multidrug-resistant-TB (MDR-TB). Long-term follow-up to Week 120 in participants of Cohort 1 (⩾12 to <18 years of age) and Cohort 2 (⩾5 to <12 years of age) have also been submitted. 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 11.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and introduce minor changes to the PI

15.3.7. Bempedoic acid - NILEMDO (CAP) - EMEA/H/C/004958/WS2798/0045; Bempedoic acid, ezetimibe - NUSTENDI (CAP) - EMEA/H/C/004959/WS2798/0050

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.2, 4.4, and 5.2 of the SmPC in order to amend information concerning renal impairment based on the final results from Study 1002-071 listed as a category 3 study in the RMP; this is a phase 1, open-label, single-dose study to evaluate the pharmacokinetics of bempedoic acid in healthy subjects with normal renal function and subjects with end-stage renal disease receiving HD; the Package Leaflet is updated accordingly. The RMP version 7.0 has also been submitted

15.3.8. Daratumumab - DARZALEX (CAP) - EMEA/H/C/004077/II/0077, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include daratumumab for the treatment of adult patients with smouldering multiple myeloma (SMM) at high risk of developing multiple myeloma based on results from studies 54767414SMM3001 (AQUILA) and 54767414SMM2001 (CENTAURUS). SMM3001 (AQUILA) is a Phase 3 Randomized, Multicentre Study of Subcutaneous Daratumumab Versus Active Monitoring in Subjects with High-risk Smoldering Multiple Myelom. SMM2001 (CENTAURUS) is a Randomized Phase 2 Trial to Evaluate Three Daratumumab Dose Schedules in Smoldering Multiple Myeloma.
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 11.2 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the PI in accordance with the latest EMA excipients guideline

15.3.9. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0024

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include in combination with androgen deprivation therapy (ADT) the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) for NUBEQA, based on final results from study 21140 (ARANOTE); this is a randomised, double-blind, placebo-controlled Phase 3 study of darolutamide to demonstrate the superiority of darolutamide in addition to ADT over placebo plus ADT in patients with

mHSPC. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor editorial changes to the PI and update the Package Leaflet to more patient friendly wording based on patient council feedback

15.3.10. Dupilumab – DUPIXENT (CAP) - EMA/VR/0000248778

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of adults with bullous pemphigoid (BP) for DUPIXENT, based on final results from study R668-BP-1902 (LIBERTY-BP ADEPT); this is a phase 2/3, multicentre, randomised, double blind, placebo-controlled, parallel group study to assess the efficacy and safety of dupilumab in adult patients with bullous pemphigoid; As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 12.0 of the RMP has also been submitted

15.3.11. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0073

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include IMFINZI in combination with cisplatin-based chemotherapy as neoadjuvant treatment, followed by IMFINZI as monotherapy adjuvant treatment after radical cystectomy, for the treatment of adults with muscle invasive bladder cancer (MIBC), based on an ongoing pivotal study D933RC00001 (NIAGARA); this is a phase 3, randomised, open-label, multi-centre, global study to determine the efficacy and safety of durvalumab in combination with gemcitabine+cisplatin for neoadjuvant treatment followed by durvalumab alone for adjuvant treatment in patients with muscle-invasive bladder cancer. As a consequence, sections 4.1, 4.2, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. The RMP version 13 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes and update the PI according to the Excipients Guideline

15.3.12. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/II/0025

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Submission of the final integrated analysis report for bone biomarkers based on GO40782 [STARTRK-2], CO40778 [STARTRK-NG], and BO41932 [TAPISTRY] studies (PAESs). The RMP version 6 has also been submitted

15.3.13. Etrasimod – VELSIPITY (CAP) - EMA/VR/0000249630

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Bolin

Scope: Update of sections 4.4, and 4.6 of the SmPC in order to amend an existing warning

and information on pregnancy regarding reduced the contraceptive washout period from 14 to 7 days based on the results of recently completed DDI studies; the Package Leaflet is updated accordingly. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet and to introduce editorial changes in the PI

15.3.14. Faricimab - VABYSMO (CAP) - EMEA/H/C/005642/II/0016

Applicant: Roche Registration GmbH

PRAC Rapporteur: Carla Torre

Scope: Update of section 5.1 of the SmPC to reflect the long-term safety profile of faricimab in patients with diabetic macular edema (DME) based on the final results from study GR41987 (Rhone-X) listed as a category 3 study of the RMP. Rhone-X was a phase III interventional, multicentre, open-label extension study to evaluate the long-term safety and tolerability of faricimab in patients with diabetic macular oedema. The RMP version 7.0 has also been submitted.

15.3.15. Formoterol, glycopyrronium bromide, budesonide - RILTRAVA AEROSPHERE (CAP) - EMEA/H/C/005311/WS2780/0017; Formoterol, glycopyrronium bromide, budesonide - TRIXEO AEROSPHERE (CAP) - EMEA/H/C/004983/WS2780/0024

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Quality variations

The RMP version 2 has also been submitted.

15.3.16. Guselkumab – TREMFYA (CAP) - EMA/VR/0000257669

Applicant: Janssen Cilag International

PRAC Rapporteur: Gabriele Maurer

Scope: Quality variations

The changes result in amendments to the Annex A, SmPC, Labeling and Package Leaflet. An updated EU RMP (Version 11.1) is also included

15.3.17. Guselkumab – TREMFYA (CAP) - EMA/VR/0000257541

Applicant: Janssen Cilag International

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2, 4.5, 4.8, 5.1, and 5.2 of the SmPC in order to add subcutaneous induction dosing for the ulcerative colitis (UC) indication based on interim results from study CNTO1959UCO3004 listed as a category 3 study in the RMP; this is a phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicentre study to evaluate the efficacy and safety of guselkumab subcutaneous induction therapy in participants with moderately to severely active UC; the Package Leaflet is updated

accordingly. The RMP version 11.1 has also been submitted. In addition, the MAH took the opportunity to bring editorial changes to the PI

15.3.18. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) - EMA/X/0000243671

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Sonja Hrabcik

Scope: Extension application to introduce a new pharmaceutical form (suspension for injection in pre-filled syringe)

15.3.19. Lebrikizumab – EBGLYSS (CAP) - EMA/VR/0000249804

Applicant: Almirall S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of:

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

C.I.4: Update of section 5.1 of the SmPC in order to update information on clinical efficacy based on final results from study J2T-AP-KGBQ (Advantage); this is a randomised, double-blind, placebo-controlled phase 3 clinical trial to assess the efficacy and safety of lebrikizumab in combination with topical corticosteroids up to 52 weeks in patients with moderate to-severe atopic dermatitis who were not adequately controlled with ciclosporin or non-eligible for cyclosporine

15.3.20. Lenacapavir - SUNLENCA (CAP) - EMEA/H/C/005638/II/0022/G

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouping of two type II variations:
- Update of section 5.1 of the SmPC to include efficacy and resistance data based on week 156 interim data from Study GS-US-200-4625; a phase 2/3 study to evaluate the safety and efficacy of long-acting capsid inhibitor GS-6207 in combination with an optimised background regimen in heavily treatment experienced people living with HIV-1 infection with multidrug resistance (category 3 study in the RMP). Additionally, upon request by the CHMP following the assessment of II/0013, the MAH proposes to update section 4.8 of the SmPC to include information related to injection site nodules and induration that were non-resolved at the end of follow-up.
- Provision of the final study report of Study GS-US-200-4334: a phase 2 randomised, open label, active controlled study evaluating the safety and efficacy of long-acting capsid inhibitor GS-6207 in combination with other antiretroviral agents in people living with HIV

(category 3 study in the RMP).
An updated RMP version 2.1 was included as part of the application

15.3.21. Mavacamten – CAMZYOS (CAP) - EMA/VR/0000249369

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Submission of the final report from long-term follow-up study MYK-461-017/CV027006 listed as a category 3 study in the RMP. This is a phase 3, randomised, double-blind, placebo-controlled study to evaluate mavacamten in adults with symptomatic obstructive hypertrophic cardiomyopathy who are eligible for septal reduction therapy (VALOR-HCM). The RMP version 5.0 has also been submitted

15.3.22. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/II/0150

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to modify administration instructions to add the option for self-administration or administration by a caregiver and to update educational guidance, based on supportive data including final results from study 101MS330; this is a Single-Arm, Open-Label, Phase 3 Study to Evaluate the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Multiple Doses of Natalizumab Administered to Japanese Participants With Relapsing-Remitting Multiple Sclerosis via a Subcutaneous Route of Administration. The Annex II, Labelling and Package Leaflet are updated accordingly. The RMP version 32.1 has also been submitted

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

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

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

15.3.24. Pegcetacoplan - ASPAVELI (CAP) - EMEA/H/C/005553/II/0028, Orphan

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.8 of the SmPC in order to add urticaria/hives to the list of adverse drug reactions (ADRs) with frequency "common" and to add anaphylactic reaction and anaphylactic shock to the list of ADRs with frequency "uncommon", based on post-marketing data and literature; the Package Leaflet is updated accordingly. The RMP version 3.1 has also been submitted

15.3.25. Pyronaridine, artesunate - PYRAMAX (Art 58[39]) - 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

15.3.26. Olipudase alfa - XENPOZYME (CAP) - EMEA/H/C/004850/II/0012/G, Orphan

Applicant: Sanofi B.V.

PRAC Rapporteur: Martin Huber

Scope: A grouped application consisting of:
C.I.4: Update of sections 4.4 and 4.8 of the SmPC in order to update safety information based on final results from study DFI12712 ASCEND, listed as a category 3 study in the RMP; this is a Phase 2/3, multicentre, randomised, double-blinded, placebo-controlled, repeat-dose study to evaluate the efficacy, safety, pharmacodynamics and pharmacokinetics of olipudase alfa in patients with AMSD. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.4 and to implement editorial changes to the SmPC.
C.I.4: Update of sections 4.4 and 4.8 of the SmPC in order to update safety information based on final results from study LTS13632 listed as a category 3 study in the RMP; this is a long-term study the ongoing safety and efficacy of olipudase alfa in patients with ASMD. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted

15.3.27. rADAMTS13 – ADZYNMA (CAP) - EMA/VR/0000255553

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Maia Uusküla

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

15.3.28. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – MRESVIA (CAP) - EMA/VR/0000248175

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

[39] 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)

Scope: To modify the approved therapeutic indication to include active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by Respiratory Syncytial Virus (RSV) in individuals 18 through 59 years of age who are at increased risk for LRTD caused by RSV for mRESVIA, based on results from Study mRNA-1345-P303 (Part A) - A Phase 3 Study to Evaluate the Immunogenicity and Safety of mRNA-1345, an mRNA Vaccine Targeting Respiratory Syncytial Virus, in High-risk Adults. As a consequence, sections 4.1, 4.6, 4.8 and 5.1 of the SmPC and the corresponding sections of the Package Leaflet are updated accordingly. The updated RMP Version 1.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI. As part of the application, the MAH also requests an extension of the market protection by one additional year

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

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

15.3.30. Retifanlimab – ZYNYZ (CAP) - EMA/VR/0000247788

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include in combination with carboplatin and paclitaxel treatment of adult patients with metastatic or with inoperable locally recurrent squamous cell carcinoma of the anal canal (SCAC) for ZYNYZ, based on interim results from study INCMGA 0012-303 (POD1UM-303/InterAACT-2); this is a phase 3 global, multicentre, double-blind randomised study of carboplatin-paclitaxel with retifanlimab or placebo in participants with inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal not previously treated with systemic chemotherapy; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce editorial changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection

15.3.31. Solriamfetol - SUNOSI (CAP) - EMEA/H/C/004893/II/0026

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Julia Pallos

Scope: Update of sections 4.6 and 5.2 of the SmPC in order to update information on

lactation and breast-feeding based on results from the post-marketing lactation study JZP110-401 listed as a category 3 study in the RMP. This was a Phase 4, open-label, single-dose study to evaluate the PK of solriamfetol in the breast milk and plasma of healthy postpartum women following oral administration of a 150 mg solriamfetol tablet. The Package Leaflet is updated accordingly. The RMP version 1.3 has also been submitted

15.3.32. Spesolimab – SPEVIGO (CAP) - EMA/VR/0000249137

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Zoubida Amimour

Scope: Update of sections 4.4, and 4.8 of the SmPC in order to add a new warning on hypersensitivity and add hypersensitivity to the list of adverse drug reactions (ADRs) with frequency 'not known' based on data from clinical trials and post-marketing data sources; the Package Leaflet is updated accordingly. The RMP version 4.0 has also been submitted

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

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

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

15.3.34. Tislelizumab - TEVIMBRA (CAP) - EMEA/H/C/005919/II/0017

Applicant: Beigene Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include, in combination with gemcitabine and cisplatin, the first-line treatment of adult patients with recurrent or metastatic nasopharyngeal carcinoma (NPC) for TEVIMBRA based on final results from study BGB-A317-309 (study 309). Study 309 was a phase 3 randomised, double-blind, placebo-controlled, Asia-only study that compared the efficacy and safety of tislelizumab combined with gemcitabine plus cisplatin (GC) versus placebo combined with GC as first line treatment for recurrent or metastatic NPC. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.6 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce editorial and administrative changes to the PI as well as to update the PI in line with the Excipients Guideline

15.3.35. Tralokinumab – ADTRALZA (CAP) - EMA/VR/0000254976

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update clinical efficacy and safety information based on the final clinical trial report of the open-label extension PASS study LP0162-1337 (ECZTEND), listed as a category 3 study in the RMP. This is a phase 3 open-label, single-arm, multi-centre, long-term extension trial to evaluate the safety and efficacy of tralokinumab in subjects with moderate-to-severe atopic dermatitis who participated in previous tralokinumab clinical trials. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the PI according to the updated EU Excipient guideline to include a warning regarding polysorbate as well as to include minor editorial changes and to update the list of local representatives in the Package Leaflet

15.3.36. Ustekinumab - PYZCHIVA (CAP) - EMEA/H/C/006183/X/0006

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new strength (45 mg solution for injection in a vial) for partial use in paediatric patients.

15.3.37. Vedolizumab – ENTYVIO (CAP) - EMA/VR/0000255408

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

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

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

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

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

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

16.1.1. Alglucosidase alfa - MYOZYME (CAP) - PSUSA/00000086/202409

Applicant: Sanofi B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

16.1.2. Amikacin[40] - ARIKAYCE LIPOSOMAL (CAP) - PSUSA/00010882/202409

Applicant: Insmed Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.1.3. Atogepant - AQUIPTA (CAP) - PSUSA/00000100/202409

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

16.1.4. Aztreonam, avibactam - EMBLAVEO (CAP) - PSUSA/00011055/202410

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure

16.1.5. Brolucizumab - BEOVU (CAP) - PSUSA/00010829/202410

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.6. COVID-19 Vaccine (recombinant, adjuvanted) - BIMERVAX (CAP) - PSUSA/00011045/202409

Applicant: Hipra Human Health S.L.

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

[40] Centrally authorised product(s) only

16.1.7. COVID-19 vaccine (Ad26.COV2-S [recombinant]) - JCOVDEN (CAP)[41] - PSUSA/00010916/202402

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.1.8. Dacomitinib - VIZIMPRO (CAP) - PSUSA/00010757/202409

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.9. Daptomycin - CUBICIN (CAP) - PSUSA/00000931/202409

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Pernille Harg

Scope: Evaluation of a PSUSA procedure

16.1.10. Darunavir, cobicistat, emtricitabine, tenofovir alafenamide - SYMTUZA (CAP) - PSUSA/00010646/202409

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.1.11. Erdafitinib - BALVERSA (CAP) - PSUSA/00011072/202410

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.12. Etrasimod - VELSIPITY (CAP) - PSUSA/00000273/202410

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[41] European Commission decision for withdrawal of marketing authorisation for Jcovden (COVID-19 Vaccine Janssen (Ad26.COV2.S)) in the European Union (EU) is dated 26 July 2024. The withdrawal was at the request of the marketing authorisation holder, Janssen-Cilag International N.V., which notified the European Commission of its decision to permanently discontinue the marketing of the product for commercial reasons.

16.1.13. Futibatinib - LYTGOBI (CAP) - PSUSA/00000068/202409

Applicant: Taiho Pharma Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.14. Hepatitis A (inactivated), hepatitis B (rDNA[42]) vaccines (adsorbed) - AMBIRIX (CAP); TWINRIX ADULT (CAP); TWINRIX PAEDIATRIC (CAP) - PSUSA/00001593/202409

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.15. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - PSUSA/00010678/202410

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.16. Histamine[43] - CEPLENE (CAP) - PSUSA/00001610/202410

Applicant: Laboratoires Delbert

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.1.17. Lasmiditan - RAYVOW (CAP) - PSUSA/00011011/202410

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

16.1.18. Lopinavir, ritonavir - ALUVIA (Art 58[44]) - EMEA/H/W/000764/PSUV/0121

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Zoubida Amimour

[42] Ribosomal deoxyribonucleic acid
[43] Indicated for acute myeloid leukaemia
[44] 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)

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

16.1.19. Lopinavir, ritonavir - KALETRA (CAP) - PSUSA/00001905/202409

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.20. Macitentan, tadalafil - YUVANCI (CAP) - PSUSA/00011090/202410

Applicant: Janssen - Cilag International

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.21. Maralixibat - LIVMARLI (CAP) - PSUSA/00011032/202409

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.22. Mirikizumab - OMVOH (CAP) - PSUSA/00000049/202409

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.23. Nintedanib[45] - OFEV (CAP) - PSUSA/00010319/202410

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.24. Niraparib, abiraterone acetate - AKEEGA (CAP) - PSUSA/00011051/202410

Applicant: Janssen-Cilag International N.V.

[45] Respiratory indication only

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.25. Olipudase alfa - XENPOZYME (CAP) - PSUSA/00011003/202409

Applicant: Sanofi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.26. Oseltamivir - TAMIFLU (CAP) - PSUSA/00002225/202409

Applicant: Roche Registration GmbH

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.27. Pandemic influenza vaccine (H5N1)[46] - FOCLIVIA (CAP); zoonotic influenza vaccine (H5N1) AFLUNOV (CAP); zoonotic influenza vaccine (H5N8)[47] - ZOONOTIC INFLUENZA VACCINE SEQIRUS (CAP) - PSUSA/00010008/202410

Applicant: Seqirus S.r.l (Aflunov, Foclivia), Seqirus S.r.l. (Zoonotic Influenza Vaccine Seqirus)

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.28. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/202410

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.29. Pemigatinib - PEMAZYRE (CAP) - PSUSA/00010923/202410

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

[46] Surface antigen, inactivated, adjuvanted
[47] Surface antigen, inactivated, adjuvanted

16.1.30. Riociguat - ADEMPAS (CAP) - PSUSA/00010174/202409

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.31. Selumetinib - KOSELUGO (CAP) - PSUSA/00010936/202410

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.32. Talazoparib - TALZENNA (CAP) - PSUSA/00010781/202410

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.33. Tofersen - QALSODY (CAP) - PSUSA/00011064/202410

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

16.1.34. Trastuzumab - HERCEPTIN (CAP); HERWENDA (CAP); HERZUMA (CAP); KANJINTI (CAP); OGIVRI (CAP); ONTRUZANT (CAP); TRAZIMERA (CAP); TUZNUE (CAP); ZERCEPAC (CAP) - PSUSA/00003010/202409

Applicant: Roche Registration GmbH (Herceptin), Sandoz GmbH (Herwenda), Celltrion Healthcare Hungary Kft. (Herzuma), Amgen Europe B.V., BREDA (Kanjinti), Biosimilar Collaborations Ireland Limited (Ogivri), Samsung Bioepis NL B.V. (Ontruzant), Pfizer Europe MA EEIG (Trazimera), Prestige Biopharma Belgium (Tuznue), Accord Healthcare S.L.U. (Zercepac)

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.35. Vortioxetine - BRINTELLIX (CAP) - PSUSA/00010052/202409

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

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

16.2.1. Filgrastim - ACCOFIL (CAP); FILGRASTIM HEXAL (CAP); GRASTOFIL[48]; NIVESTIM (CAP); RATIOGRASTIM (CAP); TEVAGRASTIM (CAP); ZARZIO (CAP); NAP - PSUSA/00001391/202409

Applicant(s): Accord Healthcare S.L.U. (Accofil, Grastofil), Hexal AG (Filgrastim Hexal), Pfizer Europe MA EEIG (Nivestim), ratiopharm GmbH (Ratiograstim), TEVA GmbH (Tevagrastim), Sandoz GmbH (Zarzio), various

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

16.2.2. Rivaroxaban - XARELTO (CAP); NAP - PSUSA/00002653/202409

Applicant(s): Bayer AG (Xarelto), various

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.2.3. Sodium oxybate[49] - XYREM (CAP); NAP - PSUSA/00010612/202410

Applicant(s): UCB Pharma S.A. (Xyrem), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.2.4. Teriparatide - FORSTEO (CAP); KAULIV (CAP); LIVOGIVA (CAP); MOVYMIA (CAP); SONDELBAY (CAP); TERIPARATIDE SUN (CAP); TERROSA (CAP); NAP - PSUSA/00002903/202409

Applicant(s): Accord Healthcare S.L.U. (Sondelbay), Eli Lilly Nederland B.V. (Forsteo), Strides Pharma (Cyprus) Limited (Kauliv), Sun Pharmaceutical Industries Europe B.V. (Teriparatide SUN), Gedeon Richter Plc. (Terrosa), Theramex Ireland Limited (Livogiva), STADA Arzneimittel AG (Movymia), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

[48] European Commission (EC) decision on the marketing authorisation (MA) withdrawal for Grastofil, dated 13 January 2025
[49] For oral use only

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

16.3.1. Alfentanil (NAP) - PSUSA/00000082/202409

Applicant(s): various

PRAC Lead: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.3.2. Atenolol, chlortalidone (NAP) - PSUSA/00000260/202409

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure

16.3.3. Betamethasone, tetryzoline (NAP) - PSUSA/00010072/202409

Applicant(s): various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure

16.3.4. Carmustine[50] (NAP) - PSUSA/00010348/202409

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.3.5. Hexaminolevulinate hydrochloride (NAP) - PSUSA/00001606/202409

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.3.6. Opium (NAP) - PSUSA/00010670/202409

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.3.7. Phloroglucinol (NAP); phloroglucinol, trimethylphloroglucinol (NAP); phloroglucinol, simeticone (NAP) - PSUSA/00010355/202409

Applicant(s): various

[50] Implant

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

16.3.8. Pramiracetam (NAP) - PSUSA/00002492/202409

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

16.3.9. Sodium oxybate[51] (NAP) - PSUSA/00010613/202410

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.3.10. Trifarotene (NAP) - PSUSA/00010929/202410

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

16.3.11. Zidovudine (NAP) - PSUSA/00003143/202409

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

16.4. Follow-up to PSUR/PSUSA procedures

16.4.1. Ocrelizumab - OCREVUS (CAP) - EMA/PAM/0000255140

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: LEG to further clarify Febrile Neutropenia and agranulocytosis events following EMEA/H/C/PSUSA/00010662/202403: provision of a cumulative review of all cases from clinical trials, post-marketing and literature reporting the MedDRA PTs "Febrile neutropenia" and "Agranulocytosis" associated with ocrelizumab treatment. The MAH is welcome to include further PTs in its search, provided it is justified and reasonable. Possible pathophysiologic mechanisms and the need to revise the product information and/or the risk management plan should be discussed

[51] For intravenous use only

16.4.2. Ocrelizumab - OCREVUS (CAP) - EMA/PAM/0000255181

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: LEG to further clarify alopecia events following EMEA/H/C/PSUSA/00010662/202403: provision of information on alopecia events from the controlled treatment periods of its pivotal clinical studies OPERA I/II and ORATORIO and report incidence rates per 100 per year in the ocrelizumab versus comparator arms (i.e., interferon beta-1a and placebo) and presentation in a tabular format, cases reporting alopecia which fulfilled established diagnostic criteria, are not confounded by other risk factors for alopecia, are not concomitantly treated with other drugs known to cause alopecia, and time to onset. Narratives of these cases should be presented

16.5. Variation procedure(s) resulting from PSUSA evaluation

16.5.1. Human thrombin, human fibrinogen - TACHOSIL (CAP) - EMEA/H/C/000505/II/0131

Applicant: Corza Medical GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 4.2 of the SmPC to emphasise correct product handling and section 4.8 of the SmPC to reflect the fact that cases of product non-adhesion issues have been reported, upon request by PRAC following the outcome of the PSUR procedure EMEA/H/C/PSUSA/00010297/202306. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC.

16.5.2. Saxagliptin, metformin hydrochloride – EBYMECT (CAP); KOMBOGLYZE (CAP); XIGDUO (CAP) - EMA/VR/0000258017

Applicant: AstraZeneca AB

PRAC Rapporteur: Bianca Mulder

Scope: C.I.3.z: To update section 4.4 of the SmPC to implement the signal recommendations from PSUR outcome for the metformin PSUSA/00002001/202404. Section 2 of the Package Leaflet was updated accordingly

Action: For adoption of PRAC Assessment Report

16.5.3. Sitagliptin, metformin hydrochloride - EFFICIB (CAP); JANUMET (CAP); RISTFOR (CAP); VELMETIA (CAP) - EMA/VR/0000253633

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: C.I.3.z: To update section 4.4 of the SmPC to implement the signal recommendations from PSUR outcome for the metformin PSUSA/00002001/202404. Section 2 of the Package Leaflet was updated accordingly.

In addition, the Product Information was brought in line with the latest QRD template (version 10.4).

Minor editorial corrections have also been implemented.

The MAH also took the opportunity to update the contact details of the local representatives.

Action: For adoption of PRAC Assessment Report

16.5.4. Vildagliptin, metformin hydrochloride- EUCREAS (CAP); ICANDRA (CAP); ZOMARIST (CAP) - EMA/VR/0000261605

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: To update section 4.4 (Special warnings and precautions for use) of the SmPC and section 2 (Warnings and precautions) of the Package Leaflet of Eucreas, Icandra and Zomarist with MELAS syndrome (Mitochondrial Encephalopathy, myopathy, Lactic acidosis and Stroke-like episodes) or Maternal inherited diabetes and deafness (MIDD) following PRAC recommendation regarding signal assessment of MELAS Syndrome/MIDD.

The MAH took the opportunity to correct the EU numbers in section 8 of the SmPC for the Icandra and Zomarist Croatian (HR) annexes

16.6. Expedited summary safety reviews[52]

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)[53]

17.1.1. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMA/PASS/0000256848

Applicant: Janssen Cilag International; ATMP

PRAC Rapporteur: Jo Robays

Scope: PASS 107o [PASS protocol amendment]: Substantial amendment to a PASS Study 68284528MMY4009: A Post-authorization Safety Study to Evaluate the Safety of Multiple Myeloma Patients Treated with Ciltacabtagene Autoleucel

17.1.2. Topiramate - EMEA/H/N/PSP/J/0106.2

Applicant: Janssen (on behalf of a consortium)

[52] 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

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

PRAC Rapporteur: Karin Bolin

Scope: MAH's response to PSP/0106.1 [DUS to evaluate the effectiveness of the implemented risk minimisation measures, particularly focusing on preventing pregnancies and further characterising the prescribing patterns for topiramate in the target populations for pregnancy prevention] as per the request for supplementary information (RSI) adopted in January 2025.

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[54]

17.2.1. Bimekizumab - BIMZELX (CAP) - EMA/PAM/0000249072

Applicant: UCB Pharma

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of a PASS protocol version 2 amendment #4 for the Cohort Study PS0037 to Evaluate Foetal and Infant Outcomes following Maternal Exposure to bimekizumab during Pregnancy

17.2.2. Deucravacitinib - SOTYKTU (CAP) - EMA/PAM/0000263305

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Protocol for PASS IM011194: Long-term, observational cohort study of adults with plaque psoriasis, who are new users of deucravacitinib, non-TNFi (tumour necrosis factor inhibitor) biologics, TNFi biologics, or non-biologic systemic therapy in the real-world clinical setting to evaluate the long-term safety of deucravacitinib

17.2.3. Marstacimab - HYMPAVZI (CAP) - EMA/PAM/0000255006

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

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

17.2.4. Risankizumab- SKYRIZI (CAP) - EMA/PAM/0000254975

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: PASS study protocol P23-653: Pregnancy Exposures and Outcomes in Women with Inflammatory Bowel Disease Treated with Risankizumab.

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

17.2.5. Risankizumab - SKYRIZI (CAP) - EMA/PAM/0000254982

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: Protocol amendment PASS study P23-654: Comparative Cohort Study of Long-term Safety Outcomes of Risankizumab Compared to Biologic Treatments for Ulcerative Colitis and Crohn's Disease in a Real-world Setting in Sweden and Denmark

17.2.6. Selexipag - UPTRAVI (CAP) - EMA/PAM/0000256686

Applicant: Janssen Cilag International

PRAC Rapporteur: Zoubida Amimour

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

17.2.7. Spesolimab - SPEVIGO (CAP) - EMA/PAM/0000254921

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Zoubida Amimour

Scope: Response to MEA 003.2 RSI adopted in January 2025 - amended protocol of PASS 1368-0128 (Non-imposed/Non-interventional). A 5-year active surveillance, post-authorisation safety study to characterise the safety of spesolimab for flare treatment in patients with GPP

17.3. Results of PASS imposed in the marketing authorisation(s)[55]

None

17.4. Results of PASS non-imposed in the marketing authorisation(s)[56]

17.4.1. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0090

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.2 of the SmPC in order to update information on posology based on the non-interventional study CICL670A2429 listed as a category 3 study in the RMP. This is a survey to assess physicians' knowledge of Exjade posology and biological monitoring recommendations as described in the Educational Materials (EMs).

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

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

Applicant: Sandoz GmbH

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

17.4.3. Human C1-esterase inhibitor - CINRYZE (CAP) - EMEA/H/C/001207/II/0104

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.6, 5.1 and 5.3 of the SmPC based on final results from the Icatibant Outcome Survey (IOS), listed as an imposed PASS in the Annex II. This is a prospective, observational disease registry. The Package Leaflet is updated accordingly. The RMP version 11.1 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 product information in line with the latest QRD template version 10.4 and to update Annex II of the PI

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

17.5.1. Avapritinib – AYVAKYT (CAP) - EMA/PAM/0000256424

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Submission of interim results from Study BLU-285-1406 [SOB 3]: In order to further confirm the safety and efficacy of avapritinib in the treatment of adult patients with unresectable or metastatic GIST harbouring the PDGFRA D842V mutation, the MAH should submit the results of an observational safety and efficacy study in patients with unresectable or metastatic PDGFRA D842V-mutant GIST

17.5.2. COVID-19 mRNA vaccine – SPIKEVAX (CAP) - EMA/PAM/0000248944

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Sixth Interim Update for study P910 – Natural history and clinical outcomes of vaccine associated myocarditis (EU) – Category 3 study – included in the Risk Management Plan for Spikevax and as per the request from procedure MEA065.5

17.5.3. Guselkumab – TREMFYA (CAP) - EMA/PAM/0000256444

Applicant: Janssen Cilag International

PRAC Rapporteur: Gabriele Maurer

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

17.5.4. Venetoclax – VENCLYXTO (CAP) - EMA/PAM/0000255427

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

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

17.6. Others

17.6.1. Abatacept – ORENCIA (CAP) - EMA/PAM/0000256412

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual update of the Observational Registry of Abatacept in Patients with Juvenile Idiopathic Arthritis (Study IM101240)

17.6.2. Diroximel fumarate – VUMERITY (CAP) - EMA/PAM/0000256697

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of annual progress report number 2 for Study 272MS401: A prospective observational pregnancy exposure registry to characterise how DRF may affect pregnancy and infant outcomes

17.7. New Scientific Advice

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

17.8. 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 letters)

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

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

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

18.1. Annual reassessments of the marketing authorisation

18.1.1. Afamelanotide – SCENESSE (CAP) - EMA/S/0000245110

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

18.1.2. Glucarpidase – VORAXAZE (CAP) - EMA/S/0000245171

Applicant: Serb

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

18.1.3. Pegzilarginase – LOARGYS (CAP) - EMA/S/0000247405

Applicant: Immedica Pharma AB

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

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

Applicant: Pierre Fabre Medicament; ATMP

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

18.1.5. Tagraxofusp – ELZONRIS (CAP) - EMA/S/0000244851

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Annual reassessment of the marketing authorisation

18.1.6. Tecovirimat – TECOVIRIMAT SIGA (CAP) - EMA/S/0000248804

Applicant: Siga Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Avapritinib – AYVAKYT (CAP) - EMA/R/0000257352

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.2. Elafibranor – IQIRVO (CAP) - EMA/R/0000257350

Applicant: Ipsen Pharma

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

18.2.3. Epcoritamab – TEPKINLY (CAP) - EMA/R/0000257200

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Conditional renewal of the marketing authorisation

18.2.4. Larotrectinib – VITRAKVI (CAP) - EMA/R/0000257511

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

18.2.5. Odronextamab – ORDSPONO (CAP) - EMA/R/0000254850

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Jana Lukacisinova

Scope: Conditional renewal of the marketing authorisation

18.2.6. Tafasitamab – MINJUVI (CAP) - EMA/R/0000256675

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.2.7. Valoctocogene roxaparvovec – ROCTAVIAN (CAP) - EMA/R/0000250212

Applicant: Biomarin International Limited; ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Acalabrutinib – CALQUENCE (CAP) - EMA/R/0000247050

Applicant: AstraZeneca AB

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: 5-year renewal of the marketing authorisation

18.3.2. Arsenic trioxide - ARSENIC TRIOXIDE MEDAC (CAP) - EMEA/H/C/005218/R/0006 (without RMP)

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.3. Bupivacaine – EXPAREL LIPOSOMAL (CAP) - EMA/R/0000248989

Applicant: Pacira Ireland Limited

PRAC Rapporteur: Eamon O'Murchu

Scope: 5-year renewal of the marketing authorisation

18.3.4. Inclisiran – LEQVIO (CAP) - EMA/R/0000247528

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: 5-year renewal of the marketing authorisation

18.3.5. Lumacaftor, ivacaftor – ORKAMBI (CAP) - EMA/R/0000249341

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Eamon O'Murchu

Scope: 5-year renewal of the marketing authorisation

18.3.6. Lumasiran – OXLUMO (CAP) - EMA/R/0000245133

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.7. Pegfilgrastim – NYVEPRIA (CAP) - EMA/R/0000249250

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

18.3.8. Quadrivalent influenza vaccine (recombinant, prepared in cell culture) – SUPEMTEK TETRA (CAP) - EMA/R/0000249010

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Zoubida Amimour

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 05-08 May 2025 PRAC meeting, which was held remotely. Participants marked with "a" attended the plenary session while those marked with "b" attended the ORGAM.

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	
Sonja Hrabcik [a]	Alternate	Austria	No interests declared	
Jean-Michel Dogné [a]	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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Barbara Kovacic Bytyqi [a]	Alternate	Croatia	No interests declared	
Elena Kaisis [a,b]	Member	Cyprus	No interests declared	
Panagiotis Psaras [a]	Alternate	Cyprus	No interests declared	
Eva Jirsová [a]	Member	Czechia	No interests declared	
Jana Lukacisinova [a,b]	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 deliberations and voting on:	15.3.21. Mavacamten – CAMZYOS (CAP) - EMA/VR/0000249369 17.2.2. Deucravacitinib - SOTYKTU (CAP) - EMA/PAM/0000263305 17.6.1. Abatacept – ORENCIA (CAP) - EMA/PAM/0000256412
Martin Huber [a,b]	Member	Germany	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Gabriele Maurer [a,b]	Alternate	Germany	No interests declared	
Georgia Gkegka [a]	Member	Greece	No interests declared	
Maria Poulianiti [a]	Alternate	Greece	No participation in discussion, final deliberations and voting on:	3.3.1. Dutasteride (NAP); dutasteride , tamsulosin (NAP); finasteride (NAP); finasteride, tadalafil (NAP); finasteride, tamsulosin (NAP) – EMEA/H/A-31/1539 14.1.1. Dabigatran – PRADAXA (CAP); NAP
Julia Pallos [a]	Member	Hungary	No participation in discussion, final deliberations and voting on:	15.3.21. Mavacamten – CAMZYOS (CAP) - EMA/VR/0000249369 17.2.2. Deucravacitinib - SOTYKTU (CAP) - EMA/PAM/0000263305 17.6.1. Abatacept – ORENCIA (CAP) - EMA/PAM/0000256412
Melinda Palfi [a]	Alternate	Hungary	No interests declared	
Guðrún Stefánsdóttir	Member	Iceland	No restrictions applicable to this meeting	
Guðrún Þengilsdóttir [a]	Alternate	Iceland	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
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 restrictions applicable to this meeting	
Emilio Clementi [a]	Alternate	Italy	No restrictions applicable to this meeting	
Zane Neikena [a,b]	Member	Latvia	No interests declared	
Diana Litenboka [a,b]	Alternate	Latvia	No interests declared	
Rugile Pilviniene [a]	Member	Lithuania	No restrictions applicable to this meeting	
Lina Seibokiene [a,b]	Alternate	Lithuania	No interests declared	
Magdalena Wielowieyska [a,b]	Alternate	Luxembourg	No participation in discussion, final deliberations and voting on:	15.3.27. rADAMTS13 – ADZYNMA (CAP) - EMA/VR/00002 55553 15.3.38. Vedolizumab – ENTYVIO (CAP) - EMA/VR/00002 55408 16.1.28. Parathyroid hormone - NATPAR (CAP) - PSUSA/000105 91/202410 17.4.3. Human C1-esterase inhibitor - CINRYZE (CAP) -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				EMEA/H/C/001207/II/0104
John Joseph Borg [a]	Member	Malta	No interests declared	
Liana Martirosyan [a,b]	Member (Vice-Chair)	Netherlands	No interests declared	
Bianca Mulder [a,b]	Alternate	Netherlands		
David Olsen [a,b]	Member	Norway	No participation in discussion, final deliberations and voting on:	15.3.9. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0024 16.1.30. Riociguat - ADEMPAS (CAP) - PSUSA/00010174/202409 16.2.2. Rivaroxaban - XARELTO (CAP); NAP - PSUSA/00002653/202409 18.2.4. Larotrectinib – VITRAKVI (CAP) - EMA/R/0000257511
Pernille Harg [a,b]	Alternate	Norway	No interests declared	
Adam Przybylkowski [a]	Member	Poland	No interests declared	
Katarzyna Ziolkowska [a,b]	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins [a,b]	Member	Portugal	No interests declared	
Carla Torre [a]	Alternate	Portugal	No restrictions applicable to this meeting	
Irina Sandu [a,b]	Alternate	Romania	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Anna Mareková [a,b]	Member	Slovakia	No interests declared	
Miroslava Gocova [a]	Alternate	Slovakia	No interests declared	
Polona Golmajer [a,b]	Member	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,b]	Alternate	Sweden	No interests declared	
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]	Membe	Independent scientific expert	No restrictions applicable to this meeting	
Hedvig Marie Egeland Nordeng [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Behija Hudina [a]	Expert	Croatia	No restrictions applicable to this meeting	
Gabriela Burianová [a]	Expert	Czech Republic	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Veronika Descikova [a]	Expert	Czech Republic	No interests declared	
Jana Kopecka [a]	Expert	Czech Republic	No interests declared	
Nicklas Hasselblad Lundstrøm [a]	Expert	Denmark	No interests declared	
Moritz Sander [a]	Expert	Denmark	No restrictions applicable to this meeting	
Wilma Fischer-Barth [a]	Expert	Germany	No interests declared	
Dennis Lex [a,b]	Expert	Germany	No interests declared	
Susanne Liebig [a]	Expert	Germany	No restrictions applicable to this meeting	
Dario Ortiz [a]	Expert	Germany	No interests declared	
Nina Pannwitz [a]	Expert	Germany	No interests declared	
Karin Seifert [a]	Expert	Germany	No interests declared	
Roberto Frontini [a]	Expert	Italy	No interests declared	
Salvatore Antonio Giuseppe Messana [a]	Expert	Italy	No interests declared	
Maxime Cuijpers [a]	Expert	Netherlands	No restrictions applicable to this meeting	
Paul ten Berg [a]	Expert	Netherlands	No interests declared	
Anja van Haren [a]	Expert	Netherlands	No interests declared	
Michal Rataj [a]	Expert	Poland	No interests declared	
Charlotte Backman [a,b]	Expert	Sweden	No interests declared	
Sahra Barzi [a]	Expert	Sweden	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Elin Blom [a]	Expert	Sweden	No interests declared	
Jolanta Gulbinovic [a]	Expert	Sweden	No interests declared	
Per Lindemo [a]	Expert	Sweden	No interests declared	
Malin Ohlund [a]	Expert	Sweden	No restrictions applicable to this meeting	
Anna Schölin [a]	Expert	Sweden	No interests declared	
Audrey Chigome [a]	Expert	NRA	No restrictions applicable to this meeting	
Libert Chirinda [a]	Expert	NRA	No interests declared	
Phuong Dong [a]	Expert	NRA	No restrictions applicable to this meeting	
Margaret Malatji [a]	Expert	NRA	No interests declared	
Adrien Inoubli [a]	Expert	WHO	No interests declared	
Eunmi Kim [a]	Expert	WHO	No interests declared	
Nyasha Maregere [a]	Expert	WHO	No interests declared	
A representative from the European Commission attended the meeting.				
Observers from Health Canada, FDA, 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