04 May 2026
EMA/PRAC/91330/2026
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 09-12 March 2026

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

The Chairperson opened the 09-12 March 2026 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 members of the EEA-EFTA states agreed with the recommendation of the PRAC, unless otherwise specified.

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

1.2. Agenda of the meeting on 09-12 March 2026

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 09-12 February 2026

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 09-12 February 2026 were published on the EMA website on 07 April 2026 (EMA/PRAC/59896/2026).

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing Procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

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

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

4.1.1. Gemcitabine (NAP)

Applicant(s): various

PRAC Rapporteur: Mari Thorn

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

EPITT 20256 – New signal

Lead Member State(s): SE

Background

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

Gemcitabine is a pyrimidine antimetabolite with a cytotoxic effect that is indicated in the treatment of non-small cell lung cancer, pancreatic cancer, urothelial cancer (bladder, renal pelvis, ureter, and urethra), breast cancer, ovarian cancer, cervical cancer, and biliary tract cancer, subject to certain conditions.

During routine signal detection activities, a signal of DRESS was identified by MPA (Swedish Medical Products Agency), based on 11 cases retrieved from EudraVigilance and 2 cases detected from literature. Sweden confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

PRAC appointed Mari Thörn as Rapporteur for the signal.

Having considered the available evidence from the Eudravigilance and literature, PRAC agreed that there is sufficient evidence to establish a causal association between gemcitabine and DRESS and proposed to update the product information to include DRESS as a warning and as an undesirable effect.

Summary of recommendation(s)

- The MAHs of gemcitabine containing products (CHEPLAPHARM ARZNEIMITTEL GMBH and SUN PHARMACEUTICAL INDUSTRIES EUROPE B.V.) should submit to EMA, by 8 May 2026, their comments on the proposed updates of the product information.
- A 30-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.2. Levonorgestrel intrauterine device 13.5 mg (NAP)

Applicant(s): various

PRAC Rapporteur: Dennis Lex

Scope: Signal of increased risk of ectopic pregnancy

EPITT 20251 – New signal

Background

The signal concerns levonorgestrel, which is a second-generation progestin (synthetic progesterone), when formulated in an intrauterine device (IUD) – Jaydess- for contraception and treatment of menorrhagia.

Following the results of a pharmacoepidemiological study performed by the GIS EPIPHARE on the French National Healthcare Data System (SNDS – Système National des Données de Santé), a signal of increased risk of ectopic pregnancy was identified by France. Germany confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

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

PRAC appointed Dennis Lex as Rapporteur for the signal.

Summary of recommendation(s)

- The MAH should critically appraise the study by *Roland et al.* [3] with regards to the risk of ectopic pregnancies in the light of the existing body of pharmacoepidemiologic data. This should include (but not be limited to) the two recent EU studies, namely *Meaidi et al. 2023*[4], *Kopp-Kallner et al. 2022*[5] and category 1 PASS (EURAS-LCS12) interim results.
- Based on the high proportion of nulliparous users of the low-dose hormonal IUD identified in several studies (especially *Roland et al.*[6] and ongoing PASS), the MAH is requested to discuss the current clinical evidence for administration in nulliparous and parous women and (re)evaluate the warning statement in SmPC section 4.4 "Use in nulliparous women: Jaydess is not first choice for contraception in nulliparous women as clinical experience is limited".
- The MAH should provide a postulated mechanism of action by which the use of the levonorgestrel IUD 13.5 mg leads to a higher risk of ectopic pregnancies.
- Based on the critical appraisal of the results discussed above in terms of a higher risk of ectopic pregnancies, the potential impact of ectopic pregnancy on future fertility for both nulliparous and parous women, and clinical experience in nulliparous and parous women, the MAH should discuss the need for any potential amendments and make accordingly a proposal for changes to the product information (SmPC/PL), educational material and/or the risk management plan, including the need for any further risk minimisation measures and communication aspects.
- A 60-day timetable was recommended for the assessment of the above List of Questions leading to a further PRAC recommendation.

4.2. Signals follow-up and prioritisation

4.2.1. Galantamine (NAP)

Applicant(s): various

PRAC Rapporteur: Karin Bolin

Scope: Signal of nightmares

EPITT 20196 – Follow-up to September 2025

Background

For background information, see PRAC minutes September 2025.

The MAH JANSSEN-CILAG replied to the request for information on the signal of nightmares and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance, literature, national reviews, including the cumulative review submitted by the innovator Marketing Authorisation Holder (MAH), JANSSEN-CILAG, PRAC agreed that there is sufficient evidence to establish a causal

[3] Roland, N. *et al.* Intrauterine Devices and Risk of Ectopic Pregnancy. *NEJM Evid.* 4, EVIDoa2500117 (2025).
[4] Meaidi, A., Torp-Pedersen, C., Lidegaard, Ø. & Mørch, L. S. Ectopic Pregnancy Risk in Users of Levonorgestrel-Releasing Intrauterine Systems With 52, 19.5, and 13.5 mg of Hormone. *JAMA* 329, 935– 937 (2023).
[5] Kopp-Kallner, H. *et al.* Method of Hormonal Contraception and Protective Effects Against Ectopic Pregnancy. *Obstet. Gynecol.* 139, 764 (2022).
[6] Roland, N. *et al.* Intrauterine Devices and Risk of Ectopic Pregnancy. *NEJM Evid.* 4, EVIDoa2500117 (2025).

association between developing of nightmares and galantamine administration. Therefore, the product information should be updated to add nightmares as an undesirable effect with a frequency 'uncommon'.

Summary of recommendation(s)

- The MAHs for galantamine should submit to the national competent authorities, within 60 days, a variation to update the product information[7].

4.2.2. Chikungunya vaccine (live) - IXCHIQ (CAP) - EMEA/H/C/000829/SDA/013

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Signal of new aspect of the known risk of aseptic meningitis

EPITT 20250 – Follow up to February 2026

Background

For background information, see PRAC minutes February 2026.

The MAH replied to the request for information on the signal of new aspect of the known risk of aseptic meningitis and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance including the data submitted by the MAH, PRAC agreed to include in the product information that serious adverse reactions have been reported with the use of IXCHIQ also in young adults with no relevant comorbidities, including aseptic meningitis.

Summary of recommendation(s)

- The MAH for Ixchiq (Chikungunya vaccine (live)) should submit to EMA, within 1 month, a variation to update the product information[8]. In addition, the MAH should submit an updated RMP at the next regulatory opportunity to reflect the changes to the product information agreed within this procedure. PRAC noted that in the parallel PSUSA procedure (PSUSA/00011058/202511), a more comprehensive dataset and a granular analysis of benefit-risk balance in different scenarios will be discussed and that the need for any further product information amendments beyond those endorsed as part of the signal procedure will be further considered during the assessment of the PSUSA.

4.3. Variation procedure(s) resulting from signal evaluation

None

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

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

5.1.1. Allogeneic faecal microbiota, pooled - (CAP MAA) - EMEA/H/C/006678, Orphan

Scope (pre D-180 phase): Treatment of adult patients with acute-graft-versus-host disease (aGvHD)

5.1.2. Autologous melanoma-derived tumor infiltrating lymphocytes, ex vivo-expanded - (CAP MAA) - EMEA/H/C/006563

ATMP

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

5.1.3. Camizestrant - (CAP MAA) - EMEA/H/C/006494

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

5.1.4. *Clostridium botulinum*, serotype E, neurotoxin (150 kDa) - (CAP MAA) - EMEA/H/C/006420

Scope (pre D-180 phase): Temporary improvement in the appearance of moderate to severe lines between the eyebrows

5.1.5. Linerixibat - (CAP MAA) - EMEA/H/C/006241, Orphan

Scope (pre D-180 phase): Treatment of cholestatic pruritus in adult patients with primary biliary cholangitis

5.1.6. Zopapogene imadenovec - (CAP MAA) - EMEA/H/C/006508, Orphan

ATMP

Scope (pre D-120 phase): Treatment of respiratory papillomatosis in adults

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

See Annex I 15.2.

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

See Annex I 15.3.

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. Ciltacabtagene autoleucel – CARVYKTI (CAP) – EMA/PSUR/0000311150

Applicant: Janssen Cilag International

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00011000/202508)

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Carvykti (ciltacabtagene autoleucel) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include infusion related reaction as an undesirable effect with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[9].
- In the next PSUR, the MAH should perform a detailed evaluation of the non-immune effector cell-associated neurotoxicity syndrome (ICANS) toxicities and the increase in reports. In addition, for new cases of T cell malignancies reported following ciltacabtagene autoleucel administration, the MAH should describe the action taken and the status of follow up of the vector presence in T-cell lymphoma (TCL), and integration site, if applicable.

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 early and the list of Union reference dates (EURD list) will be updated accordingly.

[9] 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

6.1.2. Dengue tetravalent vaccine (live, attenuated) – QDENGA (CAP) – EMA/PSUR/0000311184

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011034/202508)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Qdenga, a centrally authorised medicine containing dengue tetravalent vaccine (live, attenuated) 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 Qdenga (dengue tetravalent vaccine (live, attenuated)) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing warning regarding anaphylaxis to include the time to onset. Therefore, the current terms of the marketing authorisation(s) should be varied[10].

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. Dengue tetravalent vaccine (live, attenuated) – DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (Art 58) – EMA/PSUR/0000308360

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUV dengue tetravalent vaccine)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Dengue Tetravalent Vaccine (Live, Attenuated) Takeda, a centrally authorised medicine containing dengue tetravalent vaccine (live, attenuated) 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 Dengue Tetravalent Vaccine (Live, Attenuated) Takeda (dengue tetravalent vaccine (live, attenuated)) in the approved indication(s) remains unchanged.

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

- Nevertheless, the product information should be updated to amend the existing warning regarding anaphylaxis to include the time to onset. Therefore, the current terms of the marketing authorisation(s) should be varied[11].

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. Difelikefalin – KAPRUVIA (CAP) – EMA/PSUR/0000311151

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010995/202508)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Kapruvia, a centrally authorised medicine containing difelikefalin 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 Kapruvia (difelikefalin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include a warning regarding mental status changes (including confusional state). Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAH should provide a more in-depth cumulative review and analysis of all new cases of deteriorating mental state in elderly patients, including data from post-marketing setting, clinical trials and literature, along with a causality assessment and a discussion on whether an update of the product information is warranted.

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

6.1.5. Efanesoctocog alfa – ALTUVOCT (CAP) – EMA/PSUR/0000311177

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00011062/202508)

[11] 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
[12] 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

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Altuvoct (efanesoctocog alfa) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include Factor VIII inhibition as an undesirable effect with a frequency 'uncommon' in case of patients previously treated with other Factor VIII products and 'very common' in case of patients previously untreated with other Factor VIII products. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- In the next PSUR, the MAH should provide an updated cumulative analysis, including a review of the literature on infusion-related reactions (IRR), with a particular focus on IRRs potentially associated with administration methods 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. The frequency of submission of the subsequent PSURs should be changed from 6-monthly to yearly and the list of Union reference dates (EURD list) will be updated accordingly.

6.1.6. Epinephrine – EURNEFFY (CAP) – EMA/PSUR/0000311165

Applicant: Alk-Abello A/S

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011081/202508)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Eurneffy, a centrally authorised medicine containing epinephrine 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 Eurneffy (epinephrine) 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 present a review of the risk for QTc prolongation and Torsade de Pointes (TdP) in patients with congenital long QT syndrome (LQTS) or catecholaminergic polymorphic ventricular tachycardia (CPVT) following treatment with Eurneffy and propose product information updates as warranted.

[13] Update of SmPC section 4.8. 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.

6.1.7. Perampanel – FYCOMPA (CAP) – EMA/PSUR/0000311160

Applicant: Eisai GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure (PSUSA/00009255/202507)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Fycompa, a centrally authorised medicine containing perampanel 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 Fycompa (perampanel) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing wording on perampanel overdose and to add vomiting as an adverse reaction observed in the context of overdose administration. The Package leaflet should be updated accordingly. Therefore, the current terms of the marketing authorisation(s) should be varied[14].
- In the next PSUR, the MAH should continue to closely monitor cases of death, as well as paediatric cases involving off-label use or non-approved age ranges as per the approved indications. Furthermore, the MAH should provide a cumulative review of cases of bradycardia, as well as related preferred terms (PTs) from all sources, including a discussion about the possible mechanism of action and a separate analysis/discussion for cases in a context of overdose, and should discuss if further update to the product information is needed. Finally, the MAH should provide a cumulative review of toxic epidermal necrolysis (TEN) 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.

6.1.8. Teclistamab – TECVAYLI (CAP) – EMA/PSUR/0000311141

Applicant: Janssen Cilag International

PRAC Rapporteur: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00011010/202508)

[14] Update of SmPC section 4.9. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tecvayli, a centrally authorised medicine containing teclistamab 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 Tecvayli (teclistamab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include tumour flare as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[15].
- In the next PSUR, the MAH should continue to monitor cases with reintroduction of teclistamab after Grade 3 immune effector cell-associated neurotoxicity syndrome (ICANS) event and cases of hemophagocytic lymphohistiocytosis (HLH)/immune effector cell-associated HLH-like syndrome (IEC-HS). In addition, the MAH should provide a cumulative review of cases of uveitis, including data from non-clinical, clinical and post-marketing setting in order to establish/refute a possible causal association with teclistamab. Furthermore, The MAH should closely monitor cases suggestive of tumour flare in order to further identify possible specific risk factors, which would help in prompt recognition of this condition in patients treated with teclistamab.

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. Upadacitinib – RINVOQ (CAP) – EMA/PSUR/0000311064

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00010823/202508)

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Rinvoq, a centrally authorised medicine containing upadacitinib 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 Rinvoq (upadacitinib) in the approved indication(s) remains unchanged.

[15] 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

- Nevertheless, the product information should be updated to include semen discolouration as an undesirable effect with a frequency 'rare'. Therefore, the current terms of the marketing authorisation(s) should be varied[16].
- In the next PSUR, the MAH should provide a cumulative review of cases of amenorrheoea and related menstrual disorders, of rosacea and of dyspnoea, including clinical and non-clinical, literature and post-marketing data, along with a causality assessment and discuss whether an update of the product information is warranted. Furthermore, the MAH should further discuss and elucidate the mechanism of the event of semen discolouration considering that the coating of the tablets contains iron oxides (E172), which is frequently used as food colorant.

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

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

See Annex I 16.2.

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

See also Annex I 16.3.

6.3.1. Anastrozole – EMA/PSUR/0000311116

Applicants: various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure (PSUSA/00000210/202508)

Background

Anastrozole is a selective non-steroidal aromatase inhibitor indicated for the treatment of hormone receptor-positive advanced breast cancer in postmenopausal women, adjuvant treatment of hormone receptor-positive early invasive breast cancer in postmenopausal women, adjuvant treatment of hormone receptor-positive early invasive breast cancer in postmenopausal women who have received 2 to 3 years of adjuvant tamoxifen. Subject to certain conditions, anastrozole is also indicated for primary prevention of breast cancer in postmenopausal women at moderate or high risk.

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

Summary of recommendation(s) and conclusions

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of anastrozole-containing medicinal products 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.

6.3.2. Buclizine / codeine / paracetamol, acetylsalicylic acid / codeine / paracetamol, caffeine / codeine / paracetamol – EMA/PSUR/0000311120

Applicants: various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00000448/202508)

Background

Fixed dose combinations (FDCs) of caffeine/codeine/paracetamol are broadly indicated in adults and adolescents aged 12 years and older for the short-term treatment of acute mild, moderate or severe pain which is not relieved by paracetamol, ibuprofen or aspirin alone, subject to certain conditions.

FDCs of buclizine/codeine/paracetamol are indicated for the short-term relief of acute moderate pain, which is not relieved by paracetamol, ibuprofen, or aspirin alone, such as migraine attacks including the symptoms of migraine headache, nausea and vomiting, and for prophylactic and symptomatic treatment of migraine.

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

No data received for the FDC of acetylsalicylic acid/codeine/paracetamol, therefore PRAC did not adopt any recommendation for this combination. The concerned National Competent Authorities of acetylsalicylic acid/codeine/paracetamol may consider the need to follow up at national level as appropriate.

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of buclizine/codeine/paracetamol- or caffeine/codeine/paracetamol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add or amend information about opioid use disorder (OUD) and add a warning about hyperalgesia and central sleep apnoea (CSA). In addition, the PI should be updated to add the drug-drug interaction with gabapentinoids, as well as pancreatitis and sphincter of Oddi dysfunction as warning and undesirable effects with a frequency ‘not known’. Finally, the PL should be updated to highlight the need to store the product in a safe and secure place and to add a black box warning about the nature of the opioid-containing product

and the risk of dependence and addiction (all products). Therefore, the current terms of the marketing authorisation(s) should be varied[17].

- In the next PSUR, the MAH(s) should use the following minimum list of PSUR safety concerns: hepatotoxicity (relevant to codeine/paracetamol +/- other agents) and OUD (abuse, misuse, dependence, addiction, tolerance, withdrawal) as important identified risks.

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

6.3.3. Cetalkonium / choline salicylate – EMA/PSUR/0000311121

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00000626/202508)

Background

Choline salicylate is a topical non-steroidal anti-inflammatory drug (NSAID) that has anti-inflammatory, pyretic and analgesic properties. Cetalkonium chloride has an antibacterial and antifungal activity. The combination cetalkonium/choline salicylate is used for rapid relief of pain, inflammation, and discomfort associated with mouth ulcers, denture irritation, sore spots from orthodontic devices, and cold sores.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing cetalkonium/choline salicylate 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 cetalkonium/choline salicylate-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add to add a warning on the risk of using aspirin or other products containing salicylates, a warning regarding use in patients currently suffering from or with a history of peptic ulceration, and to add information regarding the use in pregnancy. Therefore, the current terms of the marketing authorisation(s) should be varied[18].
- In the next PSUR, the MAH(s) should propose similar safety concerns based on the list proposed by the MAH Reckitt with some adjustments if necessary: immune system / hypersensitivity reactions, use in the third trimester of pregnancy or during breast-feeding, and Reye's syndrome as important identified risks; concomitant use of acetylsalicylic acid or other salicylates, use beyond the recommended maximum duration may delay treatment of more serious underlying conditions, off-label use in

[17] Update of SmPC sections 4.2, 4.4, 4.5 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.
[18] Update of SmPC sections 4.4 and 4.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.

children under 4 months of age, and use during the first and second trimesters of pregnancy as important potential risks; none as missing information. The MAH(s) should also closely monitor any case or new information regarding bronchospasm and asthma. The MAH Lavipharm should closely monitor any case or any new information associated to a drug-drug interaction with uricosurics. The MAH Pierre Fabre should closely monitor any case or any new information associated to a drug-drug interaction with uricosurics.

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

6.3.4. Epinephrine (except for nasal use) – EMA/PSUR/0000311134

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00001232/202507)

Background

Epinephrine (except for nasal use) is a cardiac stimulant indicated for the emergency treatment of severe acute allergic reactions (anaphylaxis) triggered by allergens in foods, medicines, insect stings or bites, and other allergens as well as for exercise-induced or idiopathic anaphylaxis, cardio-vascular arrest (cardiopulmonary resuscitation), anaphylactic shock, severe anaphylactic reactions (stages III and IV): Stage III is characterized by symptoms of shock, bronchospasm with threatening dyspnoea and clouding of consciousness, stage IV by cardiovascular or respiratory arrest, and non-primary treatment in septic shock, vasoconstrictive additive to local anaesthetics.

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of epinephrine (except for nasal use)-containing medicinal products in the approved indication(s) remains unchanged.

  Nevertheless, the product information (PI) should be updated to add a warning regarding the risk of QTc prolongation and Torsade de Pointes in predisposed patients (patients with congenital long QT syndrome or catecholaminergic polymorphic ventricular tachycardia). Therefore, the current terms of the marketing authorisation(s) should be varied[19].

- In the next PSUR, the MAH(s) should provide a cumulative safety review of all adverse events associated with extravasation/paravenous administration/incorrect route of administration as well as a discussion on the need to update the PI. The MAH(s) should continue monitoring the risk of hypotension (in particular when used as adjunct to local

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

anaesthetic solutions) and review the interaction with ergot-type oxytocic drugs and discuss the need for a PI update, as warranted. In addition, the MAH Mercury should provide further details on the analysis performed during signal detection 'hypotension in quetiapine overdose', while all MAHs are requested to comment whether cumulative data would warrant a PI update. Finally, the MAH(s) should review the PSUR safety concerns as follows: for products with intramuscular administration (anaphylactic indication) to maintain drug administration error including accidental injection, lack of drug effect and auto-injector not working as important identified risks; for products with an IV administration (for indications: cardio-vascular arrest (cardiopulmonary resuscitation) anaphylactic shock, severe anaphylactic reactions, non-primary treatment in septic shock, vasoconstrictive additive to local anaesthetics, local application for vasoconstriction) to have hypertension and related complications especially cerebral haemorrhages in elderly, cardiac dysfunctions (including ventricular arrhythmia, angina, etc.), cardiac arrhythmias, bradycardia, cardiac arrest (related to drug interaction) and medication error leading to overdose as important identified risks, and use during pregnancy and labour as important potential risks.

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

6.3.5. Pethidine – EMA/PSUR/0000311131

Applicants: various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00002357/202508)

Background

Pethidine is a synthetic opioid drug indicated for the treatment of moderate to severe pain.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing pethidine 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 pethidine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add or amend information about opioid use disorder (OUD), and add a warning about hyperalgesia**,** sleep-related breathing disorders, and sphincter of Oddi dysfunction. In addition, the PI should be updated to add the drug-drug interaction with gabapentinoids and anticholinergics/drugs with anticholinergic activity. Finally, the PL should be updated to add a black box warning about the nature of the opioid-containing product and the risk

of dependence and addiction. Therefore, the current terms of the marketing authorisation(s) should be varied[20].

- In the next PSUR, the MAH(s) should provide a cumulative review of pethidine-specific data on hyperalgesia. The MAH(s) should review all the data related to the risk of sphincter of Oddi dysfunction and pancreatitis and discuss the need to update the PI, as warranted. The MAH(s) should further monitor pethidine-specific data on sleep-related breathing disorders.

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

6.3.6. Piretanide / ramipril, piretanide – EMA/PSUR/0000311146

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00002434/202508)

Background

Piretanide is diuretic, indicated for the treatment of arterial hypertension. Ramipril is an angiotensin converting enzyme inhibitor used for arterial hypertension. The combination piretanide/ramipril is indicated for the treatment of essential hypertension in patients whose blood pressure could not be sufficiently lowered with ramipril mono-component.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing piretanide/ramipril or piretanide 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 piretanide/ramipril- or piretanide-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning regarding angioedema to specify that in case of angiotensin-converting enzyme inhibitors induced angioedema, the use of epinephrine may be ineffective, and to remove the existing wording concerning emergency therapy of angioedema. Therefore, the current terms of the marketing authorisation(s) should be varied[21].
- In the next PSUR, the MAH Zentiva should continue to closely monitor and discuss any new case of DRESS. The MAH Sanofi should revise its list of safety concerns for the next PSUR in order to remove the safety concerns corresponding to important identified risks.

[20] Update of SmPC sections 4.2, 4.4, 4.5 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.
[21] Update of SmPC sections 4.4 and 4.9. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.

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

6.4. Follow-up to PSUR/PSUSA procedures

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

See also Annex I 16.5.

6.5.1. Apalutamide – ERLEADA (CAP) – EMA/VR/0000319048

Applicant: Janssen Cilag International

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 4.5 of the SmPC in order to include information regarding apalutamide interference with a digoxin laboratory test based on a cumulative safety review, following the PRAC request in procedure PSUSA/00010745/202502. In addition, the MAH took the opportunity to introduce minor editorial changes and to update the list of local representatives in the Package Leaflet.

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 provide a cumulative review on the risk of laboratory interference leading to falsely elevated digoxin plasma levels and an update of the product information, as warranted. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation. For further background, see PRAC minutes September 2025.

Summary of recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed to update the product information to reflect the potential for laboratory interference leading to falsely elevated digoxin levels by apalutamide when chemiluminescent microparticle immunoassay (CMIA) test is used.

6.6. Expedited summary safety reviews[22]

None

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

7. Post-authorisation safety studies (PASS)

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

See Annex I 17.1.

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

See Annex I 17.2.

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

See Annex I 17.3.

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

See also Annex I 17.4.

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: A grouped application consisting of:

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

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

Background

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

As stated in the RMP of Orencia (abatacept), the MAH conducted two category 3 non-imposed noninterventional PASS (IM101803 and M101816) aimed to provide information on the risk of malignancies, especially melanoma, non-melanoma skin cancer, basal cell carcinoma, and squamous cell carcinoma in abatacept-treated patients with rheumatoid

[23] In accordance with Article 107n of Directive 2001/83/EC
[24] In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004
[25] In accordance with Article 107p-q of Directive 2001/83/EC
[26] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

arthritis or psoriatic arthritis. The Rapporteur assessed the MAH's final study reports. For further background, see PRAC minutes November 2025[27].

Summary of advice

- Based on the available data, the MAH's responses to the request for supplementary information (RSI) and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be recommended for approval.
- PRAC considered that the product information (SmPC section 4.8 Description of selected adverse reactions subsection Malignancies) should be updated to reflect the final results of the studies IM101803 and IM101816. Regarding the risk management plan, PRAC agreed with the removal of the following safety concerns from the RMP: 'malignancies' and 'immunogenicity in paediatric patients'. In addition, PRAC agreed that the MAH should provide an analysis of cases of infusion- and injection-related hypersensitivity reactions in the next PSUR (submission date: 22 March 2026), along with an assessment on the classification of these reactions as safety concerns in the RMP and a reassessment of the need for additional risk minimisation measures to mitigate these risks.

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

See Annex I 17.5.

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

[27] Held on 27-30 October 2025.

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.

None

9.3. Others

None

10. Other safety issues for discussion requested by the Member States, CHMP or the EMA

10.1.1. Ocrelizumab – OCREVUS (CAP) – EMA/VR/0000313041

Applicant: Roche Registration GmbH

PRAC Rapporteur: Dirk Mentzer

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on 'Liver Injury' and to add it to the list of adverse drug reactions (ADRs) with frequency 'rare', based on a cumulative safety review. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to submit a DHPC Letter and to introduce minor changes to the PI, including the Labelling section.

Background

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

A type II variation proposing to update the product information of Ocrevus (ocrelizumab) regarding liver injury is under evaluation at CHMP. PRAC was requested to provide advice on this variation.

Summary of advice

- Based on the review of the available information, PRAC recommended to update the product information to add drug-induced liven injury (DILI) as a warning and an undesirable effect with a frequency to be re-calculated by the MAH. Further, PRAC advised adding DILI as an important identified risk in the RMP, and that this risk should be monitored in the ongoing PASS BA39730. Thereby, an amendment of the protocol for this PASS is needed. PRAC did not find additional risk minimisation measures being necessary in light of the current knowledge. In addition, PRAC advised updating the product information to add hepatic transaminases increased as an undesirable effect with frequency 'common'. PRAC also agreed with the dissemination of a DHPC, noting that its content should be updated in accordance with the revisions to the SmPC.

11. Scientific advice procedures

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

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

The PRAC Chair welcomed Dennis Lex as the new PRAC member for Germany.

12.1.2. PRAC working group - Best Practice Guide (BPG) implementation goals and statistics - update

PRAC lead: Ulla Wandel Liminga

At the organisational, regulatory and methodological matters (ORGAM) meeting on 26 March 2026, the PRAC Secretariat presented to PRAC the new implementation goals and process for collecting PRAC statistics to be implemented from 2026. Among other changes, starting in 2026 the Committee will be informed on the statistics on an annual basis. PRAC agreed with the proposal.

12.1.3. Nominated proxy

None

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. European Network Training Centre (EU NTC) – Pharmacogenomics – New training curriculum

The PRAC Secretariat presented background information and outlined the rationale supporting the development of the pharmacogenomics training curriculum, as well as the launch of the initial modules. The objective of the curriculum is to support the development of an expert and harmonised workforce across the Network. The training is delivered through the EU Network Training Centre (EU NTC) and contributes to the long-term objectives of the EMANS 2028 strategy. A call for interest was launched to allow experts to contribute to the development and review of the future training modules .

12.5. Cooperation with International Regulators

None

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

None

12.7. PRAC work plan

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Petar Mas

The EMA Secretariat presented to PRAC for adoption a minor update regarding the inclusion of synonyms to the Official request form for addition/amendments to the EU reference dates (EURD) list, following agreement by the GPAG. PRAC agreed with the proposal. After the adoption, the document will be uploaded on the EMA website at the next opportunity.

12.10.3. PSURs repository

None

12.10.4. Revisions of the Questions and Answers for assessors on Periodic safety update reports (PSUSA), PSUSA assessment report template and Explanatory Note to Good Pharmacovigilance Practice (GVP) Module VII

PRAC lead: Ulla Wändel Liminga

At the organisational, regulatory and methodological matters (ORGAM) meeting on 26 March 2026, the EMA Secretariat presented to PRAC the latest updates following the commenting phase (for background, see Minutes of PRAC meeting on 24-27 November 2025). Several additional comments were raised during the discussion and PRAC members were invited to comment on the updated documents by 17 April 2026.

Post-meeting note: As there were no additional comments received by 17 April 2026, the documents (PSUSA AR template, Explanatory note to GVP Module VII and Questions and answers document for assessors) are considered endorsed by PRAC. The documents will be published on the EMA website in the next period, as per the EMA internal processes.

12.10.5. 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 March 2026, 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 March 2026, the updated EURD list was adopted by CHMP and CMDh at their March 2026 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. Reflection paper on particulars for signal detection for (traditional) herbal medicinal products

PRAC lead: Julia Pallos

At the organisational, regulatory and methodological matters (ORGAM) meeting on 26 March 2026, the HMPC and PRAC Leads presented to PRAC the draft reflection paper on particulars for signal detection for (traditional) herbal medicinal products, including the background and the main points discussed during the drafting process. The PRAC members were invited to provide their comments in writing. The reflection paper will be released for public consultation later this year. PRAC noted the information.

12.11.2. Signals and safety analytics project – update and change management plan for the National Competent Authorities (NCAs) rollout

PRAC lead: To be appointed

The EMA Secretariat presented an update of the project, as well as the change management strategy for national competent authorities. A call for interest was launched to replace

Martin Huber as a signals and safety analytics sponsor, following his departure from PRAC.

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. EudraVigilance annual report 2025

The EMA Secretariat presented the annual report related to EudraVigilance activities on the reporting of adverse drug reactions as well as an analysis on signal detection and signal outcomes for the year 2025.

12.13.3. EudraVigilance – Expert Working Group (EV-EWG) - nomination of PRAC representative

The EMA Secretariat launched a call to replace Martin Huber as PRAC representative in the EV-EWG following his departure from PRAC. PRAC members should send their interest in writing.

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. CHMP assessment report (AR) template – Revamp Project - report on the completed pilot

The EMA Secretariat presented a summary of the report on the outcomes of a pilot initiative. PRAC noted the information.

12.21.2. PRAC Assessors trainings - update

PRAC Lead(s): Liana Martirosyan, Ulla Wändel Liminga

At the organisational, regulatory and methodological matters (ORGAM) meeting on 26 March 2026, the EMA Secretariat provided the plan for PRAC Assessors trainings for 2026, with several short webinar sessions scheduled around the year. PRAC welcomed the proposal and noted the information.

12.21.3. Draft Questions and Answers (Q&A) on EMA Guidance on the use of Real-World Data

PRAC Lead: Carla Torre

The EMA Secretariat and the PRAC Lead presented activities around the update of the Q&A on the use of real-world data including patient registries for regulatory purposes. This document has been developed under the umbrella of the Methodology Working Party (MWP) to address questions raised by stakeholders with regard to the currently available EU regulatory guidance documents, more specifically the reflection paper on the use of real-world data in non-interventional studies to generate real-world evidence for regulatory purposes, the guideline on registry-based studies and the HMA-EMA Data quality framework for medicines regulation. After endorsement at the level of MWP, PRAC members will be invited to provide their comments on the document. PRAC will be kept informed about the progress of the consultation phase.

12.21.4. Guidance on how to best involve PRAC's members nominated by the European Commission in PRAC activities – update

At the organisational, regulatory and methodological matters (ORGAM) meeting on 26 March 2026, the EMA Secretariat presented to PRAC a brief update of the guidance on involving PRAC members nominated by the European Commission in PRAC activities. PRAC noted the information.

12.21.5. Real World Evidence (RWE) project related to Alzheimer's disease and Duchenne muscular dystrophy – update

PRAC Lead(s): Carla Torre, Patricia McGettigan, Ulla Wändel Liminga

The EMA Secretariat and the PRAC Leads presented to PRAC an overview of the ongoing RWE activities and projects related to Alzheimer's disease and Duchenne muscular dystrophy, including their objectives and deliverables for the upcoming year. PRAC noted the information.

12.21.6. Artificial Intelligence in pharmacovigilance guidance development - update

PRAC Lead(s): Jean-Michel Dogné, Milou-Daniel Drici

At the organisational, regulatory and methodological matters (ORGAM) meeting on 26 March 2026, the EMA Secretariat presented to PRAC the ongoing and upcoming activities in the field of artificial intelligence, in line with the provisions of the EU Biotech Act, with a particular focus on the development of guidance on the use of AI in pharmacovigilance. PRAC noted the information.

13. Any other business

None

Annex I – Signals assessment and prioritisation[28]

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[29].

14. Signals assessment

None

14.2. Signals follow-up and prioritisation

None

14.3. Variation procedure(s) resulting from signal evaluation

None

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

None

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. Avatrombopag – DOPTELET (CAP) – EMA/VR/0000296242

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Maria Martinez Gonzalez

Scope: A grouped application consisting of:
C.I.11 for RMP: Submission of an updated RMP version 4.0 to propose the removal of missing information Use in splenectomy patients with chronic liver disease, Use in patients

[28] 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
[29] 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

receiving interferon products and Safety in patients undergoing invasive procedures.
C.I.11 for RMP: Submission of an updated RMP version 4.0 to propose to remove Targeted Medical Event Questionnaires.
C.I.11 for RMP: Submission of an updated RMP version 4.0 to update information on immune thrombocytopenia (ITP) PASS and chronic liver disease (CLD) PASS studies.

15.2.2. Lecanemab – LEQEMBI (CAP) – EMA/VR/0000302769

Applicant: Eisai GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Submission of an updated RMP version 1.1 in order to propose an update to PASS study deadlines. In addition, the MAH has taken the opportunity to update Annex II accordingly.

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

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Liana Martirosyan

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

15.2.4. Lenalidomide – LENALIDOMIDE KRKA (CAP); NAP – EMA/VR/0000310403

Applicants: KRKA tovarna zdravil d.d. Novo mesto, various

PRAC Rapporteur: Tiphaine Vaillant

Scope: C.I.11.z - to update Annex IID and the RMP following the outcome of the renewal procedure (EMA/R/0000272358).
The RMP has been updated in accordance with the changes to the reference product's RMP as requested.

15.2.5. Siponimod – MAYZENT (CAP) – EMA/VR/0000317924

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: A grouped application consisting of:
Type II (C.I.13): Submission of the final report from study CBAF312A2006 listed as a category 3 study in the RMP. This is a survey conducted among healthcare professionals and Multiple Sclerosis patients/caregivers in selected European countries plus Canada to evaluate the knowledge required for the safe use of Mayzent (siponimod). The RMP version 8.0 has also been submitted.
Type IB (C.I.11): Submission of an updated RMP version 8.0 in order to update the siponimod exposure data in accordance with the results of the drug-drug interaction study CBAF312A02101 in alignment with the EMA/VR/0000255116 procedure.

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

15.3.1. Beclometasone / Formoterol / Glycopyrronium bromide – TRIMBOW (CAP) – EMA/VR/0000315173

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include treatment of asthma for TRIMBOW 88/5/9 mcg DPI, based on existing data from the development of Trimbow 87/5/9 mcg pressurised metered dose inhaler in COPD and Asthma, Trimbow 172/5/9 mcg pressurised metered dose inhaler in Asthma and Trimbow 88/5/9 mcg Dry powder inhaler in COPD, as well as on new data coming from the PK 2 study (CLI-05993BB1-01) and on the interim results of the ongoing PASS (TRIBE) study in COPD. As a consequence, sections 4.1, 4.2, 4.4, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 11.1 of the RMP has also been submitted.

15.3.2. Bulevirtide – HEPCLUDEX (CAP) – EMA/VR/0000320140

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application consisting of:
C.I.4: Update of section 4.8 of the SmPC in order to remove a statement regarding bile acid elevations based on results from study MYR301, listed as a Category 3 study in the RMP. This is a Multicenter, Open-label, Randomized Phase 3 Clinical Study to Assess Efficacy and Safety of Bulevirtide in Patients With Chronic Hepatitis Delta to address the safety concern of 'Long-term safety of bile acid elevations' (Missing information). The RMP version 7.1 has also been submitted.
C.I.11.b: Submission of an updated RMP version 7.1 in order to propose the removal of Study GS-US-589-6206 as a Category 3 Pharmacovigilance Commitment from the RMP for safety concern of 'Long-term safety of bile acid elevations' (Missing information).

15.3.3. Datopotamab deruxtecan – DATROWAY (CAP) – EMA/VR/0000316654

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include, as monotherapy, the first-line treatment of adult patients with unresectable or metastatic triple-negative breast cancer (TNBC) who are not candidates for PD-1/PD-L1 inhibitor therapy for DATROWAY, based on final results from study D926PC00001 (TROPION-Breast02). This is a Phase 3, randomised, open-label, 2 arm, multicentre, international study assessing the efficacy and safety of Dato-DXd compared with investigator's choice chemotherapy in participants with locally recurrent inoperable or metastatic TNBC who are not candidates for PD-1/PD-L1 inhibitor therapy. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.4. Delgocitinib – ANZUPGO (CAP) – EMA/VR/0000315280

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Extension of indication to include treatment of adolescents 12 years and older with moderate to severe chronic hand eczema (CHE) for whom topical corticosteroids are inadequate or inappropriate for ANZUPGO, based on final results from study LP0133-1426 (DELTA TEEN); this is a phase 3 pivotal clinical trial to evaluate efficacy and safety of twice-daily applications of delgocitinib cream compared with cream vehicle for a 16-week treatment period in adolescents 12-17 years of age with moderate to severe chronic hand eczema. The trial is a randomized, double-blind, vehicle-controlled study. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 1.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet.

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

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Martirosyan

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

15.3.6. Dimethyl fumarate – TECFIDERA (CAP) – EMA/VR/0000320745

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Dennis Lex

Scope: Submission of the final study results from 109MS306 (CONNECT) Part 2 listed as a category 3 study in the RMP; this is a phase 3 efficacy and safety study of BG00012 in pediatric subjects with relapsing-remitting multiple sclerosis (RRMS). The primary objective of Part 2 is to evaluate the long-term safety of BG00012 in subjects who completed Week 96 in Part 1 of Study 109MS306. The secondary objective of Part 2 is to describe the long-term multiple sclerosis outcomes of BG00012 in subjects who completed Week 96 in Part 1 of Study 109MS306. The RMP version 17.1 has also been submitted.

15.3.7. Glecaprevir / Pibrentasvir – MAVIRET (CAP) – EMA/VR/0000316551

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Extension of indication to include treatment of Acute HCV for MAVIRET, based on final results from study M20-350; this is a multicenter, single-arm prospective study to evaluate safety and efficacy of GLE/PIB 8-week treatment in adults and adolescents with acute hepatitis C virus (HCV) infection. 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 10.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet.

15.3.8. Ipilimumab – YERVOY (CAP); Nivolumab – OPDIVO (CAP) – EMA/VR/0000319172

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add 'Myocarditis-Myositis-Myasthenia Gravis Overlap Syndrome' to the list of adverse drug reactions (ADRs) with frequency 'Uncommon' based on postmarketing data and literature. The Package Leaflet is updated accordingly. The RMP version 46 and 52 respectively, had also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.

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

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Maria Martinez Gonzalez

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

15.3.10. Ivacaftor / Tezacaftor / Elexacaftor – KAFTRIO (CAP) – EMA/VR/0000320413

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Dennis Lex

Scope: Submission of Part A (week 96) clinical study report for study VX21-445-125 (study 125). This is a Phase 3, open-label study to evaluate the long-term safety, tolerability, efficacy, and pharmacodynamics of elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) in cystic fibrosis (CF) subjects ≥6 years of age who have qualifying non-F508del ELX/TEZ/IVA-responsive CFTR mutations. RMP version 10.3 has also been submitted.

15.3.11. Lumacaftor / Ivacaftor – ORKAMBI (CAP) – EMA/VR/0000320822

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Eamon O Murchu

Scope: Submission of the final report from study VX18-809-128 (study 128), listed as an obligation in the Annex II of the Product Information. This is a 6-year, observational, post-authorization efficacy study (PAES) in young children with cystic fibrosis (CF) aged 1 through 5 years at the time of Orkambi initiation. This study evaluated disease progression and safety using observational cohorts of children receiving therapy in a "real-world" setting. The Annex II and the RMP version 12.0 are updated accordingly.

15.3.12. Lutetium (177Lu) vipivotide tetraxetan – PLUVICTO (CAP) – EMA/VR/0000288073

Applicant: Novartis Europharm Limited

PRAC Rapporteur: John Joseph Borg

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

15.3.13. Maralixibat – LIVMARLI (CAP) – EMA/VR/0000320544

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application consisting of:
C.I.13: Submission of the final report from study MRX- 503 listed as category 3 study in the RMP. This is a phase 3 study to Evaluate the Long-Term Safety and Efficacy of Maralixibat in the Treatment of Subjects with Progressive Familial Intrahepatic Cholestasis (PFIC). The RMP version 7.2 has also been submitted.
C.I.13: Submission of the final report for a retrospective study titled ''Analysis of Clinical Outcomes in PFIC: Comparison of Maralixibat from Studies MRX-502/503 and MRX-801 versus Natural History (NAtural course and Prognosis of PFIC and Effect of biliary Diversion [NAPPED])''.

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

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication for MENQUADFI to include the active immunisation of patients from 6 weeks of age based on final results from study MET58 and additional supportive clinical studies. Study MET58 is a Phase 3, immunogenicity and Safety Study of an Investigational Quadrivalent Meningococcal Conjugate Vaccine when Administered

Concomitantly with Routine Pediatric Vaccines in Healthy Infants and Toddlers in Europe. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. An updated Risk Management Plan (RMP) version 4.0 is also included.

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

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

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

15.3.16. Osilodrostat – ISTURISA (CAP) – EMA/VR/0000315678

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include the treatment of endogenous Cushing's syndrome in adolescents and children aged 6 years and older for ISTURISA, based on results from study CLCI699C2203; this is a Phase II, multicenter, open-label, non-comparative study to evaluate the pharmacokinetics, pharmacodynamics, and tolerability of osilodrostat in children and adolescent patients with Cushing's disease. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted.

15.3.17. Palbociclib – IBRANCE (CAP) – EMA/VR/0000316536

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Extension of indication to include, in combination with anti-HER2 and endocrine therapies, the maintenance treatment of adult patients with HR-positive, HER2-positive locally advanced or metastatic breast cancer (MBC) following induction treatment for IBRANCE, based on the interim results from the open-label Phase 3 study PATINA (AFT-38/WI215662). This is a randomized, open-label Phase 3 study evaluating the efficacy and safety of IBRANCE (palbociclib) in combination with anti-HER2 therapy and endocrine therapy compared to anti-HER2 therapy and endocrine therapy alone as a first-line maintenance therapy (following induction chemotherapy treatment) for patients with HR

positive, HER2-positive MBC. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. RMP version 1.10 has also been submitted.

15.3.18. Pembrolizumab – KEYTRUDA (CAP) – EMA/VR/0000316576

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: A grouped application consisting of:
C.I.6. Extension of indication for KEYTRUDA for subcutaneous use to include treatment of melanoma for adolescents aged 12 years and older based on an extrapolation approach from adults to adolescents using pharmacokinetics modelling and simulation. 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 52.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder took the opportunity to implement some minor editorial and formatting changes in the PI.
C.I.6. Extension of indication for KEYTRUDA for subcutaneous use to include treatment of classical Hodgkin lymphoma for adolescents aged 12 years and older based on an extrapolation approach from adults to adolescents using pharmacokinetics modelling and simulation. 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.

15.3.19. Pertuzumab – PERJETA (CAP) – EMA/VR/0000307073

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update safety and efficacy data, based on final results from post-authorisation efficacy study BO25126 (APHINITY) listed as a specific obligation in the Annex II; this is a phase III, randomized multicenter, double-blind, placebo-controlled comparison of chemotherapy plus trastuzumab plus placebo versus chemotherapy plus trastuzumab plus pertuzumab as adjuvant therapy in patients with operable HER2-positive primary breast cancer; the Package Leaflet and Annex II are updated accordingly. The RMP version 15.0 has also been submitted. In addition, the MAH took the opportunity to introduce editorials changes to the PI.

15.3.20. Pirtobrutinib – JAYPIRCA (CAP) – EMA/VR/0000316267

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adult patients with chronic lymphocytic leukaemia (CLL) for JAYPIRCA, based on interim results from studies LOXO-BTK-20023 (BRUIN-CLL-313) and LOXO-BTK-20030 (BRUIN-CLL-314). Study 20023 is a phase 3 open-label, randomized study of pirtobrutinib (LOXO-305) versus bendamustine plus rituximab in untreated patients with CLL/SLL. Study 20030 is a phase 3 open-label, randomized study of pirtobrutinib (LOXO-305) versus ibrutinib in patients with CLL/SLL. As a consequence,

sections 4.1, 4.8, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted.

15.3.21. Pneumococcal polysaccharide conjugate vaccine (21-valent) – CAPVAXIVE (CAP) – EMA/VR/0000294070

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include active immunization of children and adolescents 2 to less than 18 years of age for CAPVAXIVE, based on final results from study V116-013 (P013V116); this is a phase 3, randomized, double-blind study to evaluate the safety, tolerability, and immunogenicity of V116 in children and adolescents with increased risk of pneumococcal disease; As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted.

15.3.22. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – MRESVIA (CAP) – EMA/VR/0000320244

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

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 mRESVIA in immunocompromised individuals 18 years of age and older, based on interim results from study mRNA-1345-P303 Part B; this is a Phase 3 study to evaluate the immunogenicity and safety of mRNA-1345, an mRNA vaccine targeting respiratory syncytial virus, in high-risk adults. The updated RMP version 6.0 has also been submitted.

15.3.23. Ruxolitinib – OPZELURA (CAP) – EMA/VR/0000313318

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of moderate atopic dermatitis in adult patients who are inadequately controlled with, have a contraindication to, or are intolerant to topical corticosteroids and topical calcineurin inhibitors for OPZELURA, based on the results of the pivotal Phase III study INCB 18424-326 and the two supportive Phase III studies INCB 18424-303 and INCB 18424-304. INCB 18424-326 is a Phase 3b, double-blind, multicenter, randomized, vehicle-controlled, efficacy, and safety study of ruxolitinib cream in adults with moderate atopic dermatitis. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.0 of the RMP has also been submitted.

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

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jan Neuhauser

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

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

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jan Neuhauser

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

15.3.26. Somapacitan – SOGROYA (CAP) – EMA/VR/0000264734

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Dennis Lex

Scope: Grouped extension of indication application to include treatment of children born small for gestational age (SGA), Noonan syndrome (NS) and idiopathic short stature (ISS) for SOGROYA, based on interim results from the pivotal, confirmatory phase 3 study NN8640-4467 supported by the phase 3 study NN8640-4469 and the phase 2 study NN8640-4245. Study 4467 is a study comparing the effect and safety of once weekly dosing of somapacitan with daily Norditropin as well as evaluating long-term safety of somapacitan in a basket study design in children with short stature either born small for gestational age or with Turner syndrome, Noonan syndrome, or idiopathic short stature. Study 4469 is a study evaluating the safety and efficacy of once-weekly dosing of somapacitan in a basket study design in paediatric participants with short stature either born small for gestational age or with turner syndrome, Noonan syndrome or idiopathic short stature. Study 4245 is a dose-finding trial evaluating the effect and safety of once-weekly treatment of somapacitan compared to daily Norditropin in children with short stature born small for gestational age with no catch-up growth by 2 years of age or older. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.4. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.27. Tofersen – QALSODY (CAP) – EMA/VR/0000296462

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.8, 5.1, and 5.2 of the SmPC to numerically update the summary of safety profile and description of selected adverse reactions, as well as, to update clinical efficacy and pharmacokinetic information based on final integrated analysis from Study 233AS101 and Study 233AS102. Submission of the final results of Study 233AS102 is listed as a specific obligation in the Annex II and a category 2 study in the RMP. Study 233AAS102 was an open label extension study to assess the long-term safety, tolerability, pharmacokinetics, and effect on disease progression of tofersen administered to previously treated adults with amyotrophic lateral sclerosis caused by superoxide dismutase 1 mutation. The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to update the Annex II.

15.3.28. Ustekinumab – STELARA (CAP) – EMA/VR/0000316205

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include treatment of ulcerative colitis in paediatric patients from the age of 2 years and older for STELARA, based on results from study CNTO1275PUC3001; this is a Phase 3 Study of the Efficacy, Safety and Pharmacokinetics of Ustekinumab as Open-label Intravenous Induction Treatment Followed by Randomized Double-blind Subcutaneous Ustekinumab Maintenance in Pediatric Participants (2 to <18 Years of Age) with Moderately to Severely Active Ulcerative Colitis. 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 32.2 of the RMP has also been submitted.

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

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

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

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

16.1.1. Agalsidase beta – FABRAZYME (CAP) – EMA/PSUR/0000311185

Applicant: Sanofi B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000070/202507)

16.1.2. Belzutifan – WELIREG (CAP) – EMA/PSUR/0000311168

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00011107/202508)

16.1.3. Catumaxomab – KORJUNY (CAP) – EMA/PSUR/0000311171

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011108/202508)

16.1.4. Chikungunya vaccine (recombinant, adsorbed) – VIMKUNYA (CAP) – EMA/PSUR/0000311187

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011118/202508)

16.1.5. Crovalimab – PIASKY (CAP) – EMA/PSUR/0000311169

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011071/202508)

16.1.6. Dapivirine – DAPIVIRINE VAGINAL RING 25 MG (Art 58) – EMA/PSUR/0000313080

Applicant: International Partnership For Microbicides

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUV Dapivirine)

16.1.7. Daunorubicin / Cytarabine – VYXEOS LIPOSOMAL (CAP) – EMA/PSUR/0000311133

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010701/202508)

16.1.8. Dronedarone – MULTAQ (CAP) – EMA/PSUR/0000311124

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001180/202507)

16.1.9. Elranatamab – ELREXFIO (CAP) – EMA/PSUR/0000311115

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00000225/202508)

16.1.10. Fedratinib – INREBIC (CAP) – EMA/PSUR/0000311144

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010909/202508)

16.1.11. Fosdenopterin – NULIBRY (CAP) – EMA/PSUR/0000311166

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00011017/202508)

16.1.12. Glecaprevir / Pibrentasvir – MAVIRET (CAP) – EMA/PSUR/0000311147

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010620/202507)

16.1.13. Imlifidase – IDEFIRIX (CAP) – EMA/PSUR/0000311139

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010870/202508)

16.1.14. Lefamulin – XENLETA (CAP) – EMA/PSUR/0000311158

Applicant: Venipharm

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00010872/202508)

16.1.15. Lenacapavir – SUNLENCA (CAP); YEYTUO (CAP) – EMA/PSUR/0000311172

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00011012/202508)

16.1.16. Lenacapavir – LENACAPAVIR GILEAD (Art 58) – EMA/PSUR/0000310870

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUV lenacapavir)

16.1.17. Lonapegsomatropin – SKYTROFA (CAP) – EMA/PSUR/0000311154

Applicant: Ascendis Pharma Endocrinology Division A/S

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00010969/202508)

16.1.18. Mirdametinib – EZMEKLY (CAP) – EMA/PSUR/0000311173

Applicant: Springworks Therapeutics Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011161/202508)

16.1.19. Odronextamab – ORDSPONO (CAP) – EMA/PSUR/0000311164

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00011074/202508)

16.1.20. Omaveloxolone – SKYCLARYS (CAP) – EMA/PSUR/0000311117

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000245/202508)

16.1.21. Patisiran – ONPATTRO (CAP) – EMA/PSUR/0000311137

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00010715/202508)

16.1.22. Pegaspargase – ONCASPAR (CAP) – EMA/PSUR/0000311176

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010457/202507)

16.1.23. Polihexanide – AKANTIOR (CAP) – EMA/PSUR/0000311167

Applicant: SIFI S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011082/202508)

16.1.24. Pretomanid – DOVPRELA (CAP) – EMA/PSUR/0000311186

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010863/202508)

16.1.25. Risdiplam – EVRYSDI (CAP) – EMA/PSUR/0000311153

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010925/202508)

16.1.26. Seladelpar lysine dihydrate – LYVDELZI (CAP) – EMA/PSUR/0000311174

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00011119/202508)

16.1.27. Sofosbuvir / Velpatasvir / Voxilaprevir – VOSEVI (CAP) – EMA/PSUR/0000311119

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010619/202507)

16.1.28. Sotrovimab – XEVUDY (CAP) – EMA/PSUR/0000311183

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010973/202508)

16.1.29. Sparsentan – FILSPARI (CAP) – EMA/PSUR/0000311163

Applicant: Vifor France

PRAC Rapporteur: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00011060/202508)

16.1.30. Talquetamab – TALVEY (CAP) – EMA/PSUR/0000311118

Applicant: Janssen Cilag International

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00000099/202508)

16.1.31. Tiratricol – EMCITATE (CAP) – EMA/PSUR/0000311170

Applicant: Rare Thyroid Therapeutics International AB

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00011114/202508)

16.1.32. Tisagenlecleucel – KYMRIAH (CAP) – EMA/PSUR/0000311179

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010702/202508)

16.1.33. Valoctocogene roxaparvovec – ROCTAVIAN (CAP) – EMA/PSUR/0000311159

Applicant: Biomarin International Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00011009/202508)

16.1.34. Vosoritide – VOXZOGO (CAP) – EMA/PSUR/0000311145

Applicant: Biomarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure (PSUSA/00010952/202508)

16.1.35. Voxelotor – OXBRYTA (CAP) – EMA/PSUR/0000311152

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00010983/202508)

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

16.2.1. Human protein C – CEPROTIN (CAP); NAP – EMA/PSUR/0000311155

Applicants: Takeda Manufacturing Austria AG, various

PRAC Rapporteur: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00002563/202507)

16.2.2. Lamivudine – ZEFFIX (CAP); NAP – EMA/PSUR/0000311149

Applicants: Glaxosmithkline Trading Services Limited, various

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00001824/202507)

16.2.3. Leuprorelin – CAMCEVI (CAP); NAP – EMA/PSUR/0000311157

Applicants: Accord Healthcare S.L.U., various

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010877/202507)

16.2.4. Palonosetron – ALOXI (CAP); NAP – EMA/PSUR/0000311140

Applicants: Helsinn Birex Pharmaceuticals Limited, various

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00002268/202507)

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

16.3.1. Ademetionine – EMA/PSUR/0000310823

Applicants: various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000061/202508)

16.3.2. Amoxicillin / clarithromycin / pantoprazole – EMA/PSUR/0000311136

Applicants: various

PRAC Lead: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00002286/202508)

16.3.3. Beclometasone / formoterol (inhalative application) – EMA/PSUR/0000311156

Applicants: various

PRAC Lead: Dennis Lex

Scope: Evaluation of a PSUSA procedure (PSUSA/00010068/202507)

16.3.4. Cetylpyridinium / lysozyme, lysozyme / pyridoxine – EMA/PSUR/0000311122

Applicants: various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00000640/202508)

16.3.5. Cisatracurium – EMA/PSUR/0000311123

Applicants: various

PRAC Lead: Veronika Macurova

Scope: Evaluation of a PSUSA procedure (PSUSA/00000777/202507)

16.3.6. Copper chloride dihydrate / manganese chloride tetrahydrate / potassium iodide / sodium fluoride / sodium selenite anhydrous / zinc chloride – EMA/PSUR/0000311161

Applicants: various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00010803/202508)

16.3.7. Diclofenac / misoprostol – EMA/PSUR/0000311125

Applicants: various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00001040/202507)

16.3.8. Dimetindene / phenylephrine – EMA/PSUR/0000311126

Applicants: various

PRAC Lead: Jana Pecherova

Scope: Evaluation of a PSUSA procedure (PSUSA/00001102/202507)

16.3.9. Escherichia coli lysate – EMA/PSUR/0000311128

Applicants: various

PRAC Lead: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00001263/202507)

16.3.10. Flutrimazole – EMA/PSUR/0000311129

Applicants: various

PRAC Lead: Maria Martinez Gonzalez

Scope: Evaluation of a PSUSA procedure (PSUSA/00001456/202508)

16.3.11. Fosphenytoin – EMA/PSUR/0000311127

Applicants: various

PRAC Lead: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00001476/202508)

16.3.12. Glyceryl trinitrate – EMA/PSUR/0000311175

Applicants: various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure (PSUSA/00001552/202507)

16.3.13. Human plasma protease C1 inhibitor (nationally authorised products) – EMA/PSUR/0000311178

Applicants: various

PRAC Lead: Dirk Mentzer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010163/202508)

16.3.14. Hydrocortisone / natamycin / neomycine sulphate – EMA/PSUR/0000311130

Applicants: various

PRAC Lead: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00001672/202508)

16.3.15. Iodine (123i) iobenguane – EMA/PSUR/0000311135

Applicants: various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00001763/202508)

16.3.16. Octenidine – EMA/PSUR/0000311148

Applicants: various

PRAC Lead: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00010748/202507)

16.3.17. Pitavastatin – EMA/PSUR/0000311143

Applicants: various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010502/202507)

16.3.18. Poliovirus type 1 / poliovirus type 2 / poliovirus type 3 vaccine (oral, live, attenuated), poliovirus type 1 / poliovirus type 3 vaccine (oral, live, attenuated),poliovirus type 1 (oral, live, attenuated) vaccine, poliovirus type 2 (oral, live, attenuated) vaccine,poliovirus type 3 (oral, live, attenuated) vaccine – EMA/PSUR/0000311142

Applicants: various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010801/202507)

16.3.19. Ziprasidone – EMA/PSUR/0000311138

Applicants: various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00003146/202507)

16.4. Follow-up to PSUR/PSUSA procedures

None

16.5. Variation procedure(s) resulting from PSUSA evaluation

16.5.1. Tafamidis – VYNDAQEL (CAP) – EMA/VR/0000297114

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Zoubida Amimour

Scope: Update of sections 4.4 and 4.5 of the SmPC in order to add a new warning on co-administration tafamidis meglumine/tafamidis and BCRP substrates, update drug-drug interaction information with BCRP sustrates following the PRAC PSUR assessment report for procedure no.: EMEA/H/C/PSUSA/00002842/202405. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to update the European Medicines Agency website address in line with the latest EU CP QRD template version 10.4.

16.6. Expedited summary safety reviews[30]

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.

[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

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

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Veronika Macurova

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

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

17.2.1. Cladribine – MAVENCLAD (CAP) – EMA/PAM/0000319565

Applicant: Merck Europe B.V.

PRAC Rapporteur: Carla Torre

Scope: Protocol amendment for PASS MS 700568-0002: Long-term prospective, observational cohort study evaluating the safety profile, in terms of incidence of adverse events of special interest, in patients with highly active relapsing multiple sclerosis (RMS) newly started on oral cladribine (CLARION)

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

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Liana Martirosyan

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

17.2.3. Galcanezumab – EMGALITY (CAP) – EMA/PAM/0000322252

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: PAM MEA to present a protocol substantial amendment to the category 3 PASS "A retrospective cohort study to assess drug utilisation and long-term safety of galcanezumab in European patients in the course of routine clinical care." Study identifier: I5Q-MC-B002.

17.2.4. Metreleptin – MYALEPTA (CAP) – EMA/PAM/0000319187

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Adam Przybylkowski

[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

Scope: Protocol amendment for Metreleptin effectiveness and safety registry (MEASURE): a non-interventional, multicenter, prospective, observational study of patients initiating treatment with metreleptin for lipodystrophy in the US and EEA.

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

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Following Omvoh line extension procedure EMEA/H/C/005122/X/0006/G to include Crohn's Disease (CD) as a new indication: Protocol amendment to I6T-MC-B003: Observational Study of Pregnancy and Infant Outcomes Among Women Exposed to Mirikizumab During Pregnancy in US-based Administrative Claims Data. Protocol amendment to I6T-MC-B004: Observational Secondary Database Study to Assess the Long-Term Safety of Mirikizumab in Routine Clinical Practice Using US Administrative Claims Data.

17.2.6. Ravulizumab – ULTOMIRIS (CAP) – EMA/PAM/0000321330

Applicant: Alexion Europe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Post-authorization measure to amend the protocol for Study M11-001, an observational, non-interventional, multi-center, multi-national study of patients with Atypical Hemolytic-Uremic syndrome. This is a Category 3 study (required additional pharmacovigilance activity). The main revision to the M11-001 protocol (amendment 7 dated 08 Dec 2025) is as follows: The registry will transition from a disease-based design to a drug-based design aligned with current risk management plan objectives and ongoing pharmacovigilance needs following fulfilment of the EMEA/H/C/000791/MEA/062.3 on 25 July 2024.

17.2.7. Romosozumab – EVENITY (CAP) – EMA/PAM/0000320086

Applicant: UCB Pharma

PRAC Rapporteur: Tiphaine Vaillant

Scope: Protocol amendment for PASS No. OP0005: European non-interventional PASS related to adherence to the risk minimization measures.

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Dirk Mentzer

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

17.2.9. Vorasidenib – VORANIGO (CAP) – EMA/PAM/0000320338

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Jo Robays

Scope: To assess the safety of vorasidenib in paediatric patients 12 years of age and older based on a clinical trial in paediatric patients following exposure to vorasidenib - Final protocol for study (S095032-236) "A Phase 2, single arm, open-label study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of vorasidenib in pediatric participants aged 12 to < 18 years old with Grade 2 astrocytoma or oligodendroglioma with an IDH1 or IDH2 mutation".

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

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Veronika Macurova

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

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

17.4.1. Dapagliflozin – EDISTRIDE (CAP); FORXIGA (CAP); Dapagliflozin / Metformin – EBYMECT (CAP); XIGDUO (CAP); Saxagliptin / Dapagliflozin – QTERN (CAP) – EMA/VR/0000308587

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report from the Cancer PASS study D1690R00007 listed as a category 3 study in the RMP. This is a post-authorisation observational study, final (120-month) report: comparison of the risk of cancer between patients with type 2 diabetes exposed to dapagliflozin and those exposed to other antidiabetic treatments. The RMP versions 32.0 for Forxiga & Edistride, 16.0 for Xigduo & Ebymect and 11.0 for Qtern have also been submitted.

17.4.2. Dexmedetomidine – DEXDOR (CAP) – EMA/VR/0000316395

Applicant: Orion Corporation

PRAC Rapporteur: Karin Bolin

Scope: Submission of the final report from study ANZIC-RC/YS003 listed as a category 3 PASS in the RMP. It concerns sedation practice in intensive care evaluation [SPICE] III, early

[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

goal directed sedation compared with standard care in mechanically ventilated patients in intensive care. The RMP version 10.0 has also been submitted.

17.4.3. Ivacaftor / Tezacaftor / Elexacaftor – KAFTRIO (CAP) – EMA/VR/0000319887

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Dennis Lex

Scope: Submission of the final report from the 5-year Post Authorisation Safety Study (PASS) VX20-445-120, listed as a category 3 study in the RMP. This is a longitudinal, registry based study evaluating the real-world effects and utilisation patterns of elexacaftor, tezacaftor, and ivacaftor combination therapy (ELX/TEZ/IVA) in patients with cystic fibrosis (CF). The RMP version 10.2 has also been submitted.

17.4.4. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) – MOSQUIRIX (CAP) – EMA/VR/0000319297

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: A grouped application consisting of:

C.I.13: Submission of the final report from post authorisation safety study EPI-MAL-005 listed as a category 3 study in the RMP. This is an epidemiology study to assess Plasmodium falciparum parasite prevalence and malaria control measures in catchment areas of two interventional studies pre- and post RTS,S/AS01E introduction (EPI-MAL-002 and EPI-MAL-003) to assess, in field conditions, vaccine benefit:risk in children in sub-Saharan Africa. RMP version 7.0 has also been submitted.
C.I.13: Submission of the final report from post authorisation safety study EPI-MAL-010 listed as a category 3 study in the RMP. This is a phase IV, longitudinal, cross-sectional, retrospective, ancillary epidemiology study of the EPI-MAL-005 study to evaluate the genetic diversity in the Plasmodium falciparum parasite circumsporozoite sequences before and after the implementation of the RTS,S/AS01E vaccine in malaria-positive subjects ranging from 6 months to less than 5 years of age.

17.4.5. Ponesimod – PONVORY (CAP) – EMA/VR/0000320506

Applicant: Laboratoires Juvise Pharmaceuticals

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the final report from non-interventional post authosiration safety study PCSNSP003693 listed as a category 3 study in the RMP. This is a Survey to Assess the Effectiveness of Ponvory Educational Materials for Additional Risk Minimization Measures in the European Union.

17.4.6. Romosozumab – EVENITY (CAP) – EMA/VR/0000320170

Applicant: UCB Pharma

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report of the EU PASS study OP0006 listed as a category 3 study in the RMP. The OP0006 EU PASS study is a European non-interventional post authorization safety study related to serious infections for romosozumab. The RMP version 3.0 has also been submitted.

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

17.5.1. COVID-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP) – EMA/PAM/0000317252

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Dirk Mentzer

Scope: Third Interim Report for PASS 2019nCoV-404: US Post-authorisation safety study to evaluate the pooled risk of selected Adverse Events of Special Interest (AESI) within specified time periods after vaccination with Nuvaxovid using a claim and/or EHR database.

17.5.2. COVID-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP) – EMA/PAM/0000317251

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Dirk Mentzer

Scope: Revised Third Interim Report for PASS 2019nCoV-402: UK A Study Using the Clinical Practice Research Datalink (CPRD): A surveillance study to characterise the safety profile of Nuvaxovid in adults aged 18 years and older in the real-world setting using the UK CPRD.

17.5.3. Dinutuximab beta – QARZIBA (CAP) – EMA/PAM/0000303342

Applicant: Recordati Netherlands B.V.

PRAC Rapporteur: Dirk Mentzer

Scope: An interim report for the non-interventional post-authorisation safety study (PASS) titled: A Patient Registry of Patients with High-Risk Neuroblastoma Being Treated with the Monoclonal Antibody Dinutuximab Beta" (EUSA DB 0001)

17.5.4. Dupilumab – DUPIXENT (CAP) – EMA/PAM/0000320087

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: [Interim Report #2 for PASS Study CSA0014]: A registry-based non-interventional post- authorization safety study (PASS) to evaluate the long-term safety of dupilumab in children aged ≥6 months to <6 years with moderate-to-severe atopic dermatitis using the PEDISTAD registry.

17.5.5. Filgotinib – JYSELECA (CAP) – EMA/PAM/0000319177

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: Progress report for Study GLPG0634-CL-413: a non-interventional, post-authorisation safety study of filgotinib in patients with moderately to severely active ulcerative colitis - a European multi registry-based study.

17.5.6. Fingolimod – GILENYA (CAP) – EMA/PAM/0000320326

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 6th Annual Interim Report of Study CFTY720D2311: A two-year, double-blind, randomized, multicenter, active-controlled Core Phase study to evaluate the safety and efficacy of fingolimod administered orally once daily versus interferon β-1a i.m. once weekly in pediatric patients with multiple sclerosis with five-year fingolimod Extension Phase.

17.5.7. Guselkumab – TREMFYA (CAP) – EMA/PAM/0000320084

Applicant: Janssen Cilag International

PRAC Rapporteur: Dirk Mentzer

Scope: Interim study results for PCSIMM001324 - A Retrospective Cohort Study Using Health Administrative Claims Databases to Assess Adverse Pregnancy and Infant Outcomes in Women With Psoriasis Who Were Exposed to Guselkumab Versus Other Biologic Therapies During Pregnancy.

17.5.8. Guselkumab – TREMFYA (CAP) – EMA/PAM/0000320085)

Applicant: Janssen Cilag International

PRAC Rapporteur: Dirk Mentzer

Scope: Interim study results for PSOLAR - A Multicenter, Open Registry of Patients with Psoriasis Who Are Candidates for Systemic Therapy Including Biologics.

17.5.9. Neratinib – NERLYNX (CAP) – EMA/PAM/0000319826

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Bianca Mulder

Scope: Interim report for the primary endpoint of the category 3 PASS DIANER study (PUMA-NER-6202): a randomized phase II study to evaluate the incidence of discontinuations due to diarrhoea at 3 cycles in patients with early stage HER2-positive (HER2+), Hormone Receptor-positive (HR+) breast cancer treated with neratinib plus loperamide prophylaxis versus neratinib with initial dose escalation plus PRN loperamide prophylaxis versus neratinib plus loperamide plus colesevelam prophylaxis.

17.5.10. Nirmatrelvir / Ritonavir – PAXLOVID (CAP) – EMA/PAM/0000320342

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Dennis Lex

Scope: The second interim (31 December 2025) report for study PASS C4671037, Safety of Paxlovid During Pregnancy.

17.5.11. Octocog alfa – KOVALTRY (CAP) – EMA/PAM/0000324429

Applicant: Bayer AG

PRAC Rapporteur: Dirk Mentzer

Scope: Submission of the 17th Annual EUHASS Report (reporting end: 31 Dec 2024) and the product specific report for Kovaltry as interim results for RMP registry study 14149.
PAM MEA: Kovaltry EMEA/H/C/003825/MEA/004.9

17.5.12. Ofatumumab – KESIMPTA (CAP) – EMA/PAM/0000321410

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Fourth interim study report for PASS Study COMB157G2407: Evaluation of pregnancy and infant outcomes in Kesimpta patients using Pregnancy outcomes Intensive Monitoring (PRIM) data – The Kesimpta-PRIM study.

17.5.13. Pegvaliase – PALYNZIQ (CAP) – EMA/PAM/0000319850

Applicant: Biomarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: First interim report for study BM 165-503: a multicenter, prospective, longitudinal study evaluating immunologic, inflammatory, and laboratory parameters associated with long-term Palynziq (pegvaliase) treatment in subjects with phenylketonuria (PKU) in the United States.

17.5.14. Pegvaliase – PALYNZIQ (CAP) – EMA/PAM/0000317250

Applicant: Biomarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Third interim report for study BM 165-504: a global multicentre study to assess maternal, foetal and infant outcomes of exposure to Palynziq (pegvaliase) during pregnancy and breastfeeding.

17.5.15. Pegvaliase – PALYNZIQ (CAP) – EMA/PAM/0000319171

Applicant: Biomarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Third interim study report for study BM 165-501: a multi-centre observational study to evaluate the long-term safety of subcutaneous injections of Palynziq (pegvaliase) in subjects with phenylketonuria.

17.5.16. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – MRESVIA (CAP) – EMA/PAM/0000316615

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Assessment of Post-Authorisation Active Surveillance Safety Studies Using Secondary Data to Monitor Real-World Safety of the mRNA-1345 Vaccine for respiratory syncytial virus (RSV) in the United States and in Europe (interim results for mRNA-1345-P902 and mRNA-1345-P903).

17.5.17. Respiratory syncytial virus vaccine (bivalent, recombinant) – ABRYSVO (CAP) – EMA/PAM/0000321444

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of 2nd progress report for PASS study C3671026 - A post-authorisation safety study of Abrysvo in pregnant women and their offspring in a real world setting in Europe and UK

17.5.18. Romosozumab – EVENITY (CAP) – EMA/PAM/0000319563

Applicant: UCB Pharma

PRAC Rapporteur: Tiphaine Vaillant

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

17.5.19. Ruxolitinib – OPZELURA (CAP) – EMA/PAM/0000317014

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the first study progress report for study INCB 88888-037: an observational post-authorisation study assessing the long-term risk of Non-Melanoma Skin Cancer (NMSC) among new users of Opzelura (ruxolitinib) cream in a vitiligo patient population.

17.5.20. Sotatercept – WINREVAIR (CAP) – EMA/PAM/0000319268

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Annual Report Data Cutoff Date: 14-APR-2025. An Open-label Long-term Follow-up Study to Evaluate the Effects of Sotatercept When Added to Background

Pulmonary Arterial Hypertension (PAH) Therapy for the Treatment of PAH (MK-7962-004). This stand alone MEA is submitted to address the Additional Pharmacovigilance Activity in the RMP approved at the time of the Marketing Authorization (MA).

17.5.21. Tildrakizumab – ILUMETRI (CAP) – EMA/PAM/0000321412

Applicant: Almirall S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Interim study results for the PASS M14745-40 of tildrakizumab in European Psoriasis Registries

17.5.22. Upadacitinib – RINVOQ (CAP) – EMA/PAM/0000320093

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Progress report for study P21-824: a study of growth and development in adolescents with atopic dermatitis who receive upadacitinib.

17.5.23. Upadacitinib – RINVOQ (CAP) – EMA/PAM/0000320090

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Progress report for Study P24-343: Long-Term Safety Study of Upadacitinib Use in Ulcerative Colitis and Crohn's Disease Patients in Europe.

17.5.24. Vimseltinib – ROMVIMZA (CAP) – EMA/PAM/0000321470

Applicant: Deciphera Pharmaceuticals (Netherlands) B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Feasibility report PASS DCC-3014-04-002
Long-term safety and tolerability of vimseltinib and further characterise the safety concerns of arterial hypertension, drug-induced livery injury (DILI), muscle injury/rhabdomyolysis, nephrotoxicity, cognitive disorders/CNS adverse events, and malignancies

17.6. New Scientific Advice

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

17.7. Ongoing Scientific Advice

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

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

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

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

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

18.1. Annual reassessments of the marketing authorisation

18.1.1. Defibrotide – DEFITELIO (CAP) – EMA/S/0000316340

Applicant: Gentium S.r.l.

PRAC Rapporteur: Mari Thorn

Scope: Annual reassessment of the marketing authorisation

18.1.2. Idebenone – RAXONE (CAP) – EMA/S/0000310527

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Annual reassessment of the marketing authorisation

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

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Entrectinib – ROZLYTREK (CAP) – EMA/R/0000319073

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.2. Futibatinib – LYTGOBI (CAP) – EMA/R/0000317381

Applicant: Taiho Pharma Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.2.3. Givinostat – DUVYZAT (CAP) – EMA/R/0000316670

Applicant: Italfarmaco S.p.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Conditional renewal of the marketing authorisation

18.2.4. Mirdametinib – EZMEKLY (CAP) – EMA/R/0000323237

Applicant: Springworks Therapeutics Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.5. Obecabtagene autoleucel – AUCATZYL (CAP) – EMA/R/0000319964

Applicant: Autolus GmbH

PRAC Rapporteur: Karin Erneholm

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Cabozantinib – COMETRIQ (CAP) – EMA/R/0000316559

Applicant: Ipsen Pharma

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

18.3.2. Fingolimod – FINGOLIMOD MYLAN (CAP) – EMA/R/0000314834

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.3. Vosoritide – VOXZOGO (CAP) – EMA/R/0000314604

Applicant: Biomarin International Limited

PRAC Rapporteur: Zane Neikena

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 09-12 March 2026 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 DoI	Topics for which restriction apply
Ulla Wändel Liminga [a,b]	Chair	Sweden	No interests declared	
Sonja Radowan [a,b]	Alternate	Austria	No interests declared	
Jean-Michel Dogné [a]	Member	Belgium	No restrictions applicable to this meeting	
Jo Robays [a,b]	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva [a]	Member	Bulgaria	No interests declared	
Stanislav Stoilov [a]	Alternate	Bulgaria	No interests declared	
Petar Mas [a]	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi [a,b]	Alternate	Croatia	No interests declared	
Panagiotis Psaras [a]	Member	Cyprus	No interests declared	
Elena Kaisis [a,b]	Alternate	Cyprus	No interests declared	
Eva Jirsová [a,b]	Member	Czechia	No interests declared	
Veronika Macurova [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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Terhi Lehtinen [a,b]	Member	Finland	No interests declared	
Kimmo Jaakkola [a,b]	Alternate	Finland	No interests declared	
Tiphaine Vaillant [a,b]	Member	France	No interests declared	
Zoubida Amimour [a,b]	Alternate	France	No participation in discussion, final deliberations and voting on:	7.4.1. EMA/VR/00002 87898 15.3.5. EMA/VR/00002 82554 15.3.8. EMA/VR/00003 19172 16.1.10. EMA/PSUR/000 0311144
Dennis Lex [a,b]	Member	Germany	No interests declared	
Dirk Mentzer [a]	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:	4.1.1. Gemcitabine (NAP) 16.2.2. EMA/PSUR/000 0311157
Julia Pallos [a,b]	Member	Hungary	No participation in discussion, final deliberations and voting on:	7.4.1. EMA/VR/00002 87898 15.3.5. EMA/VR/00002 82554 15.3.8. EMA/VR/00003 19172 16.1.10. EMA/PSUR/000 0311144
Melinda Palfi [a,b]	Alternate	Hungary	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Guðrún Stefánsdóttir [a,b]	Member	Iceland	No participation in discussion, final deliberations and voting on:	17.1.1. EMA/PASS/0000263976 17.3.1. EMA/PASS/0000262863
Rhea Fitzgerald [a,b]	Member	Ireland	No interests declared	
Eamon O Murchu [a,b]	Alternate	Ireland	No interests declared	
Amelia Cupelli [a,b]	Member	Italy	No interests declared	
Zane Neikena [a,b]	Member	Latvia	No interests declared	
Diana Litenboka [a,b]	Alternate	Latvia	No interests declared	
Rugile Pilviniene [a,b]	Member	Lithuania	No restrictions applicable to this meeting	
Lina Seibokiene [a]	Alternate	Lithuania	No interests declared	
Anne-Cecile Vuillemin [a,b]	Member	Luxembourg	No interests declared	
John Joseph Borg [a]	Member	Malta	No restrictions applicable to this meeting	
Liana Martirosyan [a,b]	Member (Vice-Chair)	Netherlands	No interests declared	
Bianca Mulder [a,b]	Alternate	Netherlands	No interests declared	
David Olsen [a,b]	Member	Norway	No participation in discussion, final deliberations and voting on:	4.1.2. Levonorgestrel intrauterine device 13.5 mg (NAP) 17.5.11. EMA/PAM/0000324429

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Pernille Harg [a,b]	Alternate	Norway	No interests declared	
Adam Przybylkowski [a]	Member	Poland	No restrictions applicable to this meeting	
Ana Sofia Diniz Martins [a,b]	Member	Portugal	No interests declared	
Carla Torre [a]	Alternate	Portugal	No restrictions applicable to this meeting	
Roxana Dondera [a,b]	Member	Romania	No interests declared	
Roxana Stefania Udrescu [a,b]	Alternate	Romania	No interests declared	
Miroslava Gocova [a,b]	Member	Slovakia	No interests declared	
Jana Pecherova [a,b]	Alternate	Slovakia	No interests declared	
Marjetka Plementas [a,b]	Alternate	Slovenia	No interests declared	
Maria del Pilar Rayon [a,b]	Member	Spain	No interests declared	
Maria Martinez Gonzalez [a,b]	Alternate	Spain	No interests declared	
Mari Thorn [a,b]	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin [a,b]	Alternate	Sweden	No restrictions applicable to this meeting	
Annalisa Capuano [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Milou-Daniel Drici [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Maria Teresa Herdeiro [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Patricia McGettigan [a,b]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Hedvig Marie Egeland Nordeng [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark [a]	Member	Independent scientific expert	No restrictions applicable to this meeting	
Roberto Frontini [a,b]	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Martin Votava [a,b]	Alternate	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Yiannoula Koulla [a]	Member	Patients' Organisation Representative	No interests declared	
Michal Rataj [a]	Alternate	Patients' Organisation Representative	No interests declared	
Flora Musuamba Tshinanu [a]	Expert	Belgium	No restrictions applicable to this meeting	
Martine Sabbe [a]	Expert	Belgium	No interests declared	
Chloé Wyndham-Thomas [a]	Expert	Belgium	No restrictions applicable to this meeting	
Behija Hudina [a]	Expert	Croatia	No restrictions	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
			applicable to this meeting	
Lucie Skalova [a]	Expert	Czech Republic	No interests declared	
Thalia Marie Estrup Blicher [a]	Expert	Denmark	No interests declared	
Marian Hjortlund Allon[b]	Expert	Denmark	No interests declared	
Line Praest Lauridsen [a]	Expert	Denmark	No restrictions applicable to this meeting	
Cecilie Louise Pedersen [a,b]	Expert	Denmark	No participation in discussion, final deliberations and voting on:	15.3.26. EMA/VR/0000264734 16.1.4. EMA/PSUR/0000311187
Helle Gerda Olsen [a]	Expert	Denmark	No interests declared	
Moritz Sander [a]	Expert	Denmark	No restrictions applicable to this meeting	
Pauline Dayani [a]	Expert	France	No interests declared	
Guillaume De Preneuf [a]	Expert	France	No interests declared	
Camille De-Kervasdoue [a]	Expert	France	No interests declared	
Sara Franco [a]	Expert	France	No interests declared	
Fatiha Karam [a]	Expert	France	No interests declared	
Zina Lanseur [a]	Expert	France	No restrictions applicable to this meeting	
Nathalie Morgensztejn [a]	Expert	France	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of DoI	Topics for which restriction apply
Christopher Schulze [a]	Expert	Germany	No interests declared	
Laura Zein [a,b]	Expert	Germany	No interests declared	
Sheena Kennedy [a]	Expert	Ireland	No restrictions applicable to this meeting	
Emer Maloney [a]	Expert	Ireland	No interests declared	
Bernice Aronsson [a]	Expert	Sweden	No interests declared	
Helena Back [a]	Expert	Sweden	No interests declared	
Charlotte Backman [a,b]	Expert	Sweden	No interests declared	
Jenny Jönsson [a]	Expert	Sweden	No participation in discussion, final deliberations and voting on:	15.3.18 EMA/VR/00003 16576
Hanna Kastman [a]	Expert	Sweden	No interests declared	
Karin Mathold [a]	Expert	Sweden	No restrictions applicable to this meeting	
Erika Svedlund[b]	Expert	Sweden	No interests declared	
Linnea Willdén Melin [a]	Expert	Sweden	No interests declared	
Asimina Zisi [a]	Expert	Sweden	No interests declared	
A representative from the European Commission attended the meeting.				
Observers from Health Canada attended the meeting.				
Meeting run with support from relevant EMA staff.				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

None

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.

Article 58 of Regulation (EC) No 726/2004 (EU-M4all)

Article 58 (EU-M4all) procedure 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).

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