29 April 2025
EMA/PRAC/132323/2025
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes of PRAC meeting on 10 - 13 March 2025

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

The Chairperson opened the 10-13 March 2025 meeting by welcoming all participants.

The meeting was held remotely.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates[1] and experts and on the topics in the agenda of the meeting, the Committee Secretariat announced the restricted involvement of some Committee members, alternates and experts for concerned agenda topics. Participants were asked to declare any changes, omissions or errors to their declared interests concerning the matters for discussion. No new or additional competing interests were declared. Restrictions applicable to this meeting are captured in the List of participants included in the minutes.

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

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

1.2. Agenda of the meeting on 10-13 March 2025

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

1.3. Minutes of the previous meeting on 10-13 February 2025

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

Post-meeting note: the PRAC minutes of the meeting held on 10-13 February 2025 were published on the EMA website on 09 April 2025 (EMA/PRAC/111789/2025).

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

2.1. Newly triggered procedures

None

[1] No alternates for COMP

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

None

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

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

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

See also Annex I 14.1.

4.1.1. Binimetinib – MEKTOVI (CAP); cobimetinib – COTELLIC (CAP); dabrafenib – TAFINLAR (CAP), FINLEE (CAP); encorafenib – BRAFTOVI (CAP); trametinib – MEKINIST (CAP), SPEXOTRAS (CAP); vemurafenib – ZELBORAF (CAP)

Applicants: Novartis Europharm Limited (Finlee, Mekinist, Spexotras, Tafinlar), Pierre Fabre

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

Medicament (Braftovi, Mektovi), Roche Registration GmbH (Cotellic, Zelboraf)

PRAC Rapporteur: Mari Thorn

Scope: Signal of tattoo associated skin reaction

EPITT 20160 – New signal

Background

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

During routine signal detection activities, a signal of tattoo associated skin reaction was identified by EMA, based on the literature and 27 cases retrieved from EudraVigilance for BRAF/MEK inhibitors. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from case reports in EudraVigilance and the literature, PRAC considered that further evaluation on the signal of tattoo associated skin reaction following administration of BRAF/MEK inhibitors is warranted.

Summary of recommendation(s)

- The MAHs for Mektovi (binimetinib), Cotellic (cobimetinib), Braftovi (encorafenib), Zelboraf (vemurafenib), dabrafenib-containing medicinal products Tafinlar and Finlee, and the trametinib-containing products Mekinist and Spexotras should submit to EMA, by 28 May 2025, a cumulative review of the signal, including a text string search for the word 'tattoo' within the case narratives, reporter comments or sender comments, as well as a review of the published literature, data from spontaneous reports and reports from studies and a discussion on possible biological plausibility and mechanism of this association. The MAHs should also discuss the need for an amendment to the product information and/or the RMP, as warranted.
- A 90-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.2. Signals follow-up and prioritisation

4.2.1. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/SDA/020; canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/SDA/017; dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/SDA/017, FORXIGA (CAP) - EMEA/H/C/002322/SDA/030, DAPAGLIFLOZIN VIATRIS, NAP; dapagliflozin, metformin - EBYMECT (CAP) - EMEA/H/C/004162/SDA/015, XIGDUO (CAP) - EMEA/H/C/002672/SDA/018, NAP; empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/SDA/019; empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/SDA/010; empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/SDA/012; ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/SDA/008; ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/SDA/006; ertugliflozin, sitagliptin - STEGLUJAN (CAP) -

EMEA/H/C/004313/SDA/007; saxagliptin, dapagliflozin - QTERN (CAP) - EMEA/H/C/004057/SDA/010

Applicants: AstraZeneca AB (Ebymect, Edistride, Forxiga, Qtern, Xigduo), Boehringer Ingelheim International GmbH (Glyxambi, Jardiance, Synjardy), Janssen-Cilag International N.V. (Invocana, Vokanamet), Merck Sharp & Dohme B.V. (Segluromet, Steglatro, Steglujan), Viatris Limited (Dapagliflozin Viatris), various

PRAC Rapporteur: Mari Thorn

Scope: Signal of sarcopenia

EPITT 20111 – Follow-up to September 2024

Background

For background information, see PRAC minutes September 2024.

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

Discussion

Having considered the available evidence from EudraVigilance, the literature and the responses of the MAHs, PRAC agreed that the current evidence is insufficient to establish a causal relationship between the sodium-glucose transporter 2 (SGLT2) inhibitors and sarcopenia to further warrant an update to the product information and/or the in light of the current knowledge.

Summary of recommendation(s)

- The MAHs for Invokana (canagliflozin), Vokanamet (canagliflozin/metformin), the dapagliflozin-containing products including Dapagliflozin Viatris, Edistride, Forxiga and its combinations with metformin including Ebymect and Xigduo, as well as Qtern (saxagliptin/dapagliflozin),Jardiance (empagliflozin), Glyxambi (empagliflozin/ linagliptin), Synjardy (empagliflozin/metformin), Steglatro (ertugliflozin), Segluromet (ertugliflozin/metformin hydrochloride) and Steglujan (ertugliflozin/sitagliptin) should continue to monitor sarcopenia events as part of routine pharmacovigilance.

4.2.2. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/SDA/006

Applicant: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of demyelinating disorders

EPITT 20124 – Follow-up to November 2024

Background

For background information, see PRAC minutes November 2024[4].

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

[4] Held 28 – 31 October 2024

Discussion

Having considered the available data from the published literature, spontaneous reports and reports from studies including all cases in the EudraVigilance database, and the responses of the MAH, PRAC agreed that the current evidence is insufficient to establish a causal relationship between ixekizumab and demyelinating disorders to further warrant an update to the product information and/or RMP in light of the current knowledge.

Summary of recommendation(s)

- The MAH for Taltz (ixekizumab) should continue to monitor these events as part of routine pharmacovigilance activities.

4.2.3. Tegafur, gimeracil, oteracil - TEYSUNO (CAP) - EMEA/H/C/001242/SDA/015

Applicant: Nordic Group B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Signal of hyperammonaemia

EPITT 20115 – Follow-up to November 2024

Background

For background information, see PRAC minutes November 2024.

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

Discussion

Having considered the available evidence in EudraVigilance, the literature, and the cumulative review submitted by the MAH and also biologically plausible mechanism, PRAC concluded that there is sufficient evidence to establish a causal association between Teysuno (tegafur/gimeracil/oteracil) and hyperammonaemia. Therefore, the product information should be updated to add hyperammonaemia as a warning and undesirable effect with a frequency 'rare'.

Summary of recommendation(s)

- The MAH for Teysuno (tegafur/gimeracil/oteracil) should submit to EMA, within 60 days, a variation to amend the product information[5].

4.3. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

PRAC provided advice to CHMP on the proposed RMPs for a number of products (identified by active substance below) that are under evaluation for initial marketing authorisation.

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

Information on the PRAC advice will be available in the European Public Assessment Reports (EPARs) to be published at the end of the evaluation procedure.

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

See also Annex I 15.1.

5.1.1. Autologous cartilage-derived articular chondrocytes, in-vitro expanded - (CAP MAA) - EMEA/H/C/004594

ATMP

Scope (pre D-180 phase): Repair of symptomatic, localised, full-thickness cartilage defects of the knee joint grade III or IV

5.1.2. Obecabtagene autoleucel - (CAP MAA) - EMEA/H/C/005907, PRIME, Orphan

Applicant: Autolus GmbH, ATMP

Scope (pre D-180 phase): Treatment of patients with relapsed or refractory B cell precursor acute lymphoblastic leukaemia (ALL)

5.1.3. Resmetirom - (CAP MAA) - EMEA/H/C/006220

Scope (pre D-180 phase): Treatment of adults with non-alcoholic steatohepatitis (NASH)/metabolic dysfunction-associated steatohepatitis (MASH) with liver fibrosis

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 also Annex I 15.3.

5.3.1. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/II/0036, Orphan

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: Update of sections 4.8, and 5.1 of the SmPC in order to update the list of adverse drug reactions (ADRs), and update clinical efficacy and safety information based on second interim analysis from study 68284528MMY3002 (CARTITUDE-4); this is a phase 3 randomized study comparing ciltacabtagene autoleucel, a chimeric antigen receptor T cell (CAR-T) therapy directed against BCMA, versus Pomalidomide, Bortezomib and Dexamethasone (PVd) or Daratumumab, Pomalidomide and Dexamethasone (DPd) in subjects with relapsed and lenalidomide-refractory multiple myeloma; The RMP version 5.3 has also been submitted. In addition, the MAH took the opportunity 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.

CHMP is evaluating a type II variation for Carvykti, a centrally authorised product containing ciltacabtagene autoleucel, to update the product information in order to update the list of adverse drug reactions (ADRs), and to update clinical efficacy and safety information based on second interim analysis from study 68284528MMY3002 (CARTITUDE-4). PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

Summary of advice

- The RMP version 5.6 for Carvykti (ciltacabtagene autoleucel) in the context of the variation under evaluation by CHMP is considered acceptable.
- PRAC agreed to update the product information to add myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) as warnings under the existing warning of 'secondary malignancies including myeloid and T-cell origin', as well as to classify them as important identified risks in the RMP. In addition, PRAC agreed to update the product information to add 'secondary malignancy of myeloid origin' as an undesirable effect with a frequency 'common'. Finally, PRAC agreed to update the important potential risk of 'secondary malignancy (except secondary malignancy of T-cell)' to 'secondary malignancy (except secondary malignancy of T-cell or myeloid origin)'.

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

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

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

Background

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

CHMP is evaluating a type II variation for Tysabri, a centrally authorised product containing natalizumab to update the product information to modify administration instructions to add the option for self-administration or administration by a caregiver and to update educational guidance, based on supportive data including final results from study 101MS330. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

Summary of advice

- The RMP for Tysabri (natalizumab) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 32.1 is submitted.
- PRAC considered that the patient card should be updated to include the message that the patients need to seek medical attention whenever they experience new symptoms indicative of progressive multifocal leukoencephalopathy (PML). In addition, the MAH should propose an updated checklist which (i) includes symptoms of PML, (ii) is to be used both by healthcare professionals outside a clinical setting (OCS) and by patients and caregivers when the patient or caregiver administers natalizumab subcutaneous (SC), and (iii) needs to be completed prior to each injection. This checklist should be listed in the RMP and in Annex II of the product information as an educational tool.

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) - PSUSA/00011000/202408

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

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.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should submit a comprehensive evaluation of cases of GIT lymphoma.

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.

Please also see section 5.3.1. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/II/0036, Orphan.

6.1.2. Dengue tetravalent vaccine (live, attenuated) - DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (Art 58[6]) - EMEA/H/W/005362/PSUV/0019

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUR procedure

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.
- Nevertheless, the product information should be updated to add petechia and thrombocytopenia as undesirable effects with frequency 'rare' and 'very rare', respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[7].
- In the next PSUR, the Scientific Opinion Holder (SOH) should discuss all cases concerning rhabdomyolysis and Guillain-Barré syndrome that have been reported without co-administration of other vaccines and other causes, such as wild-type dengue virus infection.

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

6.1.3. Dengue tetravalent vaccine[8] (live, attenuated) - QDENGA (CAP) - PSUSA/00011034/202408

Applicant: Takeda GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Background

[6] Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)
[7] 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.
[8] Dengue virus, serotype 2, expressing Dengue virus, serotype 1, surface proteins, live, attenuated / Dengue virus, serotype 2, expressing Dengue virus, serotype 3, surface proteins, live, attenuated / Dengue virus, serotype 2, expressing Dengue virus, serotype 4, surface proteins, live, attenuated / Dengue virus, serotype 2, live, attenuated

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 add petechia and thrombocytopenia as undesirable effects with frequency 'rare' and 'very rare', respectively. Therefore, the current terms of the marketing authorisation(s) should be varied[9].
- In the next PSUR, the MAH should discuss all cases concerning rhabdomyolysis and Guillain-Barré syndrome that have been reported without co-administration of other vaccines and other causes, such as wild-type dengue virus infection.

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

6.1.4. Lisocabtagene maraleucel - BREYANZI (CAP) - PSUSA/00010990/202408

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Breyanzi, a centrally authorised medicine containing lisocabtagene maraleucel 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 Breyanzi (lisocabtagene maraleucel) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning regarding virus reactivation by adding reactivation of John Cunningham virus leading to progressive multifocal leukoencephalopathy (PML). Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAH should provide a cumulative review of myelodysplastic syndrome (MDS) and/or acute myeloid leukaemia (AML) including cases from randomised controlled clinical studies, and should discuss the need to amend the product information and/or the RMP as warranted. In addition, the MAH should present an update on the progress to improve second primary malignancy (SPM) sample follow-

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

up and testing, indicating also the number of interval sample requests, samples tested and subsequent results or test failures.

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.

6.1.5. Natalizumab - TYRUKO (CAP); TYSABRI (CAP) - PSUSA/00002127/202408

Applicant: Sandoz GmbH (Tyruko), Biogen Netherlands B.V. (Tysabri)

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of the natalizumab-containing products Tyruko and Tysabri in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.

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 MAH Biogen Netherlands B.V. should address, within an upcoming regulatory procedure affecting the RMP or at the latest by 07 February 2026, a revision of the educational materials, focusing on the most practical information to prevent and manage the risk of progressive multifocal leukoencephalopathy (PML), while reducing academic aspects such as MRI guides, as well as reviewing the overall number of documents both for health care professionals and patients/care givers. This simplification should then also be reflected in Annex II of the product information.

6.1.6. Saxagliptin, dapagliflozin - QTERN (CAP) - PSUSA/00010520/202407

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Qtern, a centrally authorised medicine containing saxagliptin/dapagliflozin 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 Qtern (saxagliptin/dapagliflozin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding increased haematocrit. Therefore, the current terms of the marketing authorisation(s) should be varied[11].
- In the next PSUR, the MAH should provide a cumulative review of (groin) abscesses on different locations and discuss any potential amendments on the product information as warranted. In addition, the MAH follow the outcome of the upcoming PSUSA for dapagliflozin (PSUSA/00010029/202410) regarding the request to review all cases of Fournier's gangrene reported with dapagliflozin in the context of urological surgery, and act as warranted.

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

6.1.7. Talquetamab - TALVEY (CAP) - PSUSA/00000099/202408

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Talvey, a centrally authorised medicine containing talquetamab 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 Talvey (talquetamab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the warning on skin toxicity to add palmar-plantar erythrodysesthesia syndrome and as undesirable effect with frequency 'common'. In addition, the existed undesirable effect of oral pain should be moved under SOC 'Gastrointestinal disorders'. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAH should continue to evaluate all available cumulative data from clinical trials, post marketing and literature on Grade 3 immune effector cell-associated neurotoxicity syndrome (ICANS), to provide the interval cases of cytokine release syndrome (CRS), and to discuss any need to update the product information, as warranted.

[11] Update of SmPC section 4.4. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[12] 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.

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. Tisagenlecleucel - KYMRIAH (CAP) - PSUSA/00010702/202408

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Kymriah, a centrally authorised medicine containing tisagenlecleucel 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 Kymriah (tisagenlecleucel) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the frequency of immune effector cell-associated neurotoxicity syndrome (ICANS) undesirable effect to 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[13].
- In the next PSUR, the MAH should continue to monitor life-threatening serious neurological adverse reactions (SNARs).

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 MAH should re-consider removing the pharmacy/cell lab/infusion centre training material from the RMP at the next regulatory opportunity, provided that all relevant information on the handling and storage of the product is available at treatment sites and that new personnel is adequately trained in its handling.

6.1.9. Upadacitinib - RINVOQ (CAP) - PSUSA/00010823/202408

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

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).

[13] Update of SmPC section 4.8. The PRAC AR and PRAC recommendation are transmitted to CAT and CHMP for adoption of an opinion.

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Rinvoq (upadacitinib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding retinal vein occlusion. Therefore, the current terms of the marketing authorisation(s) should be varied[14].
- In the next PSUR, the MAH should provide a cumulative review of cases where product residue present in stool is co-reported with lack of efficacy including data from clinical trials, literature and post-marketing sources. In addition, the MAH should provide a cumulative review with the following MedDRA preferred terms (PTs): vision blurred, amaurosis fugax, blindness transient, eye infarction, ophthalmic artery thrombosis, ophthalmic vascular thrombosis, retinal artery occlusion, retinal artery thrombosis, blindness, blindness cortical and blindness unilateral as well as embolic and thrombotic events narrow SMQ co-reported with events of blindness, blindness cortical and blindness unilateral. In addition, the MAH should continue to monitor cases of semen discolouration and eczema herpeticum. The MAH should also discuss any need to amend the product information, as warranted.

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

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

None

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

See also Annex I 16.3.

6.3.1. Anastrozole (NAP) - PSUSA/00000210/202408

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Background

Anastrazole is a selective non-steroidal aromatase inhibitor (NSAI) 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

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

tamoxifen and primary prevention of breast cancer in postmenopausal women at moderate or high risk, as warranted.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing anastrazole 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 anastrazole-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add dry eye, lichenoid eruption, tendonitis, tendon rupture and memory impairment as undesirable effects with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[15].
- In the next PSUR, the MAHs should closely monitor cases of eye disorders including macular hole, retinal vascular disorder, maculopathy, retinal haemorrhage, retinal detachment, retinal artery occlusion, retinal tear, retinal degeneration, vitreoretinal traction syndrome. In addition, the MAHs should monitor cases of memory impairment and related terms from all sources with a particular focus on the reversibility of memory impairment after cessation of anastrozole, and discuss any need to update the product information regarding the reversibility of this condition, as warranted.

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

6.3.2. Chlorocresol, chlorhexidine, hexamidine (NAP) - PSUSA/00001603/202408

Applicant(s): various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

Background

Chlorocresol/chlorhexidine/hexamidine is a combination indicated for cleansing of primary bacterial skin and mucosal disorders, and those liable to become superinfected.

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

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

- Nevertheless, the product information should be updated to amend the warning on hypersensitivity reactions to include allergic contact dermatitis with chlorocresol, as well as to amend the relevant footnotes. Therefore, the current terms of the marketing authorisation(s) should be varied[16].
- In the next PSUR, the MAHs should present and discuss data on post-authorisation use in special populations and data on other post-authorisation use.

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

6.3.3. Magnesium sulfate, sodium sulfate, potassium sulfate (NAP) - PSUSA/00010239/202408

Applicant(s): various

PRAC Lead: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

Background

Magnesium sulfate/sodium sulfate/potassium sulfate is a sulfate-based laxative indicated for bowel cleansing prior to any procedure requiring a clean bowel (e.g. bowel visualization during an endoscopic or radiological exploration or surgical procedure) in adults.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing magnesium sulfate/sodium sulfate/potassium sulfate 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 magnesium sulfate/sodium sulfate/potassium sulfate-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add cardiac arrhythmia as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[17].

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. Montelukast (NAP) - PSUSA/00002087/202407

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

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

Background

Montelukast is a leukotriene receptor antagonist indicated for the treatment of asthma and in allergic rhinitis, as warranted.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing montelukast 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 montelukast-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH Organon should provide a concise review of any new relevant data, including new data from clinical trials, epidemiological studies, post marketing setting and literature to estimate the frequencies of the existing neuropsychiatric undesirable events, including a discussion on the need to update the product information and risk minimisation measures, as warranted. In addition, the MAHs should provide an updated evaluation regarding their relevant data for the risk of neuropsychiatric events in different age groups, while the MAH Organon should also provide a literature review on the topic.

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. Naphazoline (NAP); naphazoline, zinc sulphate (NAP) - PSUSA/00010571/202407

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Background

Naphazoline is a sympathomimetic vasoconstrictor. Zinc sulphate is a topical antibacterial agent with astringent properties. Naphazoline is indicated for the symptomatic treatment of mild to severe cases of eye irritation, lacrimation, redness, burning sensation, light sensitivity, itching, congestion, and allergic and inflammatory states of the conjunctiva, as warranted. In addition, it is indicated as a nasal decongestant in acute catarrhal rhinitis and pharyngitis, allergic rhinitis, acute sinusitis and in nasal, paranasal and nasopharyngeal inflammatory processes in general, as warranted. Naphazoline/zinc sulphate is a combination indicated for redness of the eyes, sensation of a foreign body or heaviness in the eyelids.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing naphazoline and naphazoline/zinc sulphate, 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 naphazoline- and naphazoline/zinc sulphate-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add severe cardiovascular and/or cerebrovascular events related to excessive systemic exposure following acute or prolonged overdose. Therefore, the current terms of the marketing authorisation(s) should be varied[18].
- In the next PSUR, the MAHs should include 'psychoactive effects with excessive use, leading to addiction/dependence' as a new important potential risk and to continue monitoring the risk.

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

6.4. Follow-up to PSUR/PSUSA procedures

See also Annex I 16.3.1.

6.4.1. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/LEG 064.1

Applicant: Alexion Europe SAS

PRAC Rapporteur: Monica Martinez Redondo

Scope: MAH response to PSUR#19 (EMEA/H/C/PSUSA/00001198/202310) as adopted in October 2024

From PSURx (EMEA/H/C/PSUSA/00001198/202310 - #19
The MAH for Soliris is requested, to provide cumulative data from all the available sources in a tabulated format for all the hepatotoxicity cases (irrespective of whether, according to the MAH, they have alternative aetiologies) with transaminases elevation and clinical consequences, reported with eculizumab until de DLP of this PSUR.

Background

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

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit further data on hepatotoxicity. The responses were assessed by the Rapporteur for further PRAC advice. For further background, see PRAC minutes May 2024 and PRAC minutes October 2024.

Summary of advice/conclusion(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed that the product information of Soliris (eculizumab) should be updated to add liver injury as an undesirable effect with a frequency 'not known'. In the next PSUR, the MAH should

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

continue to monitor cases of hepatic failure, hepatic cirrhosis, hepatomegaly, portal hypertension and hepatosplenomegaly.

- The MAH should submit to EMA, within 60 days, a variation to update the product information[19].

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/II/0054, Orphan

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Jana Lukacisinova

Scope: To update sections 4.2, 4.4, 4.8 of the SmPC to include Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS); and to update section D of Annex II to remove educational materials for physicians, pharmacists and nurses and to include ICANS within neurologic events in educational material for patient/caregivers and patient alert card following the outcome of PSUR procedure EMEA/H/C/PSUSA/00010460/202212. The Package Leaflet is updated accordingly. The RMP version 17.0 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.

Following the evaluation of the most recently submitted PSUR(s) for the above-mentioned medicine(s), PRAC requested the MAH to submit a variation to update the product information to include ICANS as undesirable effect, as well as to update the educational materials. 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 July 2023, PRAC minutes February 2024, PRAC minutes July 2024 and PRAC minutes December 2024.

Summary of recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed with the update of the product information to include information about the risk of ICANS, including Grade 3 and higher ICANS, and recommendations on monitoring and treatment of ICANS with dexamethasone[20]. PRAC also agreed to remove the educational materials for physicians and pharmacists from Annex II-D as they are no longer considered necessary, to update the educational materials for patients (including patient card) on ICANs and to update the educational material for nurses to include the complete Cornell Assessment of Paediatric Delirium (CAPD) scoring system.

6.6. Expedited summary safety reviews[21]

None

[19] Update of SmPC section 4.8. The package leaflet is updated accordingly.
[20] Update of SmPC sections 4.2, 4.4 and 4.8. The package leaflet is updated accordingly.
[21] 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)[22]

None

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[23]

See Annex I 17.2.

7.3. Results of PASS imposed in the marketing authorisation(s)[24]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[25]

See also Annex I 17.4.

7.4.1. Brigatinib- ALUNBRIG (CAP) - EMEA/H/C/004248/II/0056

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Carla Torre

Scope: Submission of the final report from Brigatinib-5007 study listed as a category 3 study in the RMP. This is a non-interventional cohort study to provide real-world evidence of the occurrence of early-onset pulmonary events in patients with anaplastic lymphoma kinase-positive advanced non-small cell lung cancer treated with brigatinib: a post-authorisation safety study. The RMP version 7 has also been submitted. The MAH proposes the removal of the additional risk minimization measure, the Alunbrig Patient Alert Card (PAC), for the risk of early-onset pulmonary events (EOPEs). In addition, the MAH took the opportunity to introduce editorial changes to the PI

Background

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

As stated in the RMP of Alunbrig (brigatinib), the MAH conducted a non-imposed non-interventional PASS to provide real-world evidence of the occurrence of early-onset pulmonary events in patients with anaplastic lymphoma kinase-positive advanced non-small cell lung cancer treated with brigatinib. The Rapporteur assessed the MAH's final study report.

Summary of advice

- Based on the available data and the Rapporteur's review, PRAC considered that the

[22] In accordance with Article 107n of Directive 2001/83/EC
[23] 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
[24] In accordance with Article 107p-q of Directive 2001/83/EC
[25] 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

ongoing variation assessing the final study report could be recommended for approval.

- PRAC agreed with the removal of the PAC as additional risk minimisation measure to address the risk of EOPEs from the RMP and from Annex II, taking into account the results of the study, but also the totality of existing evidence and the well-characterised safety profile. PRAC also agreed to remove the EOPEs from the list of safety concerns, as well as the category 3 PASS study Brigatinib-5007 from the RMP.

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

See Annex I 17.4.1.

7.6. Others

See Annex I 17.5.1.

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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

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

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

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

8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1.

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.1.1.

8.3. Renewals of the marketing authorisation

See Annex I 18.2.1.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC membership

None

12.1.2. Vote by proxy

Rugile Pilviniene gave a proxy to Zane Neikena for 11 and 13 March 2025.

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Scientific Advice Working Party (SAWP) - SAWP-PRAC consultation procedure

The EMA Secretariat presented a proposal for a revised process for PRAC involvement in scientific advice procedures. The key changes include: implementing a single simplified process and guidance for SAWP-PRAC consultation (non-PASS) and PASS procedures, clarifications on the PRAC Peer-reviewers' role in different stages of the procedure and further updates to reflect IRIS implementation. PRAC members were invited to send their comments

Post-meeting note: The guidance document was endorsed by PRAC on 21 March 2025.

12.3.2. Patients' and Consumers' Working Party (PCWP) – revised mandate and composition

In order to align with the recent restructuring of EMA working parties, the EMA Secretariat presented to PRAC the revised mandate and composition of the PCWP. PRAC agreed with the revision.

12.3.3. Healthcare Professionals' Working Party (HCPWP) - revised mandate and composition

In order to align with the recent restructuring of EMA working parties, the EMA Secretariat presented to PRAC the revised mandate and composition of the HCWP. PRAC agreed with the revision.

12.3.4. Patients' and Consumers' Working Party (PCWP) and Healthcare Professionals' Working Party (HCPWP) - revised rules of procedure

The EMA Secretariat presented to PRAC the revised rules of procedure of the PCWP and HCPWP which aim to align with the working parties' objective to 'Contribute as appropriate to EMA's initiatives to enhance the medicines-development process, bridge gaps in

medicines development and supply as well as to address the challenges of new and emerging science', stated in their respective mandate. PRAC endorsed the revised rules of procedure, due also for adoption at the other EMA Committees.

12.4. Cooperation within the EU regulatory network

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

The EMA Secretariat presented to PRAC an update of the cases and outbreaks of measles, Mpox, and Ebola virus disease, as well as the status of the vaccination against Mpox, currently circulating COVID-19 variants and new variant-adapted COVID-19 vaccines. PRAC noted the information.

12.5. Cooperation with International Regulators

12.5.1. International Conference on Harmonisation (ICH) E22 on general considerations for patient preference studies (PPS)

The EMA Secretariat provided to PRAC an overview of the background work involved in developing the guideline on 'General Considerations for Patient Preference Studies', along with the initiative's objectives. Additionally, the EMA Secretariat elaborated on the concept of patient preference studies and outlined the current status and future steps in drafting the technical document. PRAC noted the information, and the members were invited to provide any comments in writing

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: Jana Lukacisinova

The EMA Secretariat together with the GPAG Chair presented to PRAC some proposals/actions in relation to the PRAC workload provisioned for 2025 based on the new PSUR frequencies predicted by the EURD Tool. PRAC agreed to further discuss the proposals also as part of the Strategic and Review Learning Meeting in Warsaw, Poland (01-02 April 2025).

12.10.3. PSURs repository

None

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

In line with the criteria for plenary presentation of updates to the EURD List adopted by PRAC in December 2021, PRAC endorsed the draft revised EURD list, version March 2025 reflecting the PRAC's comments impacting on the data lock point (DLP) and PSUR submission frequencies of the substances/combinations. PRAC endorsed the newly allocated Rapporteurs for upcoming PSUSAs in accordance with the principles previously endorsed by PRAC (see PRAC minutes April 2013).

Post-meeting note: following the PRAC meeting of March 2025, the updated EURD list was adopted by CHMP and CMDh at their March 2025 meetings and published on the EMA website, see: Home> Human Regulatory>Post-authorisation>Pharmacovigilance>Periodic safety update reports>> List of Union reference dates and frequency of submission of periodic safety update reports (PSURs)

12.11. Signal management

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

None

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. 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.

12.14. 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. Draft Reflection Paper on Patient Experience Data (PED) for internal consultation

PRAC lead: Ulla Wändel Liminga, Carla Torre

The EMA Secretariat provided a brief overview of PED, including types of PED and its relevance to pharmacovigilance and risk minimisation. A reflection paper was developed by a drafting group consisting of members from several EMA Committees and selected Working Parties. This paper serves as a framework for discussion, particularly in areas where scientific knowledge is fast evolving or regulatory experience is limited. PRAC members were invited to send their comments in writing on the draft reflection paper.

12.21.2. IncreaseNet - Joint Action on Capacity Building - On-the-job training and -coaching pilot plan for National Competent Authorities' assessors

PRAC lead: Martin Huber

The project lead and the PRAC member Martin Huber presented to PRAC an overview of IncreaseNET, a project co-funded by the EU4Health Programme, and coordinated by the Agency for Medicinal Products and Medical Devices of the Republic of Slovenia (JAZMP). The aim of the joint action is to strengthen capacity and competence building of European national medicines agencies in the field of medicines assessment, thereby ensuring better access to innovative, high-quality, effective and safe medicines for patients. The Federal Institute for Drugs and Medical Devices in Germany (BfArM) is leading Work Package 6, which aims to implement an on-the-job learning and -coaching programme for national competent authorities' assessors. The project started at the level of CHMP in 2024, and the

aim is to expand it to the level of PRAC in 2025. PRAC welcomed the initiative and agreed to start the project at the PRAC level, initially focusing on initial marketing authorisation applications and exploring whether other procedures like PSUSAs could be enrolled as well. However, further discussions are needed in order to clarify the practical process behind. PRAC will be informed accordingly.

12.21.3. Revision of Good Pharmacovigilance Practices (GVP) product- or Population-Specific Considerations I: Vaccines for prophylaxis against infectious diseases - update

PRAC lead: Jean-Michel Dogné

The EMA Secretariat provided an update on the ongoing work to revise the Guideline on GVP for vaccines used to prevent infectious diseases. This included identifying areas that require revision, introducing new concepts, and outlining the responsibilities of the drafting group involved in this process, which is also part of the PRAC workplan for 2025. The next steps and timelines for completing the guideline review and conducting the public consultation were also presented. PRAC agreed with the proposal.

12.21.4. Reflection paper on 'Use of real-world data to generate real-world evidence in non-interventional studies'

The EMA Secretariat presented the scope and objectives of the reflection paper, including an overview of the steps involved in its development. The EMA Secretariat also presented the comments and amendments received during the public consultation, as well as the next steps, which include publication of the reflection paper. PRAC noted the information.

12.21.5. Revision of EMA policy 0044 on handling of competing interests for scientific committees' members and experts

The main changes in the revision of policy 0044, the updated declaration of interests form and the next steps for experts were presented to the committee. Committee members and all experts are requested to submit an updated declaration of interests by 1 May 2025.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[26]

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[27].

[26] 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

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

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Leflunomide – ARAVA (CAP), LEFLUNOMIDE MEDAC (CAP), LEFLUNOMIDE RATIOPHARM (CAP), LEFLUNOMIDE ZENTIVA (CAP); NAP

Applicant(s): Medac Gesellschaft fur klinische (Leflunomide medac), Ratiopharm GmbH (Leflunomide ratiopharm), Sanofi-Aventis Deutschland GmbH (Arava), Zentiva, k.s. (Leflunomide Zentiva), various

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of pulmonary nodule

EPITT 20155 – New signal

14.2. New signals detected from other sources

None

15. Annex I – Risk management plans

15.1. Medicines in the pre-authorisation phase

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

15.1.1. Aflibercept - (CAP MAA) - EMEA/H/C/006745

Scope: Treatment of age-related macular degeneration (AMD) and visual impairment

15.1.2. Aflibercept - (CAP MAA) - EMEA/H/C/006192

Scope (pre D-180 phase): Treatment of age-related macular degeneration (AMD) and visual impairment

15.1.3. Denosumab - (CAP MAA) - EMEA/H/C/006269

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

15.1.4. Denosumab - (CAP MAA) - EMEA/H/C/006268

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

15.1.5. Denosumab - (CAP MAA) - EMEA/H/C/006526

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

15.1.6. Denosumab - (CAP MAA) - EMEA/H/C/006534

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

15.1.7. Dorocubicel, allogeneic umbilical cord-derived CD34- cells, non-expanded - (CAP MAA) - EMEA/H/C/005772, PRIME, Orphan

Applicant: Cordex Biologics International Limited, ATMP

Scope (pre D-180 phase): Treatment of adult patients with haematological malignancies

15.1.8. Emtricitabine, tenofovir alafenamide - (CAP MAA) - EMEA/H/C/006469

Scope (pre D-180 phase): For the treatment of human immunodeficiency virus type 1 (HIV-1)

15.1.9. Tegomil fumarate - (CAP MAA) - EMEA/H/C/006427

Scope (pre D-180 phase): Treatment of multiple sclerosis

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. Avanafil – SPEDRA (CAP) - EMA/VR/0000243987

Applicant(s): Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of an updated RMP version 6.0 in order to align with the GVP Module V on Risk Management Systems (EMA/838713/2011 Rev2*, 28 March 2017) and to update the list of safety concerns, according to the outcome of the latest two PSUSA procedures (EMEA/H/C/PSUSA/00010066/202006 and EMEA/H/C/PSUSA/00010066/202306)

15.2.2. Clopidogrel - ISCOVER (CAP) - EMEA/H/C/000175/WS2808/0158; Clopidogrel - PLAVIX (CAP) - EMEA/H/C/000174/WS2808/0160

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Carla Torre

Scope: C.I.11.z (IB) - To provide a new RMP version to update the FUQ in Annex 4.

Furthermore, the Marketing Authorisation Holder has taken the opportunity to update Part I Table 5 Product overview following approval of EMEA/H/C/WS/2150

15.2.3. Umeclidinium, vilanterol - ANORO ELLIPTA (CAP) - EMEA/H/C/002751/WS2815/0049;

Umeclidinium, vilanterol - LAVENTAIR ELLIPTA (CAP) - EMEA/H/C/003754/WS2815/0052

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP version 10.0 for Anoro Ellipta and Laventair Ellipta Inhalation powder, pre-dispensed [55µg/ 22µg] following completion of Category 1 PASS 201038 in order to remove the safety concerns accordingly

15.2.4. Umeclidinium bromide - INCRUSE ELLIPTA (CAP) - EMEA/H/C/002809/WS2816/0043; Umeclidinium - ROLUFTA ELLIPTA (CAP) - EMEA/H/C/004654/WS2816/0027

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP version 8.0 for Incruse Ellipta and Rolufta Ellipta in order to reflect the completion of the category 1 PASS study 201038 and remove the safety concerns accordingly

15.2.5. Zoledronic Acid – ZOLEDRONIC ACID ACCORD (CAP); NAP - EMA/VR/0000226953

Applicant(s): Accord Healthcare S.L.U., various

PRAC Rapporteur: Karin Erneholm

Scope: To align the RMP for Zoledronic Acid Accord with the RMP of the reference product. In addition for the nationally authorised products Zoledronic Acid Accord 4 mg/5 ml, 4 mg/100 ml concentrate for solution for infusion (product reference PT/H/0742/001/DC) the RMP is being merged with the RMP of the centrally authorised product

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

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

15.3.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/II/0025

Applicant: AstraZeneca AB

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Extension of indication to include CALQUENCE in combination with bendamustine and rituximab (BR) as treatment of adult patients with previously untreated Mantle Cell Lymphoma (MCL) based on interim results from study ACE-LY-308 (ECHO, D8220C00004); this is a Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter Study of Bendamustine and Rituximab (BR) Alone Versus in Combination with Acalabrutinib (ACP-196) in Subjects with Previously Untreated Mantle Cell Lymphoma. 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 6, succession 1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC. As part

of the application the MAH is requesting a 1-year extension of the market protection

15.3.2. Adagrasib - KRAZATI (CAP) - EMEA/H/C/006013/II/0010/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: A grouped application consisting of:

C.I.4: Update of section 5.1 of the SmPC based on final results from study 849-012 (KRYSTAL-12) listed as a specific obligation in the Annex II. This is a Randomized Phase 3 Study of MRTX849 versus Docetaxel in Patients with Previously Treated Non-Small Cell Lung Cancer with KRAS G12C Mutation. The Package Leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to update Annex IIE of the PI.

C.I.4: Update of section 4.8 of the SmPC in order to update safety information based on an integrated analysis of data from interventional studies 849-012 (KRYSTAL-12), 849-007 (KRYSTAL-7) and 849-001 (KRYSTAL-1)

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

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Karin Bolin

Scope: Grouped quality variations

15.3.4. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/002548/II/0053

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 9.12 to include changes made to the pharmacokinetic study CUV052 including the inclusion of adolescent patients in the protocol. CUV052 is an interventional study to evaluate the pharmacokinetics of afamelanotide in patients with Erythropoietic Protoporphyria (EPP)

15.3.5. Asciminib - SCEMBLIX (CAP) - EMEA/H/C/005605/II/0017, Orphan

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: Submission of a comprehensive final analysis of the data from study CABL001X2101, listed as a category 3 study in the RMP. This is a phase I, multicenter, open-label study of oral asciminib in patients with chronic myelogenous leukemia or Philadelphia Chromosome-positive acute lymphoblastic leukemia. The RMP version 2.0 has also been submitted

15.3.6. Avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/II/0051

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to add "neutropenia" to the list of adverse drug reactions (ADRs) with frequency "not known" based on post marketing data and literature. The Package Leaflet is updated accordingly. The RMP version 8.2 has also been submitted. In addition, the MAH took the opportunity to update the PI in accordance with the latest EMA excipients guideline

15.3.7. Bosutinib - BOSULIF (CAP) - EMEA/H/C/002373/X/0058/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Extension application to introduce a new pharmaceutical form (hard capsules) associated with two new strengths (50 mg and 100 mg) grouped with an extension of indication (C.I.6.a) to include treatment of paediatric patients greater than or equal to 1 year of age with newly-diagnosed (ND) chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukaemia (Ph+ CML) for BOSULIF, based on interim results from study ITCC-054/AAML1921 (BCHILD); this is a phase 1/2, multicenter, international, single-arm, open-label study of bosutinib in pediatric patients with newly diagnosed chronic phase or resistant/intolerant Ph+ chronic myeloid leukemia. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly. Version 7.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the Product Information

15.3.8. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/II/0040

Applicant: Ipsen Pharma

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include the treatment of adult patients with progressive extra-pancreatic (epNET) and pancreatic (pNET) neuroendocrine tumours after prior systemic therapy for CABOMETYX based on final results from study CABINET (A021602). This is a multicenter, two-arm, randomised, double-blind, placebo-controlled phase 3 study investigating cabozantinib versus placebo in patients with advanced Neuroendocrine Tumors (NET). 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 8.0 of the RMP has also been submitted

15.3.9. Dalbavancin - XYDALBA (CAP) - EMEA/H/C/002840/II/0050

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to include the treatment of acute bacterial skin and skin structure infections (ABSSSI) in paediatric patients from birth, including paediatric patients aged less than 3 months with suspected or confirmed sepsis associated with skin and subcutaneous tissue infections for Xydalba, based on final results from study DUR001-306,

together with data from three Phase 1 PK studies (A8841004, DUR001-106, and DUR001-107 (DAL-PK-02); DUR001-306 was a Phase 3, multicenter, open-label, randomized, comparator controlled trial evaluating the safety and efficacy of a single dose of IV dalbavancin and a 2-dose regimen of once weekly IV dalbavancin (for a total of 14 days of coverage) for the treatment of ABSSSI known or suspected to be due to susceptible Gram-positive organisms in children. 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 8.0 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 to update the list of local representatives in the Package Leaflet in line with the latest QRD template version 10.4

15.3.10. Elranatamab - ELREXFIO (CAP) - EMEA/H/C/005908/II/0005

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Update of section 4.2 of the SmPC to add every four-week dosing schedule after at least 24 weeks of every two-week dosing and to update the recommendations for restarting therapy following dose delay, and update of sections 4.8, 5.1 and 5.2 of the SmPC with long-term efficacy, safety, and clinical pharmacology results (≥2 years of follow-up after the last participant initial dose), based on the final study report of Study C1071003; a Phase 2, open-label, multicentre, non-randomised study of elranatamab monotherapy in participants with MM who are refractory to at least one PI, one IMiD, and one anti-CD38 Ab. The Package Leaflet has been updated in accordance. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and to update the list of local representatives in the Package Leaflet. Further, the provision of the final study report addresses SOB 001, and Annex II has been updated accordingly. A revised RMP version 1.2 was provided as part of the application

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

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

15.3.12. Enzalutamide - ENZALUTAMIDE VIATRIS (CAP) - EMEA/H/C/006299/X/0003

Applicant: Viatris Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension application to add a new strength of 160 mg for solution for film-coated tablets.
The RMP (version 1.0) is updated in accordance

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

Applicant: Marinus Pharmaceuticals Emerald Limited

PRAC Rapporteur: Adam Przybylkowski

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

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

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

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

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

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

15.3.14. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0044

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication for TREMFYA to include treatment of adult patients with moderately to severely active Crohn's disease (CD) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic treatment, based on results from GALAXI Phase 2/3 program and the GRAVITI Phase 3 study. GALAXI is a Phase 2/3, randomized, double-blind, placebo- and active-controlled, parallel-group, multicenter protocol to evaluate the efficacy and safety of guselkumab in participants with moderately to severely active CD who have demonstrated an inadequate response or failure to tolerate previous conventional or biologic therapy. GRAVITI is a Phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate the efficacy and safety of guselkumab SC induction therapy in participants with moderately to severely active CD.
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 10.1 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection

15.3.15. Herpes zoster vaccine (recombinant, adjuvanted) - SHINGRIX (CAP) - EMEA/H/C/004336/II/0076

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of sections 4.8 and 5.1 of the SmPC to include the final results of study ZOSTER-049, listed as a category 3 study in the RMP. This is a Phase 3b, open label, multi-country, long-term follow-up study that assessed the prophylactic efficacy, safety, and immunogenicity persistence of Shingrix in adults ≥50 years of age at the time of primary vaccination in studies ZOSTER 006 and ZOSTER-022. The study also assessed 1 or 2 additional doses of Shingrix on a 0 or 0, 2-month schedule in two subgroups of older adults. The updated RMP version 8.0 is also included. In addition, the MAH took the opportunity to implement editorial changes to the SmPC, Labelling and Package Leaflet; and to bring the PI in line with the latest QRD template version 10.4

15.3.16. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - FLUCELVAX (CAP) - EMEA/H/C/006532/II/0001

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of children from 6 months of age and older for FLUCELVAX, based on results from study V130_14. This is a Phase III, Randomized, Observer-blind, Multicenter Study to Evaluate the Efficacy, Immunogenicity and Safety of Seqirus Cell-Based Quadrivalent Subunit Influenza Virus Vaccine (QIVc) Compared to a Non-Influenza Vaccine When Administrated in Healthy Subjects Aged 6 Months Through 47 Months. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 4.0 of the RMP is also being submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the MAH took the opportunity to implement changes to sections 4.4 and 4.5 of the SmPC

15.3.17. Ivosidenib - TIBSOVO (CAP) - EMEA/H/C/005936/II/0012, Orphan

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of an updated RMP version 2.1 for TIBSOVO and a replacement study protocol for study S095031-218. This is a phase 1, multicenter, open-label, safety and pharmacokinetic study of orally administered ivosidenib in participants with IDH1-mutated malignancies and hepatic or renal impairment. Study milestones in RMP were updated accordingly

15.3.18. Ixekizumab - TALTZ (CAP) - EMEA/H/C/003943/II/0053

Applicant: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of juvenile idiopathic arthritis for TALTZ, based on week 16 results from study I1F-MC-RHCG; this is a multicenter, open-label, efficacy, safety, tolerability, and pharmacokinetic study (COSPIRIT-JIA) of subcutaneous ixekizumab with adalimumab reference arm, in children from 2 to less than 18 years of age with juvenile idiopathic arthritis subtypes of enthesitis-related arthritis (including juvenile-onset ankylosing spondylitis) and juvenile psoriatic arthritis was performed to evaluate the

efficacy and safety of ixekizumab for 16 weeks after treatment initiation. 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 8.1 of the RMP has also been submitted. Furthermore, the PI is in line with the latest QRD template version 10.4

15.3.19. L-lysine hydrochloride, L-arginine hydrochloride - LYSAKARE (CAP) - EMEA/H/C/004541/II/0018

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Update of sections 4.2, 4.3, 4.4, 4.8 and 5.1 of the SmPC in order to remove the contraindication and update the warning on 'Hyperkalaemia' as well as on 'Metabolic acidosis' and to update safety information based on final results from study CAAA001A12401 listed as a category 3 study in the RMP. This is a multicenter, open-label post authorization safety study to evaluate the effect of LysaKare infusion on serum potassium levels in GEP-NET patients eligible for Lutathera treatment. The RMP version 3.0 has also been submitted

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

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

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

An updated RMP version 2.1 was included as part of the application

15.3.21. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/II/0061

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Submission of the final report from study E7080-G000-307 listed as a category 3 study in the RMP. This is a multicenter, open-label, randomized, phase 3 trial to compare the efficacy and safety of lenvatinib in combination with everolimus or pembrolizumab versus sunitinib alone in first-line treatment of subjects with advanced renal cell carcinoma. The RMP version 18.0 has also been submitted

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

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

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

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

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

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

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

Applicant: Agios Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new strength (100 mg film-coated tablet) associated with a new orphan indication for the "treatment of adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassaemia". The extension application is grouped with a type II quality variation (C.I.4) to update of sections 4.2 and 5.2 of the SmPC in order to update pharmacokinetic information based on final results from study AG348-C-024 listed as a category 3 study in the RMP; this is a Phase 1, Open-label, Single-dose, Pharmacokinetic Study of Mitapivat in Subjects with Moderate Hepatic Impairment Compared to Matched Healthy Control Subjects with Normal Hepatic Function. The RMP (version 1.1) is updated in accordance

15.3.25. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/II/0056, Orphan

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from PRIMA study (PR-30-5017-C) listed as a PAES in the Annex II; this is a Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter

Study of Niraparib Maintenance Treatment in Patients with Advanced Ovarian Cancer Following Response on Front-Line Platinum-Based Chemotherapy. The RMP version 9.0 has also been submitted. In addition, the MAH took the opportunity to update section D of Annex II, and to implement editorial changes to the PI

15.3.26. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/II/0022/G, Orphan

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application including two type II variations:
- Update of sections 4.2, 4.4, 4.8, and 5.1 of the SmPC based on the clinical study report for the completed 72 weeks of Study A4250-008; an open-label, phase III study to evaluate the long-term efficacy and safety of odevixibat in children with PFIC (category 3 study in the RMP; MEA 002).
The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and the Package Leaflet. An updated RMP version 6.1 is included in this submission.
- Submission of the clinical study report for Study A4250-J001; a Phase I PK study in healthy Japanese adult male patients

15.3.27. Odevixibat - KAYFANDA (CAP) - EMEA/H/C/006462/II/0001/G

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application consisting of:
C.I.4: Update of sections 4.4, 4.8, and 5.1 of the SmPC based on results from Study A4250-015 listed as a category 3 study in the RMP; this is a Phase 3, multicentre, open-label extension study to evaluate the long-term safety and efficacy of odevixibat in patients with ALGS. The Package Leaflet is updated accordingly. The RMP version 6.2 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.
C.I.13: Submission of the 72-week report from study A4250-008. This is a Phase 3, multicentre, open-label extension study to investigate the long-term efficacy and safety of odevixibat in patients with Progressive Familial Intrahepatic Cholestasis Types 1 and 2 (PEDFIC 2)

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

Applicant: Laboratoires Juvise Pharmaceuticals

PRAC Rapporteur: Karin Erneholm

Scope: Grouped application comprised of two Type II Variations, as follows:
C.I.13: Submission of the final report from study AC-058B202; this is a Multicenter, Randomized, Double-blind, Parallel-group Extension to Study AC-058B201 to Investigate the Long-term Safety, Tolerability, and Efficacy of 10, 20, and 40 mg/day Ponesimod, an Oral S1P1 Receptor Agonist, in Patients with Relapsing-remitting Multiple Sclerosis.
C.I.13: Submission of the final report from study AC-058B303 (OPTIMUM-LT); this is a Multicenter, Non-Comparative Extension to Study AC-058B301, to Investigate the Long-

Term Safety, Tolerability, and Control of Disease of Ponesimod 20 mg in Subjects with Relapsing Multiple Sclerosis.
The RMP version 4.1 has also been submitted

15.3.29. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/II/0092, Orphan

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 4.2 of the SmPC in order to update the 'monitoring after infusion' recommendations, based on existing clinical trial data as well as literature references reporting real word experience. The Package Leaflet is updated accordingly. The RMP version 8.0 has also been submitted. In addition, the MAH took the opportunity to introduce a minor change to the HCP educational programme in the Annex II in order to enhance readability

15.3.30. Tislelizumab - TEVIMBRA (CAP) - EMEA/H/C/005919/II/0018

Applicant: Beigene Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication for Tevimbra in combination with platinum-containing chemotherapy as neoadjuvant treatment and then continued as monotherapy as adjuvant treatment, for the treatment of adult patients with resectable NSCLC based on interim results from study BGB-A317-315. Study BGB-A317-315 is a phase 3 randomized, placebo-controlled, double-blind study to compare the efficacy and safety of neoadjuvant treatment with tislelizumab plus platinum-based doublet chemotherapy followed by adjuvant tislelizumab versus neoadjuvant treatment with placebo plus platinum-based doublet chemotherapy followed by adjuvant placebo in patients with resectable Stage II or IIIA NSCLC. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.7 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. Aflibercept[28] - ZALTRAP (CAP) - PSUSA/00010019/202408

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.2. Agalsidase alfa - REPLAGAL (CAP) - PSUSA/00000069/202408

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.3. Alirocumab - PRALUENT (CAP) - PSUSA/00010423/202407

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.4. Avalglucosidase alfa - NEXVIADYME (CAP) - PSUSA/00011002/202408

Applicant: Sanofi B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.5. Bimekizumab - BIMZELX (CAP) - PSUSA/00010953/202408

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.6. Brodalumab - KYNTHEUM (CAP) - PSUSA/00010616/202407

Applicant: LEO Pharma A/S

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

16.1.7. Difelikefalin - KAPRUVIA (CAP) - PSUSA/00010995/202408

Applicant: Vifor Fresenius Medical Care Renal Pharma France

[28] Oncological indication(s) only

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.8. Efanesoctocog alfa - ALTUVOCT (CAP) - PSUSA/00011062/202408

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.9. Elranatamab - ELREXFIO (CAP) - PSUSA/00000225/202408

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

16.1.10. Eravacycline - XERAVA (CAP) - PSUSA/00010718/202408

Applicant: Paion Pharma GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.11. Fedratinib - INREBIC (CAP) - PSUSA/00010909/202408

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

16.1.12. Fosdenopterin - NULIBRY (CAP) - PSUSA/00011017/202408

Applicant: TMC Pharma (EU) Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.13. Idelalisib - ZYDELIG (CAP) - PSUSA/00010303/202407

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.14. Idursulfase - ELAPRASE (CAP) - PSUSA/00001722/202407

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.15. Imlifidase - IDEFIRIX (CAP) - PSUSA/00010870/202408

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.16. Interferon beta-1b - BETAFERON (CAP); EXTAVIA[29] - PSUSA/00001759/202407

Applicant: Bayer AG (Betaferon), Novartis Europharm Limited (Extavia)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.17. Lefamulin - XENLETA (CAP) - PSUSA/00010872/202408

Applicant: Nabriva Therapeutics Ireland DAC

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

16.1.18. Lenacapavir - SUNLENCA (CAP) - PSUSA/00011012/202408

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.1.19. Linaclotide - CONSTELLA (CAP) - PSUSA/00010025/202408

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.20. Lipegfilgrastim - LONQUEX (CAP) - PSUSA/00010111/202407

Applicant: Teva B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

16.1.21. Lonapegsomatropin - SKYTROFA (CAP) - PSUSA/00010969/202408

Applicant: Ascendis Pharma Endocrinology Division A/S

PRAC Rapporteur: Martin Huber

[29] European Commission (EC) decision on the marketing authorisation (MA) withdrawal for Extavia dated 25 November 2024

Scope: Evaluation of a PSUSA procedure

16.1.22. Melphalan flufenamide - PEPAXTI (CAP) - PSUSA/00011013/202408

Applicant: Oncopeptides AB

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.23. Mitapivat - PYRUKYND (CAP) - PSUSA/00011025/202408

Applicant: Agios Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.24. Omaveloxolone - SKYCLARYS (CAP) - PSUSA/00000245/202408

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.25. Patisiran - ONPATTRO (CAP) - PSUSA/00010715/202408

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

16.1.26. Peginterferon beta-1A - PLEGRIDY (CAP) - PSUSA/00010275/202407

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.1.27. Pioglitazone - ACTOS (CAP); glimepiride, pioglitazone - TANDEMACT (CAP); metformin, pioglitazone - COMPETACT (CAP); - PSUSA/00002417/202407

Applicant: CHEPLAPHARM Arzneimittel GmbH

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.1.28. Pretomanid - DOVPRELA (CAP) - PSUSA/00010863/202408

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.29. Risdiplam - EVRYSDI (CAP) - PSUSA/00010925/202408

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.30. Sotrovimab - XEVUDY (CAP) - PSUSA/00010973/202408

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.31. Sparsentan - FILSPARI (CAP) - PSUSA/00011060/202408

Applicant: Vifor France

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.32. Sutimlimab - ENJAYMO (CAP) - PSUSA/00011023/202408

Applicant: Sanofi B.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.33. Teclistamab - TECVAYLI (CAP) - PSUSA/00011010/202408

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

16.1.34. Valoctocogene roxaparvovec - ROCTAVIAN (CAP) - PSUSA/00011009/202408

Applicant: BioMarin International Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.35. Vosoritide - VOXZOGO (CAP) - PSUSA/00010952/202408

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

16.1.36. Voxelotor - OXBRYTA (CAP) - PSUSA/00010983/202408

Applicant: Pfizer Europe Ma EEIG

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

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

None

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

16.3.1. Alprostadil[30] (NAP) - PSUSA/00010021/202407

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

16.3.2. Amlodipine, rosuvastatin (NAP); amlodipine, perindopril, rosuvastatin (NAP) - PSUSA/00010434/202407

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

16.3.3. Benperidol (NAP) - PSUSA/00000329/202407

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.3.4. Bibrocathol (NAP) - PSUSA/00000406/202408

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.3.5. Budesonide, salmeterol (NAP) - PSUSA/00010511/202407

Applicant(s): various

PRAC Lead: Bianca Mulder

[30] Indicated for patency of the ductus arteriosus only

Scope: Evaluation of a PSUSA procedure

16.3.6. Cinchocaine hydrochloride, hydrocortisone (NAP) - PSUSA/00000761/202408

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

16.3.7. Everolimus[31] (NAP) - PSUSA/00010269/202407

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.3.8. Lactobacillus all subspecies and combinations of subspecies (NAP) - PSUSA/00010598/202407

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.3.9. Lidocaine hydrochloride, phenylephrine hydrochloride, tropicamide (NAP) - PSUSA/00010390/202407

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.3.10. Neomycin, triamcinolone (NAP) - PSUSA/00000081/202408

Applicant(s): various

PRAC Lead: Eva Jirsova

Scope: Evaluation of a PSUSA procedure

16.3.11. Tiapride (NAP) - PSUSA/00002944/202407

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

[31] Indicated for rejection of transplanted organs only

16.4. Follow-up to PSUR/PSUSA procedures

16.4.1. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/LEG 009

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: From PSUSA/00010608/202305
Response to the Rapporteur's assessment comment which was received on 11-Jan-2024 in the Final PRAC assessment report for the Refixia PSUR covering the period (01/06/2022 to 31/05/2023) concerning motor developmental delay and speech disorder.

16.4.2. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/LEG 058

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: From PSUSA/00003085/202312
The MAH should address the questions raised in the PSUSA regarding severe depression/ suicidal ideation.

16.4.3. Vildagliptin - GALVUS (CAP) - EMEA/H/C/000771/LEG 050

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: From PSUSA/00003113/202402
MAH Response to PSUSA/00003113/202402 assessment report of October 2024:
The MAH is requested a cumulative review of all cases of Severe Cutaneous Adverse Reactions MedDRA SMQ broad level, with DRESS, SJS and TEN cases associated with vildagliptin as suspect drug

16.4.4. Vildagliptin - JALRA (CAP) - EMEA/H/C/001048/LEG 034

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: From PSUSA/00003113/202402
MAH Response to PSUSA/00003113/202402 assessment report of October 2024:
The MAH is requested a cumulative review of all cases of Severe Cutaneous Adverse Reactions MedDRA SMQ broad level, with DRESS, SJS and TEN cases associated with vildagliptin as suspect drug

16.4.5. Vildagliptin - XILIARX (CAP) - EMEA/H/C/001051/LEG 034

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: From PSUSA/00003113/202402
MAH Response to PSUSA/00003113/202402 assessment report of October 2024:

The MAH is requested cumulative review of all cases of Severe Cutaneous Adverse Reactions MedDRA SMQ broad level, with DRESS, SJS and TEN cases associated with vildagliptin as suspect drug

16.4.6. Vildagliptin, metformin hydrochloride - EUCREAS (CAP) - EMEA/H/C/000807/LEG 028

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: From PSUSA/00003113/202402
MAH Response to PSUSA/00003113/202402 assessment report of October 2024:
The MAH is requested days a cumulative review of all cases of Severe Cutaneous Adverse Reactions MedDRA SMQ broad level, with DRESS, SJS and TEN cases associated with vildagliptin as suspect drug

16.4.7. Vildagliptin, metformin hydrochloride - ICANDRA (CAP) - EMEA/H/C/001050/LEG 026

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: From PSUSA/00003113/202402
MAH Response to PSUSA/00003113/202402 assessment report of October 2024:
The MAH is requested a cumulative review of all cases of Severe Cutaneous Adverse Reactions MedDRA SMQ broad level, with DRESS, SJS and TEN cases associated with vildagliptin as suspect drug

16.4.8. Vildagliptin, metformin hydrochloride - ZOMARIST (CAP) - EMEA/H/C/001049/LEG 026

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Mari Thorn

Scope: From PSUSA/00003113/202402
MAH Response to PSUSA/00003113/202402 assessment report of October 2024:
The MAH is requested a cumulative review of all cases of Severe Cutaneous Adverse Reactions MedDRA SMQ broad level, with DRESS, SJS and TEN cases associated with vildagliptin as suspect drug

16.5. Variation procedure(s) resulting from PSUSA evaluation

None

16.6. Expedited summary safety reviews[32]

None

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

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

17.1. Protocols of PASS imposed in the marketing authorisation(s)[33]

None

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

17.2.1. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/ANX 002.6

Applicant: Kite Pharma EU B.V., ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Response to MEA 002.5:
Revised Protocol #5 for Study KTE-EU-472-6036
Title: Long-term, non-interventional study of recipients of Tecartus (brexucabtagene autoleucel) for treatment of adult patients with relapsed or refractory Mantle Cell Lymphoma (MCL).

17.2.2. Danicopan - VOYDEYA (CAP) - EMEA/H/C/005517/MEA 002.1

Applicant: Alexion Europe

PRAC Rapporteur: Martin Huber

Scope: ***Revised Protocol Study ALX-PNH-502***
Title: An observational cohort study to assess long-term safety of danicopan add-on therapy in patients with paroxysmal nocturnal hemoglobinuria: analysis of IPIG-registry data.

17.2.3. Efanesoctocog alfa - ALTUVOCT (CAP) - EMEA/H/C/005968/MEA 002

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Amelia Cupelli

Scope: From initial MAA
PASS Protocol (non-imposed)
Observational registry study in Previously Untreated Patients (PUPs) with Haemophilia A

[32] 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
[33] In accordance with Article 107n of Directive 2001/83/EC
[34] 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

(ATHN)

17.2.4. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/MEA 007.3

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's responses to MEA 007.2 [***Revised Protocol***] as adopted in October 2024.
A revised protocol for the non-imposed non-interventional PASS to Evaluate the Risk of Malignancies in Patients with Myasthenia Gravis (MG) Treated with Efgartigimod should be submitted by 19/12/2024 taking into account the comments included in section 8 8.
Conclusion following assessment of MAH responses to 2nd RSI in the PRAC AR for EMEA/H/C/005849/MEA/007.2

17.2.5. Exagamglogene autotemcel - CASGEVY (CAP) - EMEA/H/C/005763/MEA 011.1

Applicant: Vertex Pharmaceuticals (Ireland) Limited, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: From intial MAA
Revised Protocol Version 2.0 for PASS no. VX24-290-102
Title: Healthcare Professional Survey (HCP) to Assess the Effectiveness of the Additional Risk Minimization Measures (aRMM) for Casgevy (exagamglogene autotemcel)

17.2.6. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 005.6

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

Scope: ***Protocol amendment (version 6.0) / Study (EP0219 [former ZX008-2102])***
Post Authorisation Safety Study (PASS): A Drug Utilisation Study of Fenfluramine In Europe (DUS)

17.2.7. Omaveloxolone - SKYCLARYS (CAP) - EMEA/H/C/006084/MEA 002.2

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: From initial MAA
Revised Protocol for PASS 296FA401 (408-C-2301)
An observational, multinational, post-marketing registry of omaveloxolone-treated patients with Friedreich’s ataxia)

17.3. Results of PASS imposed in the marketing authorisation(s)[35]

None

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

17.4. Results of PASS non-imposed in the marketing authorisation(s)[36]

17.4.1. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/II/0076

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report from study 20180204 listed as a category 3 study in the RMP. This is a non-interventional observational registry study to evaluate the use and safety of cinacalcet among paediatric patients with secondary hyperparathyroidism (HPT)

17.4.2. Ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/WS2794/0026; Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/WS2794/0025; Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/WS2794/0029

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Submission of the final report from study 8835-062 listed as a category 3 study in the RMP for Steglatro, Steglujan and Segluromet. This is a non-interventional post-authorization safety study (PASS) to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents. The RMP version 2.3 has also been submitted

17.4.3. Esketamine - SPRAVATO (CAP) - EMEA/H/C/004535/II/0026

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: Submission of the final study report for the non-interventional study PCSNSP002812 listed as a category 3 study in the RMP. This is a survey in order to assess the effectiveness of SPRAVATO educational materials for additional risk minimization measures in the European Union. The RMP version 8.1 has also been submitted

17.4.4. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0093

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Submission of the study report for additional pharmacovigilance analysis to further evaluate the risk of haemorrhage in participants receiving ibrutinib and concomitant vitamin K antagonists with or without antiplatelet drugs, listed as a category 3 study in the RMP

17.4.5. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/II/0058, Orphan

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

[36] 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

Scope: Submission of the final report from study 3000-04-001/ GSK213705 listed as a category 3 study in the RMP; this is a non-interventional PASS to evaluate the risks of myelodysplastic syndrome/acute myeloid leukaemia and second primary malignancies in adult patients with epithelial ovarian, fallopian tube, or primary peritoneal cancer receiving maintenance treatment with Zejula. The RMP version 10.0 has also been submitted

17.4.6. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0149

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final clinical study report (CSR) for the PASS study CA209234 listed as a category 3 study in the RMP. This is an observational, multicenter, prospective study in patients treated with nivolumab for melanoma and lung cancer in order assess the safety experience, survival, adverse event management, and outcomes of adverse events associated with nivolumab (monotherapy or with ipilimumab) in routine oncology care facilities. The RMP version 42.0 has also been submitted.

17.4.7. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[37]) - EMEA/H/W/002300/II/0085/G

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: A grouped application comprised of two type II variations, as follows:

C.I.4: Update of sections 4.4 and 5.1 of the SmPC in order to remove meningitis from the list of important potential risks and add effectiveness data based on EPI-MAL-003 study listed as a category 3 study in the RMP. This is a prospective study to evaluate the safety, effectiveness and impact of the RTS,S/AS01E vaccine in young children in sub-Saharan Africa countries. The Package Leaflet is updated accordingly.
The RMP version 6.0 has also been submitted.

C.I.13: Submission of the final report from study MVPE (Malaria Vaccine Pilot Evaluation) listed as a category 3 study in the RMP. This is a observational study in the context of a cluster-randomized pilot implementation in order to assess the feasibility of delivery, safety, and impact on mortality of the RTS,S/AS01E malaria vaccine delivered through the routine immunization services in Kenya, Malawi, and Ghana over 4 years

17.4.8. Trifluridine, tipiracil - LONSURF (CAP) - EMEA/H/C/003897/II/0031

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Mari Thorn

Scope: Submission of the final report from study DIM-95005-001 (PROMETCO), listed as a category 3 PASS in the RMP. This is a non-interventional, observational, real world evidence prospective cohort study in the management of metastatic colorectal cancer. The RMP

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

version 11.1 has also been submitted as the missing information "Use in patients in worse condition than ECOG 0-1" has been removed based on the results from PROMETCO. The PART II - section SVII 1 & SVII 2 has been updated to comply with GVP module V revision 2

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

17.5.1. Cabotegravir - APRETUDE (CAP) - EMEA/H/C/005756/MEA 002.1

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: From initial MAA
First Interim Report for PASS No 215325
Antiretroviral Pregnancy Registry (APR) to monitor CAB LA PrEP use in Pregnancy
The APR is an international registry that monitors prenatal exposures to antiretroviral (ARV) drugs to detect a potential increase in the risk of birth defects through a prospective exposure registration cohort. The registry's primary objective is to monitor for birth defects among ARV exposed pregnancies. The registry has been monitoring pregnancies with prenatal exposure to ARVs used for PrEP since the approval of ARVs used in oral PrEP.
The APR is a MAH-sponsored study involving the collaborative effort of multiple companies. Data from the APR will assess maternal (pregnancy outcomes, abortions, still births) and foetal outcomes (premature births and low birth weight) following CAB LA PrEP use during pregnancy. Exposure to CAB LA PrEP relative to gestation period and conception will be captured in the registry, thus enabling assessment of pre-conception exposures along with first, second and third trimester exposures

17.5.2. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/MEA 006.5

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: From initial MAA
RMP Category 3: Study No 215325
Pregnancy and Neonatal Outcomes following Prenatal Exposure to Cabotegravir: Data from The Antiretroviral Pregnancy Registry (APR).
2ND INTERIM REPORT

17.5.3. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/MEA 004.3

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: From Initial MAA:
First Interim Report for PASS to characterize the missing information on use in pregnant woman outlined in the risk management plan

17.5.4. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 016.4

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: From II/0001:
Annual Interim Report for Study GLPG0634-CL-413
Title: Non-interventional, post-authorization safety study of filgotinib in patients with moderately to severely active ulcerative colitis (a European multi registry-based study)

17.5.5. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 019

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: From initial MAA
Interim report for PASS GLPG0634-CL-403:
Non-interventional post-authorization safety study of filgotinib in the treatment of patients with moderate to severe active rheumatoid arthritis within European registries, including:
Study GS-EU-417-9046: RABBIT (MEA002)
Study GS-EU-417-9047: ARTIS (MEA 003)
Study GS-EU-417-9048: BSRBR-RA (MEA 004)
Study GS-EU-417-5882: BIOBADASER (MEA 005)
Study GS-EU-417-5883: DANBIO (MEA 006)

17.5.6. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038.8

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: From X-0044-G
5th Interim Report for 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. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 004.3

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Terhi Lehtinen

Scope: From initial MAA
Interim Study Report for I5Q-MC-B001
A Cohort Study to Assess Drug Utilisation and Long-Term Safety of Galcanezumab in US Patients in the Course of Routine Clinical Care

17.5.8. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/MEA 002.7

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: 4th Annual Interim Study Report for PASS VX20-445-120
Title: Real-World Effects and Utilisation Patterns of Elexacaftor, Tezacaftor, and Ivacaftor

Combination Therapy (ELX/TEZ/IVA) in Patients with Cystic Fibrosis (CF)

17.5.9. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 001.4

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: From initial MAA
First Interim Report for PASS IM047-009 (ORION)
Ozanimod real-world safety – a post-authorisation multi-national long-term non-interventional study

17.5.10. Plasmodium falciparum and hepatitis b vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[38]) - EMA/PAM/0000242605

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the interim analysis report for the study EPI-MAL-010: 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, together with updated statistical analysis plan (SAP)

17.5.11. Somatrogon - NGENLA (CAP) - EMEA/H/C/005633/MEA 001.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: From Initial MAA:
1st Interim Report PASS C0311023
An Active Surveillance PASS to Monitor the Real-World Long-term Safety of Somatrogon Among Paediatric Patients in Europe to estimate the incidence rates of neoplasms, diabetes mellitus type 2, and the clinical endpoints related to immunogenicity, and medication errors in paediatric patients treated with somatrogon, and paediatric patients treated with once daily somatropin, in the course of routine clinical care

17.5.12. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/MEA 005.3

Applicant: Amgen Europe B.V., ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: 6th Interim Report for PASS 20130193
A post-marketing, prospective cohort study of patients treated with talimogene laherparepvec in clinical practice to characterize the risk of herpetic illness among patients, close contacts, and healthcare providers; and long term safety in treated patients.

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

Annual interim reports to be included in the PSUR and DSUR

17.5.13. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.10

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: From Initial MAA:
5th Annual Interim Results for PASS No.: M-14745-40
Title: Tildrakizumab Post-Authorisation Safety Study (PASS) in European Psoriasis Registries.
To collect long-term safety data in particular relating to event of special interest (important potential risks and pregnancy related outcomes) for tildrakizumab. (Malignancies, MACEs, Serious infections, SIBH, Hypersensitivity, IBD, Safety in pregnant and lactating women).
To further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine clinical care

17.6. Others

17.6.1. Buprenorphine - SIXMO (CAP) - EMEA/H/C/004743/ANX 002.1

Applicant: L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: From Initial MAA:
First Progress Report for PASS MOLTeNI-2019-01 (EUPAS1000000092)
A prospective, observational (non-interventional), post-authorisation safety cohort study to evaluate the incidence of the breakages and insertion/removal complications of buprenorphine implants (Sixmo) in the routine clinical care.

17.6.2. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/MEA 011.1

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: From II/0060:
Progress Report for PASS CSA0014 DUPI PEDISTAD
Title: Registry-based study 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

17.6.3. Ganaxolone - ZTALMY (CAP) - EMEA/H/C/005825/MEA 014

Applicant: Marinus Pharmaceuticals Emerald Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: From inital MAA
One-Year-Update for CDD-IPR-CDD-01: CDKL5
Non-interventional, observational, international, prospective, natural history registry of up to 500 patients diagnosed with CDD. Deficiency Disorder (CDD) International Patient

Registry (IPR)

17.6.4. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 033.8

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Karin Bolin

Scope: From II-0063
5th Annual Progress Report for PASS No. MK-8259-050:
An observational post-approval safety study of golimumab in treatment of polyarticular Juvenile Idiopathic Arthritis (pJIA) using the German Biologics JIA Registry (BiKeR)

17.6.5. Ivosidenib - TIBSOVO (CAP) - EMEA/H/C/005936/MEA 003.2

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: ***Feasibility assessment for IMPACTA***
Cross-sectional study to assess the effectiveness of the patients' alert card to inform on the risk of differentiation syndrome in AML patients treated with TIBSOVO (Ivosidenib)

17.6.6. Plasmodium falciparum and hepatitis b vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[39]) - EMA/PAM/0000242859

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the 11th progress report for study EPI-MAL-003: a Phase IV prospective observational study to evaluate the safety, effectiveness and impact of the RTS,S/AS01E vaccine in young children in sub-Saharan Africa.

17.6.7. Naldemedine - RIZMOIC (CAP) - EMEA/H/C/004256/MEA 001.8

Applicant: Shionogi B.V.

PRAC Rapporteur: Eamon O'Murchu

Scope: From Initial MAA:
3rd Annual Progress Report for PASS / Product ref. number: S-297995
An Observational Post-Authorisation Safety Study (PASS) of Patients with Chronic Opioid Use for Non-Cancer and Cancer Pain who have Opioid-Induced Constipation (OIC) [period 01 Oct 2017 to 30 Sept 2023]

17.6.8. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/ANX 001.2

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: From initial MAA

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

6th Progress Report (yearly) for PASS NN7999-4031/Paradigm 8
A Non-Interventional Post-Authorisation Safety Study (PASS) in male haemophilia B patients receiving Nonacog Beta Pegol (N9-GP) prophylaxis treatment

17.6.9. Odevixibat - KAYFANDA (CAP) - EMEA/H/C/006462/SOB 001

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: From initial MAA
Feasibility Assessment for PASS CLIN-60240-034 (imposed/non-interventional)
Prospective Registry-Based Study of the Long-Term Safety of Odevixibat in Patients with Alagille syndrome (ALGS)

17.6.10. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 012.6

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: First annual progress report for PASS P21-825
Evaluation of the Effectiveness of Additional Risk Minimisation Measures for Upadacitinib in the Treatment of Atopic Dermatitis)

17.6.11. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 014.4

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Petar Mas

Scope: First Annual Progress Report for PASS P21-824
Title: A study of growth and development in adolescents with atopic dermatitis who receive upadacitinib

17.6.12. Vosoritide - VOXZOGO (CAP) - EMEA/H/C/005475/MEA 005.5

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: From Initial MAA:
SECOND BI-ANNUAL REPORT for PASS Study 111-603 (26 August 2023-25 August 2024):
A multicenter, non-interventional study to evaluate long-term safety in patients with achondroplasia treated with Voxzogo (vosoritide)

17.7. New Scientific Advice

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

17.8. Ongoing Scientific Advice

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

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

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

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

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

18.1. Annual reassessments of the marketing authorisation

18.1.1. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/S/0069 (without RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Mari Thorn

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/R/0026 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

18.2.2. Futibatinib - LYTGOBI (CAP) - EMEA/H/C/005627/R/0008 (without RMP)

Applicant: Taiho Pharma Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

18.2.3. Glofitamab - COLUMVI (CAP) - EMEA/H/C/005751/R/0012 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Conditional renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Amikacin - ARIKAYCE LIPOSOMAL (CAP) - EMEA/H/C/005264/R/0014 (with RMP)

Applicant: Insmed Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

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

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.3. Cabazitaxel - CABAZITAXEL ACCORD (CAP) - EMEA/H/C/005178/R/0012 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

18.3.4. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/R/0038 (without RMP)

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: 5-year renewal of the marketing authorisation

18.3.5. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/R/0059 (without RMP)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

18.3.6. Melphalan - PHELINUN (CAP) - EMEA/H/C/005173/R/0005 (without RMP)

Applicant: ADIENNE S.r.l.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.7. Methylthioninium chloride - LUMEBLUE (CAP) - EMEA/H/C/002776/R/0007 (without RMP)

Applicant: Cosmo Technologies Limited

PRAC Rapporteur: Mari Thorn

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 10-13 March 2025 PRAC meeting, which was held remotely.

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ulla Wändel Liminga	Chair	Sweden	No interests declared	
Jan Neuhauser	Member	Austria	No interests declared	
Sonja Hrabcik	Alternate	Austria	No interests declared	
Jean-Michel Dogné	Member	Belgium	No interests declared	
Jo Robays	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva	Member	Bulgaria	No interests declared	
Petar Mas	Member	Croatia	No interests declared	
Barbara Bytyqi	Alternate	Croatia	No interests declared	
Elena Kaisis	Member	Cyprus	No interests declared	
Panagiotis Psaras	Alternate	Cyprus	No interests declared	
Jana Lukacisinova	Alternate	Czechia	No interests declared	
Marie Louise Schougaard Christiansen	Member	Denmark	No interests declared	
Karin Erneholm	Alternate	Denmark	No interests declared	
Maia Uusküla	Member	Estonia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Terhi Lehtinen	Member	Finland	No interests declared	
Kimmo Jaakkola	Alternate	Finland	No interests declared	
Tiphaine Vaillant	Member	France	No interests declared	
Zoubida Amimour	Alternate	France	No participation in discussion, final deliberations and voting on:	6.1.4. Lisocabtagene maraleucel - BREYANZI (CAP) - PSUSA/00010990/202408 15.3.2. Adagrasib - KRAZATI (CAP) - EMEA/H/C/006013/II/0010 /G 16.1.11. Fedratinib - INREBIC (CAP) - PSUSA/00010909/202408 17.4.6. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0149 17.5.9. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 001.4
Martin Huber	Member	Germany	No interests declared	
Gabriele Maurer	Alternate	Germany	No interests declared	
Georgia Gkegka	Member	Greece	No interests declared	
Maria Poulianiti	Alternate	Greece	No restrictions applicable to this meeting	
Julia Pallos	Member	Hungary	No participation in discussion, final deliberations and voting on:	6.1.4. Lisocabtagene maraleucel - BREYANZI (CAP) - PSUSA/00010990/202408 15.3.2. Adagrasib - KRAZATI (CAP) - EMEA/H/C/006013/II/0010 /G

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				16.1.11. Fedratinib - INREBIC (CAP) - PSUSA/00010909/202408 17.4.6. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0149 17.5.9. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/MEA 001.4
Guðrún Þengilsdóttir	Alternate	Iceland	No interests declared	
Rhea Fitzgerald	Member	Ireland	No interests declared	
Eamon O Murchu	Alternate	Ireland	No interests declared	
Amelia Cupelli	Member	Italy	No interests declared	
Emilio Clementi	Alternate	Italy	No interests declared	
Zane Neikena	Member	Latvia	No interests declared	
Diana Litenboka	Alternate	Latvia	No interests declared	
Rugile Pilviniene	Member	Lithuania	No interests declared	
Lina Seibokiene	Alternate	Lithuania		
Anne-Cecile Vuillemin	Member	Luxembourg	No interests declared	
Magdalena Wielowieyska	Alternate	Luxembourg	No participation in discussion, final deliberations and voting on:	6.1.2. Dengue tetravalent vaccine (live, attenuated) - DENGUE TETRAVALENT VACCINE (LIVE, ATTENUATED) TAKEDA (Art 58) - EMEA/H/W/005362/PSUV/0019 6.1.3. Dengue tetravalent vaccine (live, attenuated) - QDENGA (CAP) -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				PSUSA/00011034/202408 7.4.1. Brigatinib-ALUNBRIG (CAP) - EMEA/H/C/004248/II/0056 16.1.2. Agalsidase alfa - REPLAGAL (CAP) - PSUSA/00000069/202408 16.1.14. Idursulfase - ELAPRASE (CAP) - PSUSA/00001722/202407
John Joseph Borg	Member	Malta	No interests declared	
Liana Martirosyan	Member (Vice-Chair)	Netherlands	No interests declared	
Bianca Mulder	Alternate	Netherlands	No interests declared	
David Olsen	Member	Norway	No participation in discussion, final deliberations and voting on:	16.1.16. Interferon beta-1b - BETAFERON (CAP); EXTAVIA - PSUSA/00001759/202407
Pernille Harg	Alternate	Norway	No interests declared	
Adam Przybylkowski	Member	Poland	No interests declared	
Katarzyna Ziolkowska	Alternate	Poland	No interests declared	
Ana Sofia Diniz Martins	Member	Portugal	No interests declared	
Carla Torre	Alternate	Portugal	No interests declared	
Roxana Dondera	Member	Romania	No interests declared	
Irina Sandu	Alternate	Romania	No interests declared	
Anna Mareková	Member	Slovakia	No interests declared	
Miroslava Gocova	Alternate	Slovakia	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Polona Golmajer	Member	Slovenia	No interests declared	
Marjetka Plementas	Alternate	Slovenia	No interests declared	
Maria del Pilar Rayon	Member	Spain	No interests declared	
Monica Martinez Redondo	Alternate	Spain	No interests declared	
Mari Thorn	Member	Sweden	No restrictions applicable to this meeting	
Karin Bolin	Alternate	Sweden	No interests declared	
Annalisa Capuano	Member	Independent scientific expert	No interests declared	
Milou-Daniel Drici	Member	Independent scientific expert	No interests declared	
Maria Teresa Herdeiro	Member	Independent scientific expert	No interests declared	
Patricia McGettigan	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark	Member	Independent scientific expert	No interests declared	
Roberto Frontini	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Salvatore Antonio Giuseppe Messana	Alternate	Healthcare Professionals' Representative	No interests declared	
Marko Korenjak	Member	Patients' Organisation Representative	No interests declared	
Michal Rataj	Alternate	Patients' Organisation Representative	No interests declared	
Flora Musuamba Tshinanu	Expert	Belgium	No restrictions applicable to this meeting	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Behija Hudina	Expert	Croatia	No restrictions applicable to this meeting	
Ivana Ljubicic	Expert	Croatia	No interests declared	
Lara Miletić	Expert	Croatia	No interests declared	
Lora Pavlinovic	Expert	Croatia	No interests declared	
Lucie Skalova	Expert	Czech Republic	No interests declared	
Karina Suciu-Subert	Expert	Czech Republic	No interests declared	
Lærke Nilausen	Expert	Denmark	No restrictions applicable to this meeting	
Moritz Sander	Expert	Denmark	No restrictions applicable to this meeting	
Ditte Søgaard	Expert	Denmark	No interests declared	
Kira Underbjerg	Expert	Denmark	No interests declared	
Mette Wikkelsø	Expert	Denmark	No interests declared	
Dennis Lex	Expert	Germany	No interests declared	
Anna Nickel	Expert	Germany	No interests declared	
Madeleine Berendsen	Expert	Netherlands	No interests declared	
Esther de Vries	Expert	Netherlands	No interests declared	
Olaf Klungel	Expert	Netherlands	No interests declared	
Charlotte Backman	Expert	Sweden	No interests declared	
A representative from the European Commission attended the meeting				
Observers from Health Canada (Canada), PMDA (Japan), MLHW (Japan) and WHO attended the meeting.				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

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

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

A PSUR is a report providing an evaluation of the benefit-risk balance of a medicine, which is submitted by marketing authorisation holders at defined time points following a medicine's authorisation.

PSURs summarises data on the benefits and risks of a medicine and includes the results of all studies carried out with this medicine (in the authorised and unauthorised indications).

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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