29 May 2025
EMA/PRAC/169632/2025
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Minutes for PRAC meeting on 07-10 April 2025

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

Health and safety information

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

Disclaimers

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

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

Note on access to documents

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

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1. Introduction

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

The Chairperson opened the 07-10 April 2025 meeting by welcoming all participants. The meeting was held in-person.

In accordance with the Agency's policy on handling of declarations of interests of scientific Committees' members and experts, based on the declarations of interest submitted by the Committee members, alternates[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 07-10 April 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 March 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 March 2025 were published on the EMA website on 08 May 2025 (EMA/PRAC/132323/2025).

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. Brodalumab – KYNTHEUM (CAP)

Applicant: LEO Pharma A/S

PRAC Rapporteur: Monica Martinez Redondo

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

Scope: Signal of pyoderma gangrenosum

EPITT 20162 – New signal

Lead Member State(s): ES

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 pyoderma gangrenosum was identified by EMA, based on the literature report *Salvia G. et al., 2024*[4] and 5 cases retrieved from EudraVigilance. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

Having considered the available evidence from case reports in EudraVigilance, including from literature articles, PRAC agreed that further evaluation on the signal of pyoderma gangrenosum is warranted.

Summary of recommendation(s)

- The MAH for Kyntheum (brodalumab) should submit to EMA, by 2 May 2025, a cumulative review of the signal from all available sources including post-marketing, clinical trials and literature data using the MedDRA preferred terms (PTs) pyoderma gangrenosum, acute febrile neutrophilic dermatosis and neutrophilic dermatosis, including a focus on literature data describing the plausible mechanism of action by which inhibition of IL-17 may cause the event. The MAH should also provide a proposal for amending the product information along with a proposal on the frequency for the event of pyoderma gangrenosum.
- A 30-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

4.1.2. Ibrutinib – IMBRUVICA (CAP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Signal of cough

EPITT 20161 – New signal

Lead Member State(s): HR

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.

[4] Salvia G, et al., Switch from adalimumab to brodalumab as a possible trigger factor for the onset of pyoderma gangrenosum. Australas J Dermatol. 2024;65 e111–e113; DOI: 10.1111/ajd.14266

During routine signal detection activities, a signal of cough was identified by Spain, based on cases of the Spanish spontaneous reporting database (FEDRA), literature and 191 cases retrieved from EudraVigilance. The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

Discussion

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

Summary of recommendation(s)

- In the next PSUR[5], the MAH for Imbruvica (ibrutinib) should submit to EMA a cumulative review of the signal, including a review of the published literature, data from spontaneous reports and reports from studies including all cases in EudraVigilance database, non-clinical data, as well as a discussion on possible biological plausibility and mechanism of this association. The MAH should also discuss the need for any potential amendment to the product information and/or the RMP as warranted.
- PRAC will assess the cumulative review within the PSUR procedure PSUSA/00010301/202511.

4.2. Signals follow-up and prioritisation

4.2.1. Avelumab – BAVENCIO (CAP) - EMEA/H/C/004338/SDA/013; atezolizumab – TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/028; cemiplimab – LIBTAYO (CAP) - EMEA/H/C/004844/SDA/014; dostarlimab – JEMPERLI (CAP) - EMEA/H/C/005204/SDA/008; durvalumab – IMFINZI (CAP) - EMEA/H/C/004771/SDA/015; ipilimumab – YERVOY (CAP) - EMEA/H/C/002213/SDA/050; nivolumab - OPDIVO- EMEA/H/C/003985/SDA/060; Nivolumab, relatlimab - OPDUALAG (CAP) - EMEA/H/C/005481/SDA/008; pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/044; retifanlimab – ZYNYZ (CAP) - EMEA/H/C/006194/SDA/003; tislelizumab – TEVIMBRA (CAP) - EMEA/H/C/005919/SDA/005; toripalimab – LOQTORZI (CAP) - EMEA/H/C/006120/SDA/002; tremelimumab – IMJUDO (CAP) - EMEA/H/C/006016/SDA/005

Applicant: AstraZeneca AB (Imfinzi, Imjudo), Beigene Ireland Limited (Tevimbra), Bristol-Myers Squibb Pharma EEIG (Yervoy, Opdivo, Opdualag), GlaxoSmithKline (Ireland) Limited (Jemperli), Incyte Biosciences Distribution B.V. (Zynyz), Merck Europe B.V. (Bavencio), Merck Sharp & Dohme B.V. (Keytruda), Regeneron Ireland Designated Activity Company (Libtayo), Roche Registration GmbH (Tecentriq), TMC Pharma (EU) Limited (Loqtorzi)

PRAC Rapporteur: David Olsen

Scope: Signal of scleroderma, systemic scleroderma, morphea

EPITT 20119 – Follow-up to November 2024

Background

For background information, see PRAC minutes November 2024[6].

[5] Data lock point: 12 November 2025
[6] Held 28 - 31 October 2024

The MAHs replied to the request for information on the signal of scleroderma, systemic scleroderma, morphea, and the responses were assessed by the Rapporteur.

Discussion

Having considered the available evidence in EudraVigilance, clinical studies, spontaneous reports, literature and the MAHs responses, PRAC agreed that the current evidence is insufficient to establish a causal relationship between the class of immune checkpoint inhibitors and scleroderma, systemic scleroderma and morphoea to further warrant an update to the product information and/or the RMP.

Summary of recommendation(s)

- In the next PSURs, the MAHs for Opdivo and Opdualag (nivolumab), Keytruda (pembrolizumab), Imfinzi (durvalumab), Bavencio (avelumab), Tecentriq (atezolizumab), Libtayo (cemiplimab), Jemperli (dostarlimab), Tevimbra (tislelizumab), Yervoy (ipilimumab), Imjudo (tremelimumab) and Zynyz (retifanlimab) should continue to monitor and report on new cases of scleroderma, systemic sclerosis and morphoea and related adverse event terms.

4.2.2. Emtricitabine, tenofovir disoproxil – EMTRICITABINE/TENOFOVIR DISOPROXIL KRKA, EMTRICITABINE/TENOFOVIR DISOPROXIL KRKA D.D., EMTRICITABINE/TENOFOVIR DISOPROXIL MYLAN, EMTRICITABINE/TENOFOVIR DISOPROXIL ZENTIVA, TRUVADA (CAP), NAP

Applicant(s): Gilead Sciences Ireland UC (Truvada, Emtricitabine/Tenofovir disoproxil Mylan), KRKA, d.d., Novo mesto (Emtricitabine/Tenofovir disoproxil Krka, Emtricitabine/tenofovir disoproxil Krka d.d.), Zentiva k.s. (Emtricitabine/Tenofovir disoproxil Zentiva), various

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Signal of trigeminal neuralgia

EPITT 20121 – Follow-up to December 2024

Background

For background information, see PRAC minutes December 2024[7].

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

Discussion

Having considered the available evidence from case reports in EudraVigilance, the literature and the MAH's responses, PRAC agreed that the current evidence is insufficient to establish a causal relationship between emtricitabine/tenofovir disoproxil and trigeminal neuralgia to further warrant an update to the product information and/or RMP.

Summary of recommendation(s)

- In the next PSUR, the MAH for Truvada (emtricitabine/tenofovir disoproxil) should closely monitor events indicative of trigeminal neuralgia including but not limited to

[7] Held 25 - 28 November 2024

MedDRA preferred term (PT) 'trigeminal neuralgia' and related terms, as cranial neuropathies and other cranial nerve disorders.

- PRAC also noted that the cumulative safety review on the signal of facial paraesthesia is out of the scope of the ongoing signal and should be addressed in the most appropriated regulatory procedure.

4.2.3. Oxytetracycline hydrochloride, hydrocortisone acetate, polymyxin B sulfate (ear/eye drops/suspension/ointment) (NAP)

Applicant(s): various

PRAC Rapporteur: Jo Robays

Scope: Signal of hearing and vestibular disorders

EPITT 20120 – Follow-up to October 2024

Background

For background information, see PRAC minutes October 2024[8].

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

Discussion

Having considered the available evidence in EudraVigilance and the literature, including the cumulative review submitted by the MAH, PRAC concluded that there is sufficient evidence to establish a causal association between hearing and vestibular disorders and oxytetracycline hydrochloride/hydrocortisone acetate/polymyxin B sulfate (ear or ear/eye drops/ointment). Therefore, the product information of oxytetracycline hydrochloride/hydrocortisone acetate/polymyxin B sulfate (ear or ear/eye drops/ointment) products should be updated to add a warning on ear and labyrinth disorders, while the oxytetracycline hydrochloride/hydrocortisone acetate/polymyxin B sulfate (ear or ear/eye drops) products should be further amended to add instructions on their use, as well as to add hypoacusis, deafness, tinnitus and dizziness as undesirable effects with a frequency 'not known'.

Summary of recommendation(s)

- The MAH(s) for oxytetracycline hydrochloride/hydrocortisone acetate/polymyxin B sulfate (ear/eye drops/suspension/ointment)-containing medicinal products should submit to national competent authorities, within 60 days, a variation to amend the product information[9].

4.2.4. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/SDA/015

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Signal of nephrotic syndrome

[8] Held 30 September - 03 October 2024
[9] Update of SmPC sections 4.2, 4.4 and 4.8 for oxytetracycline hydrochloride/hydrocortisone acetate/polymyxin B sulfate (ear or ear/eye drops). Update of SmPC section 4.4 for oxytetracycline hydrochloride/hydrocortisone acetate/polymyxin B sulfate (ointment). The package leaflets are to be updated accordingly.

EPITT 20123 – Follow-up to December 2024

Background

For background information, see PRAC minutes December 2024[10].

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

Discussion

Having considered the available evidence in EudraVigilance, clinical studies, literature and the MAH's responses, PRAC concluded that the current evidence is insufficient to establish a causal relationship between regorafenib and nephrotic syndrome to further warrant an update to the product information and/or RMP.

Summary of recommendation(s)

- In the next PSUR, the MAH for Stivarga (regorafenib) should include nephrotic syndrome as an important potential risk in the PSUR safety concerns, and follow-up on the new cases as warranted.

4.2.5. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/SDA/016

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Signal of hyperammonaemia, hyperammonaemic encephalopathy

EPITT 20147– Follow-up to February 2025

Background

For background information, see PRAC minutes February 2025.

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

Discussion

Having considered the available evidence in EudraVigilance, the literature and the MAH's responses, PRAC agreed that that there is sufficient evidence to establish a causal association between hyperammonaemia, hyperammonaemic encephalopathy and Stivarga (regorafenib). Therefore, the product information of Stivarga (regorafenib) should be updated to add hyperammonaemic encephalopathy as a warning and undesirable effect with a frequency 'not known'.

Summary of recommendation(s)

- The MAH for Stivarga (regorafenib) should submit to EMA, within 60 days, a variation to amend the product information[11].

4.3. Variation procedure(s) resulting from signal evaluation

None

[10] Held 25 - 28 November 2024
[11] Update of SmPC sections 4.4 and 4.8. The package leaflet is to be updated accordingly.

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

5.1.1. Autologous CD34+ haematopoietic stem cells transduced ex vivo with a lentiviral vector encoding human Wiskott-Aldrich syndrome protein - (CAP MAA) - EMEA/H/C/006525, Orphan

Applicant: Fondazione Telethon Ets, ATMP

Scope (pre D-120 phase): Treatment of patients with Wiskott-Aldrich Syndrome (WAS)

5.1.2. Belantamab mafodotin - (CAP MAA) - EMEA/H/C/006511, Orphan

Applicant: Glaxosmithkline Trading Services Limited

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

5.1.3. Delandistrogene moxeparvovec - (CAP MAA) - EMEA/H/C/005293, Orphan

Applicant: Roche Registration GmbH, ATMP

Scope (pre D-180 phase): Treatment of ambulatory patients aged 3 to 7 years old with Duchenne muscular dystrophy

5.1.4. Mirdametinib - (CAP MAA) - EMEA/H/C/006460, Orphan

Applicant: Springworks Therapeutics Ireland Limited

Scope (pre D-180 phase): Treatment of neurofibromatosis type 1

5.1.5. Nadofaragene firadenovec - (CAP MAA) - EMEA/H/C/005856

Scope (pre D-120 phase): Treatment of adult patients with high-grade (HG), Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC)

5.1.6. Vimseltinib - (CAP MAA) - EMEA/H/C/006363, Orphan

Applicant: Deciphera Pharmaceuticals (Netherlands) B.V.

Scope (pre D-180 phase): Treatment of adult patients with tenosynovial giant cell tumour (TGCT) who are not amenable to surgery

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

See also Annex I 15.2.

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

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Karin Bolin

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

Background

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

PRAC is evaluating a type II variation procedure for Idacio, a centrally authorised medicine containing adalimumab, to update the RMP to reflect the removal of the RABBIT study. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

Summary of advice

- The RMP for Idacio (adalimumab) in the context of the variation procedure under evaluation by PRAC and CHMP could be considered acceptable provided that an update to RMP version 6.2 is submitted.
- PRAC considered that in principle the discontinuation of the RABBIT study due to recruitment challenges could be accepted, pending the response to the request for supplementary information (RSI). However, PRAC agreed that the study should remain in the RMP until the final study report has been submitted and that the MAH should clarify whether the study has already been terminated, or if the final report could include data from a later cut-off date than the one proposed if the study is still ongoing. The MAH should also align the summary of safety concerns with the originator.

5.2.2. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/WS2125/0133; Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/WS2125/0047

Applicant: Alexion Europe SAS

PRAC Rapporteur: Monica Martinez Redondo

Scope: Submission of an updated RMP version 21.0 for SOLIRIS and RMP version 9.0 for ULTOMIRIS in order to revise the controlled distribution additional risk minimisation measures and to add a new post-authorisation safety study (PASS) intended to evaluate the effectiveness of the revised additional risk minimisation measures for minimising the risk of meningococcal infections in the EU, following the PRAC outcome for PSUSA/00001198/202310 for SOLIRIS. The Annex II is updated accordingly. In addition, the MAH introduced minor updates to the SmPC to align the wording with the updated Annex II

Background

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

PRAC is evaluating a type II variation procedure for Soliris, a centrally authorised medicine containing eculizumab, and for Ultomiris, a centrally authorised medicine containing ravulizumab to update the RMP to reflect the introduction of a new PASS to evaluate the effectiveness of the revised additional risk minimisation measures for minimising the risk of meningococcal infections in the EU. 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 May 2024 and PRAC minutes December 2024[12].

Summary of advice

- The RMP for Soliris (eculizumab) and for Ultomiris (ravulizumab) in the context of the work sharing variation procedure under evaluation by PRAC and CHMP is considered acceptable.
- Taking all relevant information into account, PRAC supported the discontinuation of the controlled distribution system for these two products. Furthermore, PRAC agreed with the proposal to reinforce the need for (re-)vaccination against all available serotypes with new key element in the healthcare professional and patient materials and to update the existing warnings in the product information. For Soliris (eculizumab), PRAC agreed to retain the important identified risks (IIR) of serious infections (including sepsis) in both the patient/parent information brochure and patient safety card, and of severe TMA complications due to drug discontinuation in aHUS patients in the patient/parent information brochure. For Ultomiris (ravulizumab), PRAC agreed to retain the IIR of serious infections and severe TMA complications due to drug discontinuation in aHUS patients in the patient/parent/legal guardian guide.

5.2.3. Meningococcal group B vaccine (recombinant, adsorbed) – TRUMENBA (CAP) - EMA/VR/0000247141

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of an updated RMP version 9.0 in order to propose the removal of "Use in co-administration with MMR and pneumococcal vaccines" as missing information from the safety concerns listed in the RMP and consequently, removal of the associated additional pharmacovigilance activity, study C3511006 (a Phase 3, randomized, controlled, open-label trial to assess the safety, tolerability, and immunogenicity of MenABCWY in healthy participants 12 to <24 months of age, and when administered concomitantly with MMR and pneumococcal vaccine in healthy participants ⩾12 to <16 months of age)

Background

[12] Held 25 - 28 November 2024

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

PRAC is evaluating a type II variation procedure for Trumenba, a centrally authorised medicine containing meningococcal group B vaccine (recombinant, adsorbed), to update the RMP to reflect the removal of the missing information on use in co-administration with MMR and pneumococcal vaccines, as well as the associated pharmacovigilance activity. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

Summary of advice

- The RMP version 9.0 for Trumenba (meningococcal group B vaccine (recombinant, adsorbed) in the context of the variation under evaluation by PRAC and CHMP is considered acceptable.
- PRAC agreed with the MAH's proposal to remove the missing information of 'use in co-administration with MMR and pneumococcal vaccines' from the list of safety concerns in the RMP considering that co-administration of Trumenba and MMR and/or pneumococcal vaccines is expected to be rare, no safety signals have been identified for this topic in the post-marketing data with the cumulative reporting adverse effects frequency following co-administration of Trumenba with MMR or pneumococcal vaccines in the indicated population to be very low. In addition, PRAC agreed with the removal of the planned additional pharmacovigilance activity associated with this missing information (Category 3 study C3511006). Finally, PRAC agreed that the MAH should continue to monitor any adverse effect reports describing co-administration of Trumenba with other vaccines, including MMR and pneumococcal vaccines, through routine pharmacovigilance activities.

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

See also Annex I 15.3.

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

Applicant: Sanofi B.V.

PRAC Rapporteur: Martin Huber

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

a long-term study the ongoing safety and efficacy of olipudase alfa in patients with ASMD. The Package Leaflet is updated accordingly. The RMP version 3.0 has also been submitted.

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 Xenpozyme, a centrally authorised product containing olipudase alfa, to update the product information and the RMP based on the final results from the DFI12712 ASCEND and LTS13632 studies. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure. For further background, see PRAC minutes November 2024[13] and PRAC minutes January 2025.

Summary of advice

- The RMP for Xenpozyme (olipudase alfa) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 3.2 is submitted.
- PRAC considered the MAH's responses and agreed to the maintenance of 'use in breastfeeding women' as missing information, and of the ongoing studies OBS17376, OBS18020 and OBS17422 as PASS to evaluate further the safety concerns in view of the limited data. PRAC agreed to the inclusion of the study protocols of OBS18020 and OBS17422 in the RMP, however the MAH should replace the draft protocol of study OBS17376 with the final study protocol in the RMP. Regarding the proposed MAH amendments to the key elements for the educational material to enhance safety reporting, PRAC supported that the specific follow-up questionnaires (FUQs) should be included in the RMP as routine pharmacovigilance activities, as the FUQs are considered adverse reaction specific and not product specific.

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. Abrocitinib - CIBINQO (CAP) - PSUSA/00010976/202409

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

Background

[13] Held 28 - 31 October 2024

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Cibinqo, a centrally authorised medicine containing abrocitinib and issued a recommendation on its marketing authorisation.

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Cibinqo (abrocitinib) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include neutropenia as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation should be varied[14].
- In the next PSUR, the MAH should continue to monitor cases of acute kidney injury, cases suggestive of drug-induced liver injury (DILI) and cases of hepatic transaminase elevations. In addition, the MAH should submit a cumulative review of all cases of cutaneous T-cell lymphoma in the next PSUR, including data from clinical trials, literature and post-marketing sources. The MAH should comment on potential mechanism of action and also discuss whether a product information update is warranted.

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

6.1.2. Epcoritamab - TEPKINLY (CAP) - PSUSA/00000107/202409

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

Background

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

Summary of recommendation(s) and conclusions

- Based on the review of the data on safety and efficacy, the benefit-risk balance of Tepkinly (epcoritamab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding haemophagocytic lymphohistiocytosis (HLH). Therefore, the current terms of the marketing authorisation(s) should be varied[15].
- In the next PSUR, the MAH should continue to monitor cases of HLH in order to discuss if the level of evidence has changed and further amendments to product information are warranted. In addition, the MAH should provide a cumulative review of cases of delirium and discuss whether the available evidence suggest a change regarding the risk of

[14] 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.
[15] 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.

progressive multifocal leukoencephalopathy (PML) and whether an update of the product information is warranted.

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

6.1.3. Isavuconazole - CRESEMBA (CAP) - PSUSA/00010426/202409

Applicant: Basilea Pharmaceutica Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Cresemba, a centrally authorised medicine containing isavuconazole 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 Cresemba (isavuconazole) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add hyponatremia as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[16].

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

6.1.4. Loxapine[17] - ADASUVE (CAP) - PSUSA/00010113/202408

Applicant: Ferrer Internacional s.a.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

Background

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

[16] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[17] Pre-dispensed inhalation powder only

- Nevertheless, the product information should be updated to add drug rash with eosinophilia and systemic symptoms (DRESS) as a warning. Therefore, the current terms of the marketing authorisation(s) should be varied[18].
- In the next PSUR, the MAH should add DRESS as important potential risk in the PSUR list of safety concerns. In addition, the MAH should continue monitor cases of DRESS and discuss the need for further risk minimisation measures, 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.

6.1.5. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - PSUSA/00010366/202409

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Mysimba, a centrally authorised medicine containing naltrexone hydrochloride/bupropion hydrochloride 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 Mysimba (naltrexone hydrochloride/bupropion hydrochloride) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be amended to include a statement on the availability and accessibility of the patient card for Mysimba. Therefore, the current terms of the marketing authorisation(s) should be varied[19].
- In the next PSUR, the MAH should provide reviews of cases of DRESS, chronic eosinophilic pneumonia, medication errors, off-label use and abuse, fall, injury and fracture, co-administration with other anti-obesity drugs. The MAH should also provide an effectiveness evaluation of the patient card and product information updates related to the risk of opioid interactions.

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

6.1.6. Nivolumab, relatlimab - OPDUALAG (CAP) - PSUSA/00011018/202409

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

[18] 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.
[19] 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.

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Opdualag, a centrally authorised medicine containing nivolumab/relatlimab 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 Opdualag (nivolumab/relatlimab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to include myasthenia gravis as a warning and as an undesirable effect with a frequency 'uncommon'. In addition, the product information should be updated to reflect the available data regarding the safety of patients with pre-existing autoimmune disease (AID). Therefore, the current terms of the marketing authorisation(s) should be varied[20].
- In the next PSUR, the MAH should monitor the safety of nivolumab/relatlimab fixed dose combination in patients with pre-existing autoimmune disorders and provide cumulative evidence on this aspect. Based on the available evidence, the MAH should discuss whether an update of the product information is warranted.

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

6.1.7. Pembrolizumab - KEYTRUDA (CAP) - PSUSA/00010403/202409

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Keytruda, a centrally authorised medicine containing pembrolizumab 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 Keytruda (pembrolizumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding immune-mediated adverse reactions in patients with pre-existing autoimmune disease. Therefore, the current terms of the marketing authorisation(s) should be varied[21].

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

- In the next PSUR, the MAH should provide a review of cases of immune-mediated adverse events following in utero exposure to pembrolizumab, including data from literature and post-marketing setting. In addition, the MAH should provide a cumulative review of cases of myositis/myasthenia gravis overlap syndrome, including data from literature, clinical trials and post-marketing setting and discuss the need for update of the product information, as warranted.

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

6.1.8. Somapacitan - SOGROYA (CAP) - PSUSA/00010920/202408

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Background

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Sogroya, a centrally authorised medicine containing somapacitan 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 Sogroya (somapacitan) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding the risk of risk of slipped capital femoral epiphysis (SCFE). Therefore, the current terms of the marketing authorisation(s) should be varied[22].
- In the next PSUR, the MAH should monitor the risk of SCFE and osteonecrosis (including related terms such as Legg-Calve-Perthes disease) in association with somapacitan use and provide review of such cases.

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

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

See also Annex I 16.2.

6.2.1. Glycopyrronium[23] - SIALANAR (CAP); NAP - PSUSA/00010529/202409

Applicant(s): Proveca Pharma Limited, various

[22] 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.
[23] For severe sialorrhoea indication only

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Background

Glycopyrronium bromide is a synthetic quaternary ammonium muscarinic anticholinergic agent and it is indicated for the symptomatic treatment of severe sialorrhoea in children and adolescents aged 3 years and older with chronic neurological disorders.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Sialanar, (a) centrally authorised medicine(s) containing glycopyrronium, and nationally authorised medicines containing glycopyrronium 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 glycopyrronium-containing product(s) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisations should be maintained.
- In the next PSUR, all MAHs should monitor cases of dosing errors leading to anticholinergic side effects (safety concern 'Anticholinergic side effects due to dosing errors: constipation, urinary retention, pneumonia, risk of overheating, cardiac disorders, dental caries, CNS effects') and provide an analysis of these cases with particular focus on the type of the dosing error (prescribing, dispensing).

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

6.2.2. Measles, mumps, rubella, varicella vaccines (live) - PROQUAD (CAP); NAP - PSUSA/00001936/202409

Applicants: Merck Sharp & Dohme B.V. (ProQuad), various

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Background

The vaccine is indicated for simultaneous vaccination against measles, mumps, rubella, and varicella (MMRV) in individuals 12 months to 12 years of age.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Proquad, (a) centrally authorised medicine(s) containing measles, mumps, rubella, varicella vaccines (live), and nationally authorised medicines containing measles, mumps, rubella, varicella vaccines (live) 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 measles, mumps, rubella, varicella vaccines (live)-containing product(s) in the approved indication(s) remains unchanged.

- Nevertheless, the product information for ProQuad and Priorix-Tetra should be updated to amend the recommendations for use in pregnancy. In addition, the product information for Priorix-Tetra should be updated to amend the definition of contraindication in the presence of immunosuppression. Therefore, the current terms of the marketing authorisations should be varied[24].
- In the next PSUR, the MAH(s) should perform a cumulative review of cases of hemophagocytic lymphohistiocytosis (HLH) and discuss whether genetic mutations associated with the cases of HLH were reported. In addition, the MAH of Priorix-Tetra should provide a cumulative review of cases of skin and visceral granulomas in immunocompetent patients following immunisation with rubella virus containing vaccines and discuss whether a product information update is warranted.

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

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

See also Annex I 16.3.

6.3.1. Etonogestrel (NAP) - PSUSA/00001331/202409

Applicant(s): various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

Background

Etonogestrel is a synthetic progestin hormone indicated for contraception in women.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing etonogestrel (implant) 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 etonogestrel-containing medicinal products (implant) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to remove the drug-drug interaction between etonogestrel and ritonavir. Therefore, the current terms of the marketing authorisation(s) should be varied[25].
- In the next PSUR, the MAH(s) should continue to monitor cases of insertion and removal related events and to provide an evaluation of the effectiveness of routine and/or additional risk minimisation activities to minimise the risk of deep insertions and implant migrations. The MAH(s) should discuss any available information on awareness and

[24] Update of SmPC sections 4.3 and 4.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[25] Update of SmPC section 4.5. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.

knowledge of the risk minimisation measures and whether the current additional risk minimisation measures are adequate to cover the risks of deep insertions and implant migrations. The MAH(s) should conduct a review of device breakage cases and analyse the root causes, including those related to the manufacturing process. Additionally, the MAH(s) are expected to provide a comprehensive review of the interaction between the etonogestrel implant and ulipristal. A report should be submitted detailing the proportion of cases where device removal was unsuccessful, along with available information on the long-term effects observed in these instances. The report should also address appropriate (routine) follow-up activities for managing such cases. In future PSURs, the MAH(s) are requested to take into account all cases of migration into the pulmonary artery.

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. Hydrocortisone[26] (NAP) - PSUSA/00010855/202408

Applicant(s): various

PRAC Lead: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

Background

Hydrocortisone is a glucocorticoid primarily used for its anti-inflammatory effects in disorders of many organ systems such as skin conditions, ophthalmic, rectal and ear indications.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing hydrocortisone 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 hydrocortisone-containing medicinal products (for systemic formulations except for products indicated in adrenal insufficiency in a modified release tablet formulation and except for centrally authorised products for adrenal insufficiency, paediatric use only) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning on thyrotoxic periodic paralysis (TPP). Therefore, the current terms of the marketing authorisation(s) should be varied[27].
- In the next PSUR, the MAH(s) should provide a review of cases of anaemia, aplastic anaemia, febrile neutropenia, neutropenia and thrombosis, including data from literature, clinical trials and post-marketing setting. The MAH(s) should also continue to closely monitor sinus bradycardia and oral/orofacial clefts.

[26] For systemic formulations except for products indicated in adrenal insufficiency in a modified release tablet formulation and except for centrally authorised products for adrenal insufficiency, paediatric use only
[27] Update of SmPC section 4.4. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position.

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. Meropenem (NAP) - PSUSA/00001989/202408

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Background

Meropenem is a carbapenem antibiotic, belonging to the β-lactam family of antibiotics. It is a broad-spectrum agent with in-vitro activity against multiple aerobic and anaerobic Gram-positive and Gram-negative bacteria indicated in a wide range of infections in both adults and children and in host compromised neutropenic patients, and for polymicrobial infections, such as lower respiratory tract infections, urinary tract infections including complicated infections, intra-abdominal infections, gynaecological infections including postpartum infections, skin and skin structure infections, septicaemia, meningitis. Intravenous (IV) meropenem has been used effectively in patients with cystic fibrosis and chronic lower respiratory tract infections, either as monotherapy or in combination.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing meropenem 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 meropenem-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding drug-induced liver injury (DILI) to highlight that if severe DILI occurs, treatment discontinuation should be considered as clinically appropriate and reintroduced only if assessed as essential for treatment. In addition, the product information should be updated to add hypokalaemia and DILI (including hepatitis and liver failure) as undesirable effects with frequencies 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[28].
- In the next PSUR, the MAH(s) should keep under monitoring the following topics: factor V inhibition/anti factor V antibody, hypertriglyceridemia, symmetric drug-related intertriginous and flexural exanthema (SDRIFE) and necrotising enterocolitis, and provide a review if new relevant information is identified.

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.

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

6.3.4. Oxcarbazepine (NAP) - PSUSA/00002235/202408

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

Background

Oxcarbazepine is a first-line antiepileptic agent for use as monotherapy or adjunctive therapy and it can replace other Antiepileptic Drugs (AEDs) when current therapy provides insufficient seizure control. It is indicated for the treatment of partial seizures (which include the seizure subtypes of simple, complex and partial seizures evolving to secondarily generalized seizures) and generalised tonic-clonic seizures.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing oxcarbazepine 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 oxcarbazepine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding the risk of infants being small for gestational age following use of oxcarbazepine during pregnancy. Therefore, the current terms of the marketing authorisation(s) should be varied[29].
- In the next PSUR, the MAH(s) should provide a thorough analysis on the safety of oxcarbazepine use during pregnancy, including information about number of women exposed to oxcarbazepine during pregnancy, and the pregnancy outcomes. The MAH(s) should place a special emphasis on whether this new information alters the safety profile of oxcarbazepine exposure during pregnancy and the risk of congenital malformations as well as other relevant outcomes. Based on the findings, the MAH(s) should discuss whether an update of the product information is warranted. In addition, the MAH(s) are reminded of the request in the conclusions of the previous PSUSA procedure to provide a review regarding breastfeeding in the upcoming PSURs.

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

6.4. Follow-up to PSUR/PSUSA procedures

None

6.5. Variation procedure(s) resulting from PSUSA evaluation

See also Annex I 16.5.

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

6.5.1. Mogamulizumab - POTELIGEO (CAP) - EMEA/H/C/004232/II/0026, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of section 4.8 of the SmPC in order to add 'granuloma' to the list of adverse drug reactions (ADRs) with frequency 'unknown', based on post marketing data; the Package Leaflet is updated accordingly

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 cumulative review on granuloma in the next PSUR during the procedure PSUSA/00010741/202303. The MAH submitted a variation to update the product information in order to add 'granuloma' as an undesirable effect. PRAC is responsible for adopting an outcome based on the assessment report from the PRAC Rapporteur, to be further considered at the level of CHMP, responsible for adopting an opinion on this variation.

Summary of recommendation(s)

- Based on the available data and the Rapporteur's assessment, PRAC agreed that the product information should be updated[30] to add granuloma as undesirable effect with a frequency 'not known'. PRAC also endorsed the classification of granuloma as a non-important identified risk in context of the PSUR(s).

6.6. Expedited summary safety reviews[31]

None

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[32]

See also Annex I 17.1.

7.1.1. Valproate (NAP) - EMEA/H/N/PSP/J/0108.1

Applicant: Sanofi-Aventis Recherche & Développement (on behalf of a consortium)

PRAC Rapporteur: Liana Martirosyan

Scope: MAH's response to PSP/0108 [Paternal exposure to valproate, further investigation on the risk of Neuro Developmental Disorders (NDD) and Congenital Malformation (CM) in Offspring: A Non-Interventional Post-Authorization Safety Study (PASS)] as per the request

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

for supplementary information (RSI) adopted in Oct 2024

Background

Valproic acid and the relates substances are antiepileptics indicated for the treatment of epilepsy, of bipolar disorders restricted to the treatment of manic episodes when lithium is contraindicated or not tolerated, and for the prophylaxis of migraine attacks, as warranted.

For further background on this procedure, see PRAC minutes November 2025[33].

Endorsement/Refusal of the protocol

- Having considered the draft protocol version 2.0 in accordance with Article 107n of Directive 2001/83/EC, PRAC objected to the draft protocol for the above listed medicinal product(s), as the Committee considered that that the design of the study did not fulfil the study objectives at this stage.
- PRAC requested the MAH to provide further updates of the protocol in relation to the definition of NDD, confounders and risk factors of NDD / major CM, data analyses and the statistical models to be used, and requested further sensitivity analyses.
- The MAH should submit a revised PASS protocol by 7 May 2025 to EMA. A 30 days-assessment timetable will be followed.

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

See Annex I 17.2.

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

See also Annex I 17.3.

7.3.1. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSR/S/0050

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: Final study report for a non-interventional post-authorisation safety study to investigate drug utilisation and safety monitoring patterns for Lemtrada (alemtuzumab)

Background

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

In line with the conclusions reached in 2019 of the referral procedure under Article 20 of Regulation (EC) No 726/2004 conducted by PRAC, the MAH was required to conduct a PASS to assess the implementation of the risk minimisation measures to address the new safety events such as cardiovascular disorders and immune-related disorders in routine clinical

[33] Held 28 - 31 October 2024
[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
[35] In accordance with Article 107p-q of Directive 2001/83/EC

practice (Annex II-D). In July 2021, PRAC endorsed the PASS protocol version 1.4 (dated May 2021) submitted by the MAH.

The final study report was submitted to EMA by the MAH Sanofi Belgium on 13 September 2024. PRAC discussed the final study results.

Summary of recommendation(s) and conclusions

- Based on the review of the final report of the non-interventional PASS entitled 'A non-interventional post-authorisation safety study to investigate drug utilisation and safety monitoring patterns for LEMTRADA (alemtuzumab)', PRAC considered that the benefit-risk balance of Lemtrada (alemtuzumab) remains unchanged. As a consequence, PRAC recommended that the terms of the marketing authorisation(s) for Lemtrada (alemtuzumab) should be varied to remove the PASS as an obligation from Annex-IID on the 'conditions or restrictions with regard to the safe and effective use of the medicinal product'.

7.3.2. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSR/S/0051

Applicant: Sanofi Belgium

PRAC Rapporteur: Karin Erneholm

Scope: Final study report for a non-interventional post-authorisation safety study to investigate the risk of mortality in multiple sclerosis patients treated with alemtuzumab (Lemtrada) relative to comparable multiple sclerosis patients using other disease modifying therapies: a cohort study

Background

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

In line with the conclusions reached in 2019 of the referral procedure under Article 20 of Regulation (EC) No 726/2004 conducted by PRAC, the MAH was required as a condition to the marketing authorisation (Annex II-D) to conduct a PASS to investigate the incidence of mortality in patients treated with Lemtrada compared to a relevant patient population. In July 2021, PRAC endorsed the PASS protocol version 1.4 (dated 20 May 2021) submitted by the MAH Sanofi Belgium.

The final study report was submitted to EMA by the MAH Sanofi Belgium on 11 November 2024. PRAC discussed the final study results.

Summary of recommendation(s) and conclusions

- Based on the review of the final report of the non-interventional PASS entitled 'A Non-Interventional Post-Authorisation Safety Study to Investigate the Risk of Mortality in Multiple Sclerosis Patients Treated with Alemtuzumab (LEMTRADA®) Relative to Comparable Multiple Sclerosis Patients Using Other Disease Modifying Therapies: A Cohort Study', PRAC considered that the benefit-risk balance of Lemtrada (alemtuzumab) remains unchanged. As a consequence, PRAC recommended that the terms of the marketing authorisation(s) for Lemtrada (alemtuzumab) should be varied to remove the PASS as an obligation from Annex-IID on the 'conditions or restrictions with regard to the safe and effective use of the medicinal product'.

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

See also Annex I 17.4.

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

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

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

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 Exjade (deferasirox), the MAH conducted a non-imposed non-interventional PASS to assess physicians' knowledge of Exjade posology and biological monitoring recommendations as described in the EMs. The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI).

Summary of advice

- Based on the available data, the MAH's responses to the RSI and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be considered acceptable provided that the MAH submits satisfactory responses to a RSI.
- PRAC endorsed the MAH's proposal to remove the study CICL670A2429 as an additional pharmacovigilance activity from the RMP. In addition, PRAC agreed to keep 'compliance with posology and biological monitoring' as a safety concern monitored as an important potential risk in the PSUR(s). Finally, PRAC agreed with the update of the product information (section 4.2) taking the results of the study into account, however the Committee considered that the wording should be further updated to improve readability.

7.4.2. Etanercept - ENBREL (CAP) - EMEA/H/C/000262/II/0255

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Monica Martinez Redondo

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to remove information regarding the Patient Card, based on final results from study B1801309 (BSR Register of Anti-TNF Treated Patients and Prospective Surveillance Study for Adverse Events: Enbrel). This is a non-interventional PASS study listed as a category 3 study in the RMP. The Annex II and Package Leaflet are updated accordingly. The RMP version 7.7 has also been

[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

submitted. In addition, the MAH took the opportunity to introduce minor editorial and formatting changes to the PI as well as to update the list of local representatives in the Package Leaflet and align the PI with the QRD version 10.4

Background

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

As stated in the RMP of Enbrel (etanercept), the MAH conducted a non-imposed non-interventional PASS comparing the safety profile of etanercept before and after 3 years of introduction of high-capacity manufactured product. The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI).

Summary of advice

- Based on the available data, the MAH's responses to the RSI and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be considered acceptable provided that the MAH submits satisfactory responses to a RSI.
- PRAC endorsed the removal of the non-interventional category 3 study B1801309 (BSR Register of Anti-TNF Treated Patients and Prospective Surveillance Study for Adverse Events: Enbrel) as an additional pharmacovigilance activity from the RMP. In addition, given the relevance of serious infections such as tuberculosis and the need to perform relevant test prior to start Enbrel to evaluate for both active and inactive ('latent') tuberculosis, PRAC did not endorse the MAH's proposal to remove the patient card as additional risk minimisation measures (RMMs). However, considering that the patient card does not provide additional information to that which is already included in the product information for the important identified risk of congestive heart failure in adult subjects, PRAC endorsed the removal of this risk from the patient card. Finally, the RMP should be updated to remove the following safety concerns from the list of safety specifications: aplastic anaemia and pancytopenia, congestive heart failure in adult subjects and acute ischaemic cardiovascular events in adult subjects, as well as immunogenicity profile and related clinical outcomes of etanercept manufactured using the SFPHC process in a real-life post-marketing setting which should also be removed from the patient card while the batch number should remain as a key element.
- The MAH should submit an updated RMP in line with the requested changes.

7.4.3. Influenza quadrivalent vaccine (rDNA[37]) - SUPEMTEK TETRA (CAP) - EMEA/H/C/005159/II/0020

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Zoubida Amimour

Scope: Update of section 4.6 of the SmPC in order to update pregnancy information based on final results from study VAP00007 (non-interventional PASS); this is a Phase IV, observational retrospective post-authorization, descriptive, safety surveillance study to evaluate the safety of RIV4 in pregnant women and their offspring exposed during

[37] Ribosomal deoxyribonucleic acid

pregnancy or up to 28 days preceding the estimated date of conception with regards to pregnancy, birth, and neonatal/infant outcomes

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 Supemtek Tetra, the MAH conducted a non-imposed non-interventional PASS to evaluate the safety of RIV4 in pregnant women and their offspring exposed during pregnancy or up to 28 days preceding the estimated date of conception with regards to pregnancy, birth, and neonatal/infant outcomes. The Rapporteur assessed the MAH's final study report in addition to the MAH's answers to the request for supplementary information (RSI).

Summary of advice

- Based on the available data, the MAH's responses to the RSI and the Rapporteur's review, PRAC considered that the ongoing variation assessing the final study report could be recommended for approval.
- PRAC agreed that the product information should be updated[38] to reflect that Supemtek tetra can be used during pregnancy be used during pregnancy in accordance with official recommendations, based on the final results from study VAP00007.

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

See Annex I 17.5.

7.6. Others

See Annex I 17.6.

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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

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

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

[38] Update of SmPC section 4.6

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

8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1.

8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2.

8.3. Renewals of the marketing authorisation

See Annex I 18.3.

9. Product related pharmacovigilance inspections

9.1. List of planned pharmacovigilance inspections

None

9.2. Ongoing or concluded pharmacovigilance inspections

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

9.3. Others

None

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

10.1. Safety related variations of the marketing authorisation

None

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

None

10.3. Other requests

None

10.4. Scientific Advice

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

contain commercially confidential information.

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

11.1. Safety related variations of the marketing authorisation

None

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of PRAC

12.1.1. PRAC Best Practice Guide - Recommendations on efficiency of plenary meetings - Revision 2

PRAC lead: Martin Huber

The revision 2 of the Best Practice Guide aimed at providing hands-on guidance to PRAC members/alternates was presented to PRAC following separate discussions with the established group consisting of PRAC members and EMA. The revised document was presented and discussed during the plenary and adopted by PRAC. A follow-up discussion is planned in the upcoming months related to the implementation plan.

12.1.2. PRAC membership

None

12.1.3. Vote by proxy

Annalisa Capuano gave a proxy to Milou Drici for the whole meeting.

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

None

12.4. Cooperation within the EU regulatory network

12.4.1. European medicines agencies network strategy (EMANS) to 2028

The EMA Secretariat presented to PRAC the EMANS strategy to 2028, following its adoption

by the EMA Management Board and the Heads of Medicines Agencies (HMA). The strategy is a comprehensive update of the five-year strategy developed to cover the period 2021 to 2025 (EMANS 2025) and aims to guide the European medicines regulatory network over the next few years to meet the challenges ahead, including preparing for and responding to public health emergencies and threats, as well as further changes to the technological and regulatory landscape including the revision of the pharmaceutical legislation. PRAC noted the information.

12.4.2. Exchange of views with European Commission on Pharmaceutical Legislation Reform

The PRAC members received an update on the reform of the pharmaceutical legislation, in particular on the proposed reform of the EMA committees and exchanged views with the EC Representatives.

12.5. Cooperation with International Regulators

12.5.1. International Coalition of Medicines Regulatory Authorities (ICMRA) Working Group on Real World Evidence (RWE) for Public Health Emergencies: mandate, general principles and process for conducting collaboratives studies

PRAC was informed on the goal of this ICMRA working group (WG) to create a forum to facilitate international cooperation between interested regulatory agencies to proactively enhance the efficiency of critical responses in case of new public health emergencies through collaborative studies. The EMA Secretariat presented the WG, including its mandate, general principles and processes. Through this framework, PRAC would have the possibility to request studies, that then to be run together with other agencies across the world, in view to increase sample sizes and generate meaningful evidence for regulatory assessment and decision making. PRAC members were invited to provide ideas of collaborative studies to be moved under this framework and the interactions of development of a protocol. PRAC noted the information.

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)

None

12.10.3. PSURs repository

None

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

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

12.11. Signal management

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

PRAC lead: Martin Huber

PRAC was updated on the ongoing activities of the SMART working group – work stream Methods meeting held on 20 March 2025. Among the topics discussed were the update on pilots and prototypes of the use of artificial intelligence (AI) and automation in signal detection workflow, an overview of drug interaction signals using a process developed by the EMA Health Data Lab. PRAC noted the information. For the previous update, see PRAC minutes February 2025.

12.12. Adverse drug reactions reporting and additional monitoring

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

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

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. Onboarding experience of Committee/CMD members and alternates

Topic postponed for discussion at the PRAC May 2025 meeting.

12.21.2. Real World Evidence (RWE) and Data analysis and real-world interrogation network (DARWIN EU®) – update

The EMA Secretariat presented to PRAC an update on RWE and DARWIN EU activities, including the progress on the growth of the network of data partners and an update regarding the ongoing and finalised real-world data (RWD) studies, as well as a list of new requests for studies to be performed. The EMA Secretariat also presented the upcoming events related to RWE organised by EMA and recent publications. PRAC was also informed on the ongoing discussions and reflections related to the approach to be followed when RWE studies are requested in the context of PSUSAs and signals. PRAC provided comments that will further streamline the processes.

12.21.3. Replacement of Annex C – Use of the IRIS NCA Dashboard to extract the relevant information

The EMA Secretariat presented to PRAC the new tool connected to IRIS which intends to replace the Annex C that was previously circulated, along with a demo on its use. PRAC members were invited to provide comments. EMA will keep circulating the Annex C, until further development of the tool.

13. Any other business

None

14. Annex I – Signals assessment and prioritisation[39]

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[40].

14.1. New signals detected from EU spontaneous reporting systems

14.1.1. Diazoxide (NAP)

Applicant(s): various

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of necrotising enterocolitis neonatal

EPITT 20163 – 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/006438

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

15.1.2. Aflibercept - (CAP MAA) - EMEA/H/C/006761

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

[39] 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

[40] 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

impairment

15.1.3. Aflibercept - (CAP MAA) - EMEA/H/C/006282

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

15.1.4. Denosumab - (CAP MAA) - EMEA/H/C/006436

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

15.1.5. Denosumab - (CAP MAA) - EMEA/H/C/006437

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

15.1.6. Emtricitabine, rilpivirine, tenofovir alafenamide - (CAP MAA) - EMEA/H/C/006491

Scope (pre D-180 phase): Treatment of HIV-1

15.1.7. Macitentan - (CAP MAA) - EMEA/H/C/006524

Scope (pre D-180 phase): Treatment of pulmonary arterial hypertension (PAH)

15.1.8. Macitentan - (CAP MAA) - EMEA/H/C/006523

Scope (pre D-180 phase): Treatment of pulmonary arterial hypertension (PAH)

15.1.9. Nintedanib - (CAP MAA) - EMEA/H/C/006486

Scope (pre D-180 phase): Treatment of Idiopathic Pulmonary Fibrosis (IPF), other chronic fibrosing interstitial lung diseases (ILDs) and systemic sclerosis associated interstitial lung disease (SSc-ILD)

15.1.10. Ustekinumab - (CAP MAA) - EMEA/H/C/006467

Scope (pre D-180 phase): Treatment of Crohn’s disease and ulcerative colitis, treatment of plaque psoriasis, arthritis psoriatic

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. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/II/0034, Orphan

Applicant: Janssen-Cilag International NV, ATMP

PRAC Rapporteur: Jo Robays

Scope: Submission of an updated RMP version 5.2 in order to add a new important identified risk of "Secondary malignancy of T-cell origin", to change the important potential risk of "Second primary malignancies" to "Second primary malignancy except secondary malignancy of T-cell origin", and to include an additional pharmacovigilance activity for testing of secondary malignancies of T-cell origin, following the PRAC recommendation for the Secondary malignancy of T-cell origin signal (EPITT no: 20040)

15.2.2. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0071

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP version 8.1 in order to add a medullary thyroid cancer (MTC) database linkage study (Study I8F-MC-B014) as an additional pharmacovigilance activity to evaluate the important potential risk of MTC in patients exposed to long-acting glucagon-like peptide-1 receptor agonist (GLP-1 RA) therapies. In addition, the MAH took the opportunity to include an amendment to Study H9X-MC-B013 due to the removal of the United States data source

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

Applicant: UCB Pharma SA

PRAC Rapporteur: Martin Huber

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

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

Applicant: Phoenix Labs Unlimited Company

PRAC Rapporteur: Karin Erneholm

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

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

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

15.3.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/II/0028

Applicant: AstraZeneca AB

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Extension of indication to include CALQUENCE in combination with venetoclax with or without obinutuzumab for the treatment of adult patients with previously untreated chronic lymphocytic leukemia (CLL), based on interim results from study AMPLIFY (D8221C00001). This is a Randomized, Multicenter, Open-Label, Phase 3 Study to Compare the Efficacy and Safety of Acalabrutinib in Combination with Venetoclax with and without Obinutuzumab Compared to Investigator's Choice of Chemoimmunotherapy in Subjects with Previously Untreated Chronic Lymphocytic Leukemia Without del(17p) or TP53 Mutation (AMPLIFY). 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 of the RMP has also been submitted.

15.3.2. Afamelanotide - SCENESSE (CAP) - EMA/VR/0000247271

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

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

15.3.3. Tecovirimat - TECOVIRIMAT SIGA (CAP) - EMA/VR/0000244868

Applicant: Siga Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.5 of the SmPC in order to add drug-drug interaction information with calcium acetate, lanthanum carbonate, sevelamer carbonate, and sucroferric oxyhydroxide based on final results from study SIGA-246-023. This is a safety, tolerability, and efficacy study of 4 phosphate binders on tecovirimat in adults. The Package Leaflet has been updated accordingly. The RMP version 2.1 has also been submitted

15.3.4. Tezepelumab - TEZSPIRE (CAP) - EMA/VR/0000245013

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

Scope: Extension of indication to include treatment of Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) for Tezspire, based on results from study WAYPOINT (D5242C00001); this is a global, multicentre, randomised, double-blind, parallel-group, placebo-controlled study that evaluated the efficacy and safety of tezepelumab compared with placebo in the treatment of CRSwNP. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes and to update the PI and the Package Leaflet in accordance with the latest EMA excipients guideline

15.3.5. Tolvaptan - JINARC (CAP) - EMA/VR/0000246866

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to update information based on final results from study 156-12-299 listed as a category 1 study in the RMP. This is a 7.5-year, Multicentre, Non-interventional, Post-authorisation Safety Study for Patients Prescribed JINARC for Autosomal Dominant Polycystic Kidney Disease. This study was intended to explore the safety profile and usage of Jinarc when used in the real-world setting in Europe, particularly with relation to the risk of liver injury. The Package Leaflet is updated accordingly. The RMP version 15.1 has also been submitted. In addition, the MAH took the opportunity to update Annex II section D, to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10.4

15.3.6. Venetoclax - VENCLYXTO (CAP) - EMA/VR/0000246380

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Update of sections 4.2, 4.9 and 5.2 of the SmPC in order to inform no adjustment is needed in patients with ESRD requiring dialysis and to add information on the pharmacokinetics data for patients with ESRD requiring dialysis, based on final results from study M19-065, "Evaluation of the Pharmacokinetics and Safety of Venetoclax in Subjects with Impaired Renal Function". The RMP version 10.0 has also been submitted

15.3.7. Zoonotic influenza vaccine (H5N8) (surface antigen, inactivated, adjuvanted)- ZOONOTIC INFLUENZA VACCINE SEQIRUS (CAP) - EMA/VR/0000249071

Applicant: Seqirus S.r.l.

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of individuals 6 months of age and above for Zoonotic Influenza Vaccine Seqirus based on final results from study V87_30. This is a Phase 2, Randomized, Observer-Blind, Multicenter Study to Evaluate the Immunogenicity and Safety of Several Doses of Antigen and MF59 Adjuvant Content in a Monovalent H5N1 Pandemic Influenza Vaccine in Healthy Pediatric Subjects 6 Months to < 9 Years of Age. As a consequence, sections 4.1, 4.2, 4.6, 4.7, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 6.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes to the PI

15.3.8. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0111

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication for ADCETRIS to include treatment for adult patients with previously untreated CD30+ Stage IIB with risk factors, Stage III or Stage IV HL in combination with etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone (BrECADD), based on final results from phase 3 study HD21 (NCT02661503). This study is titled Treatment Optimization Trial in the First-Line Treatment of Advanced-Stage Hodgkin Lymphoma; Comparison of 4-6 Cycles of Escalated BEACOPP With 4-6 Cycles of BrECADD.

As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 20.0 of the RMP has also been submitted.
In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to implement editorial changes to the SmPC

15.3.9. Clopidogrel - CLOPIDOGREL ZENTIVA (CAP) - EMEA/H/C/000975/II/0092

Applicant: Zentiva k.s.

PRAC Rapporteur: Carla Torre

Scope: Extension of indication to include, in combination with acetylsalicylic acid (ASA), patients with ST segment elevation acute myocardial infarction (STEMI) who are undergoing percutaneous coronary intervention (PCI) for CLOPIDOGREL ZENTIVA. As a consequence, sections 4.1, 4.2, 4.4 and 5.1 of the SmPC are updated. Version 0.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet, introduce minor editorial changes to the PI and bring it in line with the latest QRD template version 10.4

15.3.10. Concizumab - ALHEMO (CAP) - EMA/VR/0000244862

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Extension of indication to include treatment of haemophilia A without inhibitors and haemophilia B without inhibitors for ALHEMO based on final results from study NN7415-4307; this is an interventional study to investigate efficacy and safety of concizumab prophylaxis in patients with haemophilia A or B without inhibitors. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor changes to the PI

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

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

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

15.3.12. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/II/0034

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment and prophylaxis of bleeding in

previously treated patients ≥7 years of age with haemophilia A for JIVI, based on integrated analysis results from Part A of the Alfa-PROTECT study (21824) and PROTECT Kids main study (15912). Alfa-PROTECT is a Phase 3, single-group treatment, open-label study to evaluate the safety of BAY 94-9027 infusions for prophylaxis and treatment of bleeding in previously treated children aged 7 to <12 years with severe hemophilia A. PROTECT Kids is a multi-center, Phase 3, non-controlled, open-label trial to evaluate the pharmacokinetics, safety, and efficacy of BAY 94-9027 for prophylaxis and treatment of bleeding in previously treated children (age <12 years) with severe haemophilia A. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template version 10.4

15.3.13. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/X/0033/G

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to add a new strength of Jivi 4000 UI powder and solvent for solution for injection for treatment and prophylaxis of bleeding in previously treated patients ⩾ 12 years of age with haemophilia A (congenital factor VIII deficiency).
Version 3.1 of the RMP has also been submitted.
In addition, the MAH has taken the opportunity to align the product information with the pre-specified language from the updated EC Excipient Guideline.

15.3.14. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/II/0020, Orphan

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension of indication to include the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) with active disease despite treatment with corticosteroids or immunoglobulins for VYVGART, based on final results from study ARGX-113-1802; this is a pivotal study to investigate the efficacy, safety and tolerability of efgartigimod PH20 SC in adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP); and based on interim results from study ARGX-113-1902; this is an open-label extension study of the ARGX-113-1802 trial to investigate the long-term safety, tolerability and efficacy of efgartigimod PH20 SC in patients with (CIDP).
As a consequence, sections 4.1, 4.2. 4.4, 4.8, 5.1 and 5.2 of the SmPC has been updated. The Package Leaflet has been updated in accordance with the SmPC. In addition, the MAH took the opportunity to implement editorial changes to the SmPC

15.3.15. Eltrombopag - REVOLADE (CAP) - EMEA/H/C/001110/II/0077

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Extension of indication to include second-line treatment of paediatric patients aged 2 years and above with acquired severe aplastic anaemia (SAA) for REVOLADE based on the

ETB115E2201 (E2201) study primary analysis results; this is a paediatric phase II, open-label, uncontrolled, intra-patient dose escalation study to characterise the pharmacokinetics after oral administration of eltrombopag in paediatric patients with refractory, relapsed severe aplastic anaemia or recurrent aplastic anaemia. 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 56.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI

15.3.16. Florbetaben (^{18}F) - NEURACEQ (CAP) - EMA/VR/0000227744

Applicant: Life Molecular Imaging GmbH

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include monitoring of the biological treatment response to pharmacological and non-pharmacological interventions for NEURACEQ, based on supporting literature. As a consequence, sections 4.1, 4.4 and 5.1 of the SmPC are updated. The Package Leaflet (PL) is updated in accordance. Version 6.91 of the RMP has also been submitted. In addition, the MAH took the opportunity to include the proposal to discontinue the inclusion of a paper copy of the SmPC with the product package

15.3.17. Glucagon - BAQSIMI (CAP) - EMA/VR/0000244909

Applicant: Amphastar France Pharmaceuticals

PRAC Rapporteur: Eamon O'Murchu

Scope: Extension of indication to include treatment of severe hypoglycaemia in paediatric patients aged 1 and over with diabetes mellitus for BAQSIMI, based on final results from study I8R-MC-IGBO; this is an Open-Label, Multi-Center, Single-Dose Study to Assess the Safety, Tolerability, Pharmacodynamics, and Pharmacokinetics of Nasal Glucagon in Paediatric Patients with Type 1 Diabetes Aged 1 to <4 years; As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce a correction in the Package Leaflet

15.3.18. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0121

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Karin Bolin

Scope: Extension of indication to include treatment of paediatric ulcerative colitis for SIMPONI, based on results from study CNTO148UCO3003; this is a Phase 3 Randomized, Open-label Study to Assess the Efficacy, Safety, and Pharmacokinetics of Golimumab Treatment, a Human anti-TNFα Monoclonal Antibody, Administered Subcutaneously in Paediatric Participants with Moderately to Severely Active Ulcerative Colitis; As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. Version 28.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is updated in accordance with the latest EMA excipients guideline and aligned with the latest QRD template version 10.4

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

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Barbara Kovacic Bytyqi

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

15.3.20. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/X/0149

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension application to introduce a new pharmaceutical form (concentrate for solution for infusion) associated with a new strength (40 mg/ml)

15.3.21. Mercaptamine - CYSTADROPS (CAP) - EMEA/H/C/003769/II/0032, Orphan

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include treatment of children from 6 months of age for CYSTADROPS, based on final results from study CYT-C2-001. This is an Open-label, Single-arm, Multicenter Study to Assess the Safety of Cystadrops in Pediatric Cystinosis Patients from 6 Months to Less Than 2 Years Old. 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 2.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to update Annex II of the PI and the list of local representatives in the Package Leaflet

15.3.22. Mosunetuzumab - LUNSUMIO (CAP) - EMEA/H/C/005680/X/0015, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with two new strengths (5 mg and 45 mg) and new route of administration (subcutaneous use).
The RMP (version 3.0) is updated in accordance

15.3.23. Naloxone - NYXOID (CAP) - EMEA/H/C/004325/II/0019

Applicant: Mundipharma Corporation (Ireland) Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Submission of the interim report from the PAES MR903-9501 listed as an obligation in the Annex II, supported by Real World Evidence from literature and European Take-Home Naloxone programs (THN) demonstrating the effectiveness of Nyxoid in a real-world setting. Study MR903-9501 is a non-interventional multi-national, prospective, mixed methods study of the effectiveness of naloxone (including intranasal Nyxoid) administration by lay people in reversing opioid overdose. The Annex II and the RMP version 3.0 are updated accordingly. In addition, the MAH took the opportunity to introduce minor administrative changes to the Package Leaflet

15.3.24. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/II/0061/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: A grouped application comprised of a Type II Variation and a Type IB Variation, as follows:

Type II (C.I.6.a): Extension of indication to include treatment of coronavirus disease 2019 (COVID-19) in paediatric patients 6 years of age and older weighing at least 20 kg for PAXLOVID, based on the final analysis of Cohorts 1 and 2 from pivotal Study C4671026; this is a Phase 2/3, Interventional Safety, Pharmacokinetics, and Efficacy, Open-Label, Multi-Center, Single-Arm Study to Investigate Orally Administered PF 07321332 (Nirmatrelvir)/Ritonavir in Nonhospitalized Symptomatic Pediatric Participants With COVID-19 Who Are at Risk of Progression to Severe Disease. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to introduce minor changes to the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

15.3.25. Nusinersen - SPINRAZA (CAP) - EMEA/H/C/004312/X/0038, Orphan

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Karin Bolin

Scope: Extension application to add a new strength of 28 mg and 50 mg.
The RMP (version 12.x) is updated in accordance (version 12.2 is under assessment in procedure EMEA/H/C/004312/II/0034/G)

15.3.26. Obinutuzumab - GAZYVARO (CAP) - EMA/VR/0000244907

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of adult patients with active lupus nephritis who are receiving standard therapy for GAZYVARO, based on results from study

Regency (CA41705). This is an ongoing, Phase III, randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of obinutuzumab administered at standard infusion rates in patients with ISN/RPS 2003 Class III or IV lupus nephritis treated with standard-of-care therapy.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet

15.3.27. Pembrolizumab - KEYTRUDA (CAP) - EMA/VR/0000245108

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include, KEYTRUDA as monotherapy, for the treatment of resectable locally advanced head and neck squamous cell carcinoma (HNSCC) as neoadjuvant treatment, continued as adjuvant treatment in combination with radiation therapy with or without platinum-containing chemotherapy and then as monotherapy in adults, based on the results of study P689V01MK3475 (KEYNOTE-689); this is a Phase 3, randomised, open-label study evaluating pembrolizumab as neoadjuvant therapy and in combination with standard of care as adjuvant therapy for stage III or IVA, resectable, locoregionally advanced head and neck squamous cell carcinoma. Consequently, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. The RMP version 48.1 has also been submitted. In addition, the MAH took the opportunity to introduce some minor editorial changes to the PI

15.3.28. Ranibizumab - EPRUVY (CAP) - EMEA/H/C/006528/II/0002/G

Applicant: MIDAS Pharma GmbH

PRAC Rapporteur: Karin Bolin

Scope: Quality variations

The product information and the RMP (version 2.0) are updated consequentially

15.3.29. Ranibizumab - RANIVISIO (CAP) - EMEA/H/C/005019/II/0017/G

Applicant: Midas Pharma GmbH

PRAC Rapporteur: Karin Bolin

Scope: Quality variations
The product information and the RMP (version 2.0) are updated consequentially

15.3.30. Ranibizumab - RIMMYRAH (CAP) - EMA/VR/0000246182

Applicant: QILU Pharma Spain S.L.

PRAC Rapporteur: Karin Bolin

Scope: Quality variation. The RMP version 1.1 has also been submitted.

15.3.31. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0053/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Grouped application comprising two extensions of indication to include treatment of paediatric patients weighing at least 1.5 kg for VEKLURY, based on final results from study GS-US-540-5823; this is a Phase 2/3 single-arm, open-label study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of remdesivir in participants from birth to < 18 years of age with COVID-19; 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 8.1 of the RMP has also been submitted

15.3.32. Riociguat - ADEMPAS (CAP) - EMEA/H/C/002737/X/0041

Applicant: Bayer AG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (0.15 mg/ml granules for oral suspension) for the Pulmonary arterial hypertension (PAH) paediatric indication. As a consequence, the film coated tablets presentations are updated to accommodate the new pharmaceutical form. In addition, contact details for local representatives of Belgium, Luxembourg, Greece and Ireland, have also been updated

15.3.33. Ritonavir - NORVIR (CAP) - EMA/VR/0000249795

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Martirosyan

Scope: A grouped application consisting of:

Type II (C.I.6.a): To modify the approved therapeutic indication to reflect current clinical use as a pharmacokinetic enhancer of other antiretroviral products only. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.5, 4.8 and 5.1 of the SmPC. The Package Leaflet is updated accordingly. The updated RMP version 8.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.

15.3.34. Selpercatinib - RETSEVMO (CAP) - EMA/VR/0000247142

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Update of section 5.3 of the SmPC in order to update information on carcinogenesis based on results from a non-clinical 2-year carcinogenicity study of selpercatinib in rats. The RMP version 11.1 has also been submitted

15.3.35. Selumetinib - KOSELUGO (CAP) - EMEA/H/C/005244/X/0018/G, Orphan

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Extension application to introduce a new pharmaceutical form (Granules in capsules for opening) associated with new strengths (5 mg and 7.5 mg capsule) grouped with a Type II variation (C.I.4) to update sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to align the SmPC and labelling of Koselugo capsules and Koselugo granules in capsules for opening. The Package Leaflet and Labelling are updated accordingly. The RMP version 3.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

15.3.36. Selumetinib - KOSELUGO (CAP) - EMA/VR/0000245231

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication for KOSELUGO to include treatment of adults based on results from study D134BC00001 (KOMET). This is a phase III, multicentre, international study with a parallel, randomised, double-blind, placebo-controlled, 2 arm design that assesses efficacy and safety of selumetinib in adult participants with NF1 who have Symptomatic Inoperable Plexiform Neurofibromas.

As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (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

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

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include the treatment of nighttime sleep disturbances in adults with Smith Magenis Syndrome (SMS) for HETLIOZ, based on results from study VP-VEC-162-2401. This is a double-blind, randomized, two-period crossover study evaluating the effects of tasimelteon vs. placebo on sleep disturbances of individuals with Smith-Magenis Syndrome (SMS). As a consequence, sections 4.1, 4.5, 5.1, 5.2 and 5.3 of the SmPC are updated. The Labelling and Package Leaflet are updated in accordance. The RMP version 5.0 has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.4. As part of the application, the MAH is requesting a 1-year extension of the market protection

15.3.38. Ustekinumab - OTULFI (CAP) - EMEA/H/C/006544/II/0001/G

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Quality variations
The product information and the RMP (v 1.0) are updated consequentially.

15.3.39. Vutrisiran - AMVUTTRA (CAP) - EMEA/H/C/005852/II/0015, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Extension of indication to include treatment of wild-type or hereditary transthyretin-mediated amyloidosis in adult patients with cardiomyopathy (ATTR-CM), based on primary analysis results from study HELIOS-B (ALN-TTRSC02-003); a Phase 3, Randomized, Double-blind, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Vutrisiran in Patients With Transthyretin Amyloidosis With Cardiomyopathy (ATTR Amyloidosis With Cardiomyopathy). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. An updated version 1.3 of the RMP has also been submitted

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

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Bianca Mulder

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

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. Aprocitentan - JERAYGO (CAP) - PSUSA/00011067/202409

Applicant: Idorsia Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

16.1.2. Bedaquiline - SIRTURO (CAP) - PSUSA/00010074/202409

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.1.3. Cabotegravir[41] - APRETUDE (CAP) - PSUSA/00000116/202409

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.4. Caplacizumab - CABLIVI (CAP) - PSUSA/00010713/202408

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.5. Cenobamate - ONTOZRY (CAP) - PSUSA/00010921/202409

Applicant: Angelini S.p.A.

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

16.1.6. Chlormethine - LEDAGA (CAP) - PSUSA/00010587/202408

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.1.7. Cholic acid[42] - ORPHACOL (CAP) - PSUSA/00010208/202409

Applicant: Theravia

PRAC Rapporteur: Maria Poulianiti

Scope: Evaluation of a PSUSA procedure

16.1.8. Cipaglucosidase alfa - POMBILITI (CAP) - PSUSA/00011047/202409

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.9. Deferiprone - FERRIPROX (CAP) - PSUSA/00000940/202408

Applicant: Chiesi Farmaceutici S.p.A.

[41] Indicated for pre-exposure prophylaxis of HIV-1 infection

[42] For oxosteroid-reductase or hydroxy-steroid dehydrogenase deficiency indication only

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

16.1.10. Deucravacitinib - SOTYKTU (CAP) - PSUSA/00011046/202409

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure

16.1.11. Duvelisib - COPIKTRA (CAP) - PSUSA/00010939/202409

Applicant: Secura Bio Limited

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

16.1.12. Ebola vaccine (MVA-BN-Filo [recombinant]) - MVABEA (CAP); Ebola vaccine (Ad26.ZEBOV-GP [recombinant]) ZABDENO (CAP) - PSUSA/00010857/202409

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.1.13. Eliglustat - CERDELGA (CAP) - PSUSA/00010351/202408

Applicant: Sanofi B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

16.1.14. Filgotinib - JYSELECA (CAP) - PSUSA/00010879/202409

Applicant: Alfasigma S.p.A.

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure

16.1.15. Fruquintinib - FRUZAQLA (CAP) - PSUSA/00011069/202409

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

16.1.16. Ganaxolone - ZTALMY (CAP) - PSUSA/00000093/202409

Applicant: Marinus Pharmaceuticals Emerald Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.17. Gilteritinib - XOSPATA (CAP) - PSUSA/00010832/202409

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.18. Glofitamab - COLUMVI (CAP) - PSUSA/00000067/202409

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Evaluation of a PSUSA procedure

16.1.19. Gozetotide - LOCAMETZ (CAP) - PSUSA/00011030/202409

Applicant: Novartis Europharm Limited

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

16.1.20. Idebenone[43] - RAXONE (CAP) - PSUSA/00010412/202409

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.21. Influenza vaccine (intranasal, live attenuated) - FLUENZ (CAP); FLUENZ TETRA (CAP) - PSUSA/00001742/202408

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.1.22. Lacosamide - LACOSAMIDE UCB (CAP); VIMPAT (CAP) - PSUSA/00001816/202408

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Karin Bolin

Scope: Evaluation of a PSUSA procedure

16.1.23. Lorlatinib - LORVIQUA (CAP) - PSUSA/00010760/202409

Applicant: Pfizer Europe MA EEIG

[43] For centrally authorised product(s) only

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

16.1.24. Lutetium (^{177}LU) vipivotide tetraxetan - PLUVICTO (CAP) - PSUSA/00011031/202409

Applicant: Novartis Europharm Limited

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure

16.1.25. Mecasermin - INCRELEX (CAP) - PSUSA/00001942/202408

Applicant: Ipsen Pharma

PRAC Rapporteur: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure

16.1.26. Mepolizumab - NUCALA (CAP) - PSUSA/00010456/202409

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.27. Miglustat[44] - OPFOLDA (CAP) - PSUSA/00000077/202409

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.28. Momelotinib - OMJJARA (CAP) - PSUSA/00000263/202409

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.29. Moroctocog alfa - REFACTO AF (CAP) - PSUSA/00002089/202408

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

[44] For treatment of Pompe disease only

16.1.30. Naloxegol - MOVENTIG (CAP) - PSUSA/00010317/202409

Applicant: Gruenenthal GmbH (Moventig)

PRAC Rapporteur: Eamon O'Murchu

Scope: Evaluation of a PSUSA procedure

16.1.31. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - PSUSA/00010366/202409

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

16.1.32. Ofatumumab - KESIMPTA (CAP) - PSUSA/00010927/202409

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

16.1.33. Pralsetinib - GAVRETO[45] - PSUSA/00010961/202409

Applicant: Blueprint Medicines (Netherlands) B.V.

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.34. Retifanlimab - ZYNYZ (CAP) - PSUSA/00011059/202409

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

16.1.35. Rezafungin - REZZAYO (CAP) - PSUSA/00000221/202409

Applicant: Mundipharma GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

16.1.36. Ruxolitinib[46] - OPZELURA (CAP) - PSUSA/00011052/202409

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Adam Przybylkowski

[45] European Commission (EC) decision on the marketing authorisation (MA) withdrawal of Gavreto dated 3 November 2022
[46] For non-segmental vitiligo only

Scope: Evaluation of a PSUSA procedure

16.1.37. Sebelipase alfa - KANUMA (CAP) - PSUSA/00010422/202408

Applicant: Alexion Europe SAS

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.1.38. Sodium thiosulfate - PEDMARQSI (CAP) - PSUSA/00000066/202409

Applicant: Norgine B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.39. Sotatercept - WINREVAIR (CAP) - PSUSA/00011076/202409

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

16.1.40. Spesolimab - SPEVIGO (CAP) - PSUSA/00011033/202409

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure

16.1.41. Teduglutide - REVESTIVE (CAP) - PSUSA/00009305/202408

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

16.1.42. Vibegron - OBGEMSA (CAP) - PSUSA/00011068/202409

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.1.43. Zilucoplan - ZILBRYSQ (CAP) - PSUSA/00000169/202409

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.1.44. Zolbetuximab - VYLOY (CAP) - PSUSA/00011095/202409

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure

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

16.2.1. Asparaginase, crisantaspase (L-asparaginase from Erwinia chrysanthemi) - ENRYLAZE (CAP); NAP - PSUSA/00003161/202408

Applicants: Jazz Pharmaceuticals Ireland Limited (Enrylaze), various

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

16.2.2. Epoetin alfa - ABSEAMED (CAP); BINOCRIT (CAP); EPOETIN ALFA HEXAL (CAP); NAP - PSUSA/00001237/202408

Applicants: Medice Arzneimittel Pütter GmbH & Co. KG (Abseamed), Hexal AG (Epoetin alfa Hexal), Sandoz GmbH (Binocrit), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

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

16.3.1. Ciclesonide (NAP) - PSUSA/00000742/202408

Applicant(s): various

PRAC Lead: Mari Thorn

Scope: Evaluation of a PSUSA procedure

16.3.2. Dalteparin sodium (NAP) - PSUSA/00000922/202408

Applicant(s): various

PRAC Lead: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

16.3.3. Dexamfetamine (NAP) - PSUSA/00000986/202409

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

16.3.4. Estrogen, medroxyprogesterone (NAP) - PSUSA/00000582/202408

Applicant(s): various

PRAC Lead: Jana Lukačišinová

Scope: Evaluation of a PSUSA procedure

16.3.5. Hydrocortisone[47] (NAP) - PSUSA/00010856/202408

Applicant(s): various

PRAC Lead: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure

16.3.6. Lercanidipine (NAP) - PSUSA/00001841/202408

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

16.3.7. Rilmenidine (NAP) - PSUSA/00002643/202408

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

16.3.8. Sotalol (NAP) - PSUSA/00002774/202408

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure

16.3.9. Thallium [201TL] (NAP) - PSUSA/00002920/202408

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

16.4. Follow-up to PSUR/PSUSA procedures

None

[47] For all formulations apart from systemic use

16.5. Variation procedure(s) resulting from PSUSA evaluation

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

Applicant: Kyowa Kirin Holdings B.V.

PRAC Lead: Gabriele Maurer

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

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

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Lead: Karin Erneholm

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

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

16.6. Expedited summary safety reviews[48]

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)[49]

17.1.1. Cabotegravir - VOCABRIA; rilpivirine - REKAMBYS (CAP) - EMA/PASS/0000247696

Applicants: Janssen-Cilag International N.V. (Rekambys), ViiV Healthcare B.V. (Vocabria)

PRAC Rapporteur: Liana Martirosyan

Scope: Drug Utilization, Adherence, Effectiveness and Resistance: A Prospective

[48] 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

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

Observational Cohort Study in People living with HIV (PLWH) initiating ARV regimen of CAB+RPV LA in Collaboration with EuroSIDA

17.1.2. rADAMTS13 - ADZYNMA (CAP) - EMA/PASS/0000253115

Applicant: Takeda Manufacturing Austria AG

PRAC Rapporteur: Maia Uusküla

Scope: A Post-Authorization Safety Study (PASS) to Further Evaluate Real-World Safety in Patients with Congenital Thrombotic Thrombocytopenic Purpura (cTTP) Treated with Adzynma

17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[50]

17.2.1. Beclometasone, formoterol, glycopyrronium bromide – RIARIFY (CAP) - EMA/PAM/0000247638

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Revised protocol for a PASS study, non-interventional study titled: "MulTinational database cohoRt study to assess adverse cardIovascular and cereBrovascular outcomes in patiEnts (TRIBE) with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurized metered dose inhaler (pMDI)" (study code No.: CLI-05993BA1-05 CLI-05993BA1-05 (TRIBE)

17.2.2. Beclometasone, formoterol, glycopyrronium bromide –TRIMBOW (CAP) - EMA/PAM/0000247269

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Revised protocol for a PASS study, non-interventional study titled: "MulTinational database cohoRt study to assess adverse cardIovascular and cereBrovascular outcomes in patiEnts (TRIBE) with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurized metered dose inhaler (pMDI)" (study code No.: CLI-05993BA1-05 CLI-05993BA1-05 (TRIBE)

17.2.3. Beclometasone, formoterol, glycopyrronium bromide – TRYDONIS - EMA/PAM/0000247627

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Revised protocol for a PASS study, non-interventional study titled: "MulTinational database cohoRt study to assess adverse cardIovascular and cereBrovascular outcomes in

[50] 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

patiEnts (TRIBE) with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurized metered dose inhaler (pMDI)" (study code No.: CLI-05993BA1-05 CLI-05993BA1-05 (TRIBE)

17.2.4. Emicizumab – HEMLIBRA (CAP) - EMA/PAM/0000248363

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Revised protocol (version 3.0) of the protocol for study BO44691 which is a long term non-interventional safety study of Emicizumab treatment in patients with moderate haemophilia A and severe bleeding phenotype for PRAC review as a 'standalone' post-authorisation measure (PAM) application [EMEA/H/C/00406/MEA/012.3]

17.2.5. Etranacogene dezaparvovec – HEMGENIX (CAP) - EMA/PAM/0000248926

Applicant: CSL Behring GmbH, ATMP

PRAC Rapporteur: Bianca Mulder

Scope: Protocol for PASS CSL222_5001: Survey to evaluate the effectiveness of additional risk minimization measures (aRMMs) for Hemgenix among prescribers in the EU

17.2.6. Golimumab – SIMPONI (CAP) - EMA/PAM/0000248923

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Karin Bolin

Scope: PASS No. MK-8259-050: An observational post-approval safety study of golimumab in treatment of poly-articular Juvenile Idiopathic Arthritis (pJIA) using the German Biologics JIA Registry (BiKeR)

17.2.7. Human thrombin, human fibrinogen – TACHOSIL (CAP) - EMA/PAM/0000247840

Applicant: Corza Medical GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Revised protocol for PASS PasTel: Short- and long-term safety evaluation of TachoSil in paediatric population

17.2.8. Talimogene laherparepvec – IMLYGIC (CAP) - EMA/PAM/0000247962

Applicant: Amgen Europe B.V.G, ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: 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

17.2.9. Ublituximab – BRIUMVI (CAP) - EMA/PAM/0000246081

Applicant: Neuraxpharm Pharmaceuticals S.L.

PRAC Rapporteur: Liana Martirosyan

Scope: Revised protocol for PASS No. TG1101-RMS403 A registry study of pregnancy and infant outcomes in patients treated with ublituximab to characterise the safety of ublituximab use in pregnancy, including maternal, foetal and neonate/infant outcomes, in female patients with relapsing forms of multiple sclerosis

17.2.10. Velaglucerase alfa – VPRIV (CAP) - EMA/PAM/0000248394

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Martin Huber

Scope: Response to MEA/030: Study TAK-669-4018: A Survey among Patients, Caregivers and Home Infusion Nurses based in the European Union to Assess their Awareness and Understanding of Educational Materials (EM) Supporting VPRIV Infusion at Home.

Objectives: To determine whether patients/caregivers and home infusion nurses appropriately understand and implement the EM associated with VPRIV home infusion. Specifically, to assess the proportion of patients/caregivers and home infusion nurses who are aware of the EM; who understand the EM; and who use the EM

17.3. Results of PASS imposed in the marketing authorisation(s)[51]

17.3.1. Methylphenidate hydrochloride (NAP) - EMA/PASS/0000248031

Applicant(s): Medice Arzneimittel Puetter GmbH & Co. KG (Medikinet)

PRAC Rapporteur: Martin Huber

Scope: Final study report for a multi-centre, observational, prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet retard according to normal standard clinical practice

17.4. Results of PASS non-imposed in the marketing authorisation(s)[52]

17.4.1. Avelumab - BAVENCIO (CAP) - EMA/VR/0000244307

Applicant: Merck Europe B.V.

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the final report from study MS100070-0031 listed as a category 3 PASS in the RMP. This is a non-interventional cohort efficacy and safety study to assess the characteristics and management of patients with Merkel cell carcinoma (MCC) in Germany

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

17.4.2. Eliglustat - CERDELGA (CAP) - EMA/VR/0000245058

Applicant: Sanofi B.V.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study ELIGLC06913 listed as a category 3 PASS in the RMP. This is a drug utilisation study of eliglustat for the treatment of Gaucher Disease Type 1 in Europe using electronic healthcare records

17.4.3. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[53]) - 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.

17.4.4. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/II/0071

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Submission of the final report from the Mepolizumab (Nucala) Pregnancy Exposure Study 200870: a VAMPSS post marketing surveillance study of Mepolizumab safety in pregnancy, listed as a category 3 study in the RMP. This is a non-interventional study to monitor planned and unplanned pregnancies exposed to mepolizumab and to evaluate the possible teratogenic effect of this medication relative to the pregnancy outcomes of major birth defects, preterm delivery, small for gestational age infants and spontaneous abortion or stillbirth. The RMP version 13.0 has also been submitted.

17.4.5. Venetoclax - VENCLYXTO (CAP) - EMA/VR/0000245044

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final report from study P22-907 listed as a category 3 PASS in the

[53] 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)

RMP. This is a non-interventional cross-sectional study evaluating the effectiveness of venetoclax risk minimisation measures among haematologists in Europe

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

17.5.1. Burosumab – CRYSVITA (CAP) - EMA/PAM/0000248012

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: First adult interim report for PASS EUPAS32190: Non-interventional Post-Authorisation Safety Study of Burosumab in the Treatment of Children >1 year of age, Adolescents and Adults with X linked Hypophosphataemia (protocol number 2019-36-EU-CRY)

17.5.2. COVID-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP) - EMA/PAM/0000244397

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

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

17.5.3. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/MEA 008.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: From Initial MAA:
First Interim Report for PASS C4671037
Title: Use and safety of Paxlovid in pregnant and breastfeeding women

17.5.4. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/MEA 009.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: From Initial MAA:
First Interim Report for PASS C4671047
Use and safety of Paxlovid during pregnancy and among patients with moderate or severe hepatic or renal impairment

17.5.5. Ofatumumab – KESIMPTA (CAP) - EMA/PAM/0000243996

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Third Interim Report for PASS Study COMB157G2407: Evaluation of pregnancy and infant outcomes in Kesimpta patients using Pregnancy outcomes Intensive Monitoring (PRIM) data – The Kesimpta-PRIM study

17.5.6. Rurioctocog alfa pegol – ADYNOVI (CAP) - EMA/PAM/0000248808

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Bianca Mulder

Scope: 5th interim/progress report (dated 15 January 2025, with a data cut-off of 12 November 2024) for the ongoing Adynovi post-authorisation safety study (PASS) TAK-660-403 (EUPAS35698) which is a non-interventional, imposed study aimed to investigate the potential effects of PEG accumulation in the choroid plexus of the brain and other tissues/organs

17.5.7. Tofacitinib – XELJANZ (CAP) - EMA/PAM/0000247897

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Response to MEA 017.4 - an RSI adopted on 12.12.2024 following assessment of Interim Report from Study A3921352

Study A3921352 is an active surveillance, post-authorization study to characterize the safety of tofacitinib in patients with moderately to severely active ulcerative colitis in the real-world setting using data from the United Registries for Clinical Assessment and Research (UR-CARE) in the European Union (EU)

17.6. Others

17.6.1. Anifrolumab – SAPHNELO (CAP) - EMA/PAM/0000245373

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Martirosyan

Scope: Progress report for ROSE study (D3461R00028): A non-interventional multi-database post-authorisation study to assess pregnancy-related safety data from women with Systemic Lupus Erythematosus exposed to anifrolumab

17.6.2. Damoctocog alfa pegol – JIVI (CAP) - EMA/PAM/0000245659

Applicant: Bayer AG

PRAC Rapporteur: Bianca Mulder

Scope: 16th Annual Report for Study 14149: EUHASS Registry (European Haemophilia Safety Surveillance)

17.6.3. Ganaxolone – ZTALMY (CAP) - EMA/PAM/0000246069

Applicant: Marinus Pharmaceuticals Emerald Limited

PRAC Rapporteur: Adam Przybylkowski

Scope: Study LLF001 (CANDID observational study): Milestone report to be provided after 50 participants have completed the first-year visit

17.6.4. Infliximab – REMSIMA (CAP) - EMA/PAM/0000245463

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: MAH's responses to MEA 020.5 Annual Recruitment Status Report from Study CT-P13 4.8

An observational, prospective cohort study to evaluate safety of Remsima SC in patients with RA, AS, PsA and Ps

RSI as adopted in April 2024

17.6.5. Octocog alfa – KOVALTRY (CAP) - EMA/PAM/0000246076

Applicant: Bayer AG

PRAC Rapporteur: Gabriele Maurer

Scope: Study 14149: 16th Annual Report and Product Specific EUHASS Report

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. Histamine dihydrochloride - CEPLENE (CAP) - EMEA/H/C/000796/S/0049 (without RMP)

Applicant: Laboratoires Delbert

PRAC Rapporteur: Eamon O'Murchu

Scope: Annual reassessment of the marketing authorisation

18.1.2. Maralixibat - LIVMARLI (CAP) - EMEA/H/C/005857/S/0019 (without RMP)

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

18.2. Conditional renewals of the marketing authorisation

18.2.1. Fidanacogene elaparvovec - BEQVEZ (CAP) - EMA/R/0000247045

Applicant: Pfizer Europe MA EEIG, ATMP

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: 5-year renewal of the marketing authorisation

18.2.2. Imlifidase – IDEFIRIX (CAP) - EMA/R/0000249767

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

18.2.3. Meningococcal Group A, C, W and Y conjugate vaccine – MENQUADFI (CAP) - EMA/R/0000245024

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Jean-Michel Dogné

Scope: 5-year renewal of the marketing authorisation

18.2.4. Talquetamab – TALVEY (CAP) - EMA/R/0000249367

Applicant: Janssen Cilag International

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: 5-year renewal of the marketing authorisation

18.2.5. Teclistamab – TECVAYLI (CAP) - EMA/R/0000249306

Applicant: Janssen Cilag International

PRAC Rapporteur: Jana Lukacisinova

Scope: 5-year renewal of the marketing authorisation

18.3. Renewals of the marketing authorisation

18.3.1. Bevacizumab - AYBINTIO (CAP) - EMEA/H/C/005106/R/0022 (without RMP)

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Karin Erneholm

Scope: 5-year renewal of the marketing authorisation

18.3.2. Fampridine – FAMPRIDINE ACCORD (CAP) - EMA/R/0000243787

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

18.3.3. Formoterol / Glycopyrronium bromide / Budesonide – TRIXEO AEROSPHERE (CAP) - EMA/R/0000245136

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: 5-year renewal of the marketing authorisation

18.3.4. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/R/0043 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

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

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

18.3.6. Phenylephrine, ketorolac - OMIDRIA (CAP) - EMEA/H/C/003702/R/0030 (without RMP)

Applicant: Rayner Surgical (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

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 07-10 April 2025 PRAC meeting, which was held in-person.

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

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Ulla Wändel Liminga	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 restrictions applicable to this meeting	
Jo Robays	Alternate	Belgium	No interests declared	
Maria Popova-Kiradjieva	Member	Bulgaria	No interests declared	
Petar Mas	Member	Croatia	No interests declared	
Barbara Kovacic Bytyqi	Alternate	Croatia	No interests declared	
Panagiotis Psaras	Alternate	Cyprus	No interests declared	
Eva Jirsová	Member*	Czechia	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	
Krõõt Aab	Alternate*	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:	4.2.1. Avelumab – BAVENCIO (CAP) - EMEA/H/C/004338/SDA/013; atezolizumab – TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/028; cemiplimab – LIBTAYO (CAP) - EMEA/H/C/004844/SDA/014; dostarlimab – JEMPERLI (CAP) - EMEA/H/C/005204/SDA/008; durvalumab – IMFINZI (CAP) - EMEA/H/C/004771/SDA/015; ipilimumab – YERVOY (CAP) - EMEA/H/C/002213/SDA/050; nivolumab - OPDIVO- EMEA/H/C/003985/SDA/060; Nivolumab, relatlimab - OPDUALAG (CAP) - EMEA/H/C/005481/SDA/008; pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/044; retifanlimab – ZYNYZ (CAP) - EMEA/H/C/006194/SDA/003; tislelizumab – TEVIMBRA (CAP) -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				EMEA/H/C/005919/SDA/005; toripalimab – LOQTORZI (CAP) - EMEA/H/C/006120/SDA/002; tremelimumab – IMJUDO (CAP) - EMEA/H/C/006016/SDA/005 6.1.6. Nivolumab, relatlimab - OPDUALAG (CAP) - PSUSA/00011018/202409 16.1.10. Deucravacitinib - SOTYKTU (CAP) - PSUSA/00011046/202409
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:	4.2.1. Avelumab – BAVENCIO (CAP) - EMEA/H/C/004338/SDA/013; atezolizumab – TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/028; cemiplimab – LIBTAYO (CAP) - EMEA/H/C/004844/SDA/014; dostarlimab – JEMPERLI (CAP) -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				EMEA/H/C/005204/SDA/008; durvalumab – IMFINZI (CAP) - EMEA/H/C/004771/SDA/015; ipilimumab – YERVOY (CAP) - EMEA/H/C/002213/SDA/050; nivolumab - OPDIVO- EMEA/H/C/003985/SDA/060; Nivolumab, relatlimab - OPDUALAG (CAP) - EMEA/H/C/005481/SDA/008; pembrolizumab – KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/044; retifanlimab – ZYNYZ (CAP) - EMEA/H/C/006194/SDA/003; tislelizumab – TEVIMBRA (CAP) - EMEA/H/C/005919/SDA/005; toripalimab – LOQTORZI (CAP) - EMEA/H/C/006120/SDA/002; tremelimumab – IMJUDO (CAP) - EMEA/H/C/006016/SDA/005 6.1.6. Nivolumab, relatlimab - OPDUALAG (CAP) - PSUSA/00011018/202409 16.1.10. Deucravacitinib - SOTYKTU (CAP) -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				PSUSA/00011046 /202409
Guðrún Stefánsdóttir	Member	Iceland	No restrictions applicable to this meeting	
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	
Magdalena Wielowieyska	Alternate	Luxembourg	No participation in discussion, final deliberations and voting on:	15.3.8. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0111 16.1.15. Fruquintinib - FRUZAQLA (CAP) - PSUSA/00011069 /202409 16.1.41. Teduglutide - REVESTIVE (CAP) - PSUSA/00009305 /202408 16.3.9. Thallium [201TL] (NAP) - PSUSA/00002920 /202408 17.1.2. rADAMTS13 -

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				ADZYNMA (CAP) - EMA/PASS/00002 53115 17.2.10. Velaglucerase alfa – VPRIV (CAP) - EMA/PAM/00002 48394
John Joseph Borg	Member*	Malta	No interests declared	
Liana Martirosyan	Member	Netherlands	No interests declared	
Bianca Mulder	Alternate	Netherlands	No interests declared	
David Olsen	Member	Norway	No participation in discussion, final deliberations and voting on:	4.2.4. Regorafenib - STIVARGA (CAP) - EMEA/H/C/00257 3/SDA/015 4.2.5. Regorafenib - STIVARGA (CAP) - EMEA/H/C/00257 3/SDA /016 15.3.12. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/00405 4/II/0034 15.3.13. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/00405 4/X/0033/G 15.3.32. Riociguat - ADEMPAS (CAP) - EMEA/H/C/00273 7/X/0041 17.6.2. Damoctocog alfa

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
				pegol – JIVI (CAP) - EMA/PAM/00002 45659 17.6.5. Octocog alfa – KOVALTRY (CAP) - EMA/PAM/00002 46076
Pernille Harg	Alternate	Norway	No interests declared	
Adam Przybylkowski	Member	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	
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	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Patricia McGettigan	Member	Independent scientific expert	No restrictions applicable to this meeting	
Anette Kirstine Stark	Member	Independent scientific expert	No interests declared	
Hedvig Marie Egeland Nordeng	Member	Independent scientific expert	No restrictions applicable to this meeting	
Roberto Frontini	Member	Healthcare Professionals' Representative	No restrictions applicable to this meeting	
Salvatore Antonio Giuseppe Messana	Alternate	Healthcare Professionals' Representative	No interests declared	
Michal Rataj	Alternate	Patients' Organisation Representative	No interests declared	
Els Beghein	Expert	Belgium	No interests declared	
Fabrice Moore	Expert	Belgium	No interests declared	
Behija Hudina	Expert	Croatia	No restrictions applicable to this meeting	
Nina Lalić	Expert	Croatia	No restrictions applicable to this meeting	
Lora Pavlinović	Expert	Croatia	No interests declared	
Michaela Kleinova	Expert	Czech Republic	No interests declared	
Petra Vacková	Expert	Czech Republic	No interests declared	
Frederikke Hillebrand Laustsen	Expert	Denmark	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
Helle Gerda Olsen	Expert	Denmark	No interests declared	
Cecilie Louise Pedersen	Expert	Denmark	No restrictions applicable to this meeting	
Moritz Sander	Expert	Denmark	No restrictions applicable to this meeting	
Jelena Katic	Expert	Germany	No interests declared	
Dennis Lex	Expert	Germany	No interests declared	
Laura Zein	Expert	Germany	No interests declared	
Esther de Vries	Expert	Netherlands	No interests declared	
Helen Gatling	Expert	Netherlands	No interests declared	
Sara Khosrovani	Expert	Netherlands	No interests declared	
Marianne Klanker	Expert	Netherlands	No interests declared	
Anne Slomp	Expert	Netherlands	No restrictions applicable to this meeting	
Frederika Adriana Vermeij-van Nimwegen	Expert	Netherlands	No restrictions applicable to this meeting	
Consuelo Argumánez	Expert	Spain	No restrictions applicable to this meeting	
Natividad Galiana	Expert	Spain	No restrictions applicable to this meeting	
Charlotte Backman	Expert	Sweden	No interests declared	

Name	Role	Member state or affiliation	Outcome restriction following evaluation of e-DoI	Topics on agenda for which restrictions apply
Jolanta Gulbinovic	Expert	Sweden	No interests declared	
Emelie Lindberger	Expert	Sweden	No interests declared	
A representative from the European Commission attended the meeting				
Observers from Health Canada and WHO attended the meeting				
Meeting run with support from relevant EMA staff				

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

20. Annex III - List of acronyms and abbreviations

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

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

21. Explanatory notes

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

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

(Items 2 and 3 of the PRAC minutes)

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

Signals assessment and prioritisation

(Item 4 of the PRAC minutes)

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

may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet.

Risk Management Plans (RMPs)

(Item 5 of the PRAC minutes)

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

Assessment of Periodic Safety Update Reports (PSURs)

(Item 6 of the PRAC minutes)

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

Post-authorisation Safety Studies (PASS)

(Item 7 of the PRAC minutes)

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

Product related pharmacovigilance inspections

(Item 9 of the PRAC minutes)

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

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