EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Division

# Pharmacovigilance Risk Assessment Committee (PRAC)

## Minutes for PRAC meeting on 07-10 July 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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# Table of contents

# 1. Introduction

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

The Chair opened the meeting by welcoming all participants. The meeting was held in-person.

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

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

The Chair thanked the departing member(s)/alternate(s) for their contributions to the Committee.

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

The Chair announced the start of the Danish presidency of the Council of the European Union (EU).

## 1.2. Agenda of the meeting on 07-10 July 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 02-05 June 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 02-05 June 2025 were published on the EMA website on 19 August 2025 (EMA/PRAC/238878/2025).

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

## 2.1. Newly triggered procedures

None

## 2.2. Ongoing procedures

None

## 2.3. Procedures for finalisation

None

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

## 3.1. Newly triggered procedures

None

## 3.2. Ongoing procedures

None

## 3.3. Procedures for finalisation

None

### 3.3.1. Chikungunya vaccine (live) – IXCHIQ (CAP) – EMA/REF/0000269473

Applicant: Valneva Austria GmbH

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

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

**Background**

A referral procedure under Article 20 of Regulation (EC) No 726/2004 for Ixchiq (Chikungunya vaccine (live)) is to be concluded. A final assessment of the data submitted was produced by the Rapporteurs according to the agreed timetable. For further background, see PRAC minutes May 2025.

**Discussion**

PRAC reviewed all the available data, which included data provided by the MAH, as well as the adverse reactions in EudraVigilance reported following use of Ixchiq (Chikungunya vaccine (live)).

PRAC discussed the conclusion reached by the Rapporteurs. Based on the evaluated cases of serious adverse events, including three fatal cases, reported with use of Ixchiq (Chikungunya vaccine (live)), PRAC noted that the majority of the serious cases concerned individuals aged 65 years and older and individuals with multiple underlying chronic and/or uncontrolled medical conditions.

PRAC considered that elderly individuals are more likely to benefit from vaccination since this population is at increased risk of hospitalisation and of death due to severe chikungunya infection. Therefore, as the benefits of the vaccine outweigh the risks, PRAC concluded that Ixchiq (Chikungunya vaccine (live)) could be given to individuals 65 years of age and older, and thus, the temporary contraindication for this population adopted by PRAC in May 2025 should be lifted.

PRAC considered also that information on the risk of serious adverse reactions in younger adults (below 65 years of age) with underlying medical conditions is currently limited. In light of the severe reactions observed and the limited information on the risk in younger adults with underlying chronic and/or uncontrolled medical conditions, PRAC concluded that, for all individuals, Ixchiq (Chikungunya vaccine (live)) should only be given when there is a significant risk of acquiring chikungunya infection, and after careful consideration of the potential risks and benefits.

PRAC also noted cases of Ixchiq (Chikungunya vaccine (live)) use in individuals who are immunodeficient or immunosuppressed, and recommended that the wording of the contraindication in these individuals to be clarified. In addition, PRAC was of the view that the product information of Ixchiq (Chikungunya vaccine (live)) should reflect the current knowledge on the occurrence of serious adverse reactions, including the occurrence of encephalitis, and agreed to add warnings and precautions of use relating to the risks associated with the use of Ixchiq. PRAC also concluded that the product information should be updated to add encephalopathy, encephalitis and aseptic meningitis as undesirable effects with a frequency 'not known', confusional state with a frequency 'rare', as well as syncope, thrombocytopenia and malaise, and decreased appetite as undesirable effects with a frequency 'uncommon'.

In view of the above, PRAC considers that the benefit-risk balance of Ixchiq (Chikungunya vaccine (live)) remains favourable subject to the agreed amendments to the product information. As a consequence, PRAC recommended the variation to the terms of the marketing authorisation for Ixchiq (Chikungunya vaccine (live)).

**Summary of recommendation(s)/conclusions**

- PRAC adopted, by consensus, a recommendation to vary[1] the terms of the marketing authorisation for Ixchiq (Chikungunya vaccine (live)) to be considered by CHMP for an opinion.
- PRAC agreed the distribution of a direct healthcare professional communication (DHPC) together with a communication plan.

Post-meeting note 1: On 10 July 2025, the public health communication entitled 'Ixchiq: temporary restriction on vaccinating people 65 years and older to be lifted' was published on the EMA website.

Post-meeting note 2: On 25 July 2025, the public health communication entitled 'Ixchiq: temporary restriction on vaccinating people 65 years and older to be lifted' was published on the EMA website expressing the opinion of CHMP.

[1] Update of SmPC sections 4.1, 4.3, 4.4 and 4.8. The package leaflet is updated accordingly.

## 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. Valproate (NAP) and related substances[4]

Applicant(s): various

PRAC Rapporteur: Liana Martirosyan

Scope: Signal of neurodevelopmental disorders with paternal exposure

EPITT 20191 – New signal

**Background**

Valproic acid and the related 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.

During routine signal detection activities, a signal of neurodevelopmental disorders (NDD) with paternal exposure was identified by The Netherlands based on a new study by *Christensen et al, 2025*[5], following previous conclusions on the PASS EMEA/H/N/PSR/J/0043 (see PRAC minutes January 2024). The Rapporteur confirmed that the signal needed initial analysis and prioritisation by PRAC.

**Discussion**

Having considered the available evidence from the epidemiological study by *Christensen et al, 2025*, PRAC agreed that further evaluation of the signal is warranted.

PRAC appointed Liana Martirosyan as Rapporteur for the signal.

**Summary of recommendation(s)**

[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
[4] Valproic acid, sodium valproate, valproate semisodium, valpromide,
[5] Christensen J, et al. Risk of Neurodevelopmental Disorders and Paternal Use of Valproate During Spermatogenesis. JAMA Netw Open. 2025;8(5):e2512139. doi:10.1001/jamanetworkopen.2025.12139

- The MAH Sanofi as the innovator of valproate and related substances-containing medicinal products should submit to EMA, by 24 September 2025, a detailed discussion of the study results of *Christensen et al, 2025,* including strengths and limitations of the study as well as the mentioned analyses to explore the impact of methodological choices and definitions used in the paternal PASS performed by the Consortium (EMEA/H/N/PSR/J/0043). In addition, a discussion should also be provided on the previous findings related to analyses restricted to fathers with epilepsy of unknown underlying cause, which showed a higher risk (aHR > 2) and was not observed in any other analysis performed by *Christensen et al, 2025*, including a clarification on the observed differences in NDD risk observed between the paternal PASS, in particular for Denmark, and the study published by *Christensen et al, 2025*. The MAH should also provide and discuss any new additional non-clinical data or literature data available.
- A 60-day timetable was recommended for the assessment of this review leading to a further PRAC recommendation.

## 4.2. Signals follow-up and prioritisation

### 4.2.1. Ciltacabtagene autoleucel – CARVYKTI (CAP) - EMEA/H/C/005095/SDA/021; idecabtagene vicleucel – ABECMA (CAP) - EMEA/H/C/004662/SDA/024; tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/SDA/026

Applicants: Bristol-Myers Squibb Pharma EEIG (Abecma), Janssen-Cilag International NV (Carvykti), Novartis Europharm Limited (Kymriah), ATMP

PRAC Rapporteur: Gabriele Maurer

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

EPITT 20153 – Follow up to February 2025

**Background**

For background information, see PRAC minutes February 2025.

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

**Discussion**

Having considered the available evidence in EudraVigilance, including the cumulative review and the MAHs responses, the existing information on infections in the product information and the strategy in regulatory decision-making proposed by *Segec et al, 2015*[6]*,* PRAC agreed that there is sufficient evidence to support a causal association between PML and Carvykti (ciltacabtagene autoleucel), Abecma (idecabtagene vicleucel) and Kymriah (tisagenlecleucel). Therefore, the product information of Carvykti (ciltacabtagene autoleucel), Abecma (idecabtagene vicleucel) and Kymriah (tisagenlecleucel) should be updated to add a warning on viral reactivation leading to PML.

**Summary of recommendation(s)**

[6] Segec A. et al. Strategy in Regulatory Decision-Making for Management of Progressive Multifocal Leukoencephalopathy. Clin Pharmacol Ther. 2015 Nov;98(5):502-5; doi: 10.1002/cpt.199

- The MAHs for Carvykti (ciltacabtagene autoleucel), Abecma (idecabtagene vicleucel) and Kymriah (tisagenlecleucel) should submit to EMA, within 60 days, a variation[7] to amend the product information.

### 4.2.2. Clozapine (NAP)

Applicant(s): various

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of new aspect of the known risk of neutropenia/agranulocytosis with potential impact on the risk minimisation measures

EPITT 20141 – Follow up to January 2025

**Background**

For background information, see PRAC minutes January 2025.

The innovator MAH Viatris for clozapine-containing medicinal products replied to the request for information on the signal of the known risk of neutropenia/agranulocytosis with potential impact on the risk minimisation measures and the responses were assessed by the Rapporteur.

**Discussion**

Having considered the available evidence from EudraVigilance, the literature, the DARWIN EU® - Clozapine and the incidence of agranulocytosis over time study results, as well as the data provided by the innovator MAH, PRAC agreed that there is sufficient evidence to revise the current recommendations regarding blood monitoring in clozapine users to mitigate the risk of agranulocytosis. Additionally, specific thresholds for the sub-population with benign ethnic neutropenia (BEN) should be indicated.

**Summary of recommendation(s)**

- The MAHs for clozapine-containing medicinal products should submit to the national competent authorities, within 60 days, a variation[8] to amend the product information. The MAHs should also collaboratively distribute a joint direct healthcare professional communication (DHPC) to communicate the revised recommendations for routine blood monitoring for the risk of agranulocytosis.

### 4.2.3. Varicella vaccine (live) (NAP); measles, mumps, rubella and varicella vaccine (live) – PROQUAD (CAP); (NAP)

Applicant(s): MERCK SHARP & DOHME B.V. (Proquad), various

PRAC Rapporteur: Jean-Michel Dogné

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

EPITT 20180 – Follow up to June 2025

**Background**

For background information, see PRAC minutes June 2025.

[7] Update of SmPC sections 4.4.
[8] Update of SmPC section 4.2, 4.4, 4.5 and 4.8. The package leaflet is updated accordingly.

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

**Discussion**

Having considered the available evidence in EudraVigilance including the cumulative reviews submitted by the MAHs, PRAC agreed that there is sufficient evidence to support a causal association between new aspect of the known risk of encephalitis and Proquad (measles, mumps, rubella and varicella vaccine (live)) and for varicella vaccine (live)-containing medicinal products. Therefore, the product information should be updated to add encephalitis as a warning and describe further the encephalitis cases as undesirable effects including their potentially fatal outcome.

**Summary of recommendation(s)**

- The MAHs for Proquad (measles, mumps, rubella and varicella vaccine (live)) and for varicella vaccine (live)-containing medicinal products should submit to EMA, within 30 days, a variation[9] to amend the product information.
- In the next PSURs, the MAHs should discuss any new information regarding encephalitis after vaccination with the varicella vaccines (live) and the fixed combination measles, mumps, rubella and varicella vaccines.

## 4.3. Variation procedure(s) resulting from signal evaluation

None

# 5. Risk management plans (RMPs)

## 5.1. Medicines in the pre-authorisation phase

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

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

See also Annex I 15.1.

### 5.1.1. Acellular pertussis vaccine - (CAP MAA) - EMEA/H/C/006304

Scope (pre D-180 phase): Indicated as active booster immunization against pertussis of persons aged 11 years onwards and passive protection against pertussis in early infancy following maternal immunization during pregnancy

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

ATMPScope (pre D-120 phase): Treatment of melanoma

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

### 5.1.3. Brensocatib - (CAP MAA) - EMEA/H/C/005820, PRIME

Scope (pre D-120 phase, accelerated assessment): Treatment of non-cystic fibrosis bronchiectasis

### 5.1.4. Clascoterone - (CAP MAA) - EMEA/H/C/006138

Scope (re-examination): Indicated for the topical treatment of acne vulgaris in adults and adolescents

### 5.1.5. Clesrovimab - (CAP MAA) - EMEA/H/C/006497

Scope (pre D-180 phase): Prevention of infections with respiratory syncytial virus (RSV) and lower respiratory tract disease (LRTD)

### 5.1.6. Elinzanetant - (CAP MAA) - EMEA/H/C/006298

Scope (pre D-180 phase): For the treatment of moderate to severe vasomotor symptoms (VMS)

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### 5.1.7. Insulin icodec / Semaglutide - (CAP MAA) - EMEA/H/C/006279

Scope (pre D-180 phase): Treatment of adults with type 2 diabetes mellitus insufficiently controlled on basal insulin or glucagon-like peptide 1 (GLP-1) receptor agonists

### 5.1.8. Rilzabrutinib - (CAP MAA) - EMEA/H/C/006425, Orphan

Applicant: Sanofi B.V.

Scope (pre D-180 phase): For the treatment of persistent or chronic immune thrombocytopenia (ITP)

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

Scope (pre D-210 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 Annex I 15.2.

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

See also Annex I 15.3.

### 5.3.1. 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).

**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 an extension of application for Remsima, a centrally authorised product containing infliximab, to introduce a new pharmaceutical form. 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 April 2025.

**Summary of advice**

- The RMP for Remsima (infliximab) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 17.1 is submitted.
- PRAC considered that the safety specification of the RMP should be updated to include 'serious metabolic harms due to sorbitol exposure in patients with hereditary fructose intolerance (HFI)' as an important potential risk, as an inadvertent use remains a risk despite the proposed contraindication in this population. Regarding the additional risk minimisation measures, PRAC agreed that the proposed patient card should be updated to include information on contraindication on HFI, as well as that the MAH should provide a proposal on a direct health care professional communication (DHPC) and communication plan to inform health care professionals on this risk.

### 5.3.2. Marstacimab – HYMPAVZI (CAP) – EMA/VR/0000268024

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to add information regarding thromboembolic events and to add "thrombosis" to the list of adverse drug reactions (ADRs) with frequency uncommon based on a review of clinical data, post marketing data and literature. The Package Leaflet is updated accordingly. The RMP version 1.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes and corrections to the PI, including 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.

CHMP is evaluating a type II variation for Hympavzi, a centrally authorised product containing marstacimab, to update the product information based on a review of clinical data, post marketing data and literature. PRAC is responsible for providing advice to CHMP on the necessary updates to the RMP to support this procedure.

**Summary of advice**

- The RMP for Hympavzi (marstacimab) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 1.1 is submitted.
- PRAC supported the reclassification of 'thromboembolism' from an important potential risk to an important identified risk (IIR) in the RMP, as well as the inclusion of a follow-up questionnaire for 'thromboembolic events', and the implementation of additional risk minimisation measures (aRMMs) in the form of a patient card for this IIR. Furthermore, PRAC supported that the effectiveness of the patient card should be followed up with routine pharmacovigilance activities in the PSURs, but did not support the implementation of the aRMMs of a patient guide and a health care professional guide as was proposed by the MAH, in light of the current knowledge.

### 5.3.3. 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, multicentre 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.

**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 Gazyvaro, a centrally authorised product containing obinutuzumab, to extend the indication to include treatment of adult patients with active lupus nephritis who are receiving standard therapy for Gazyvaro. 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 April 2025.

**Summary of advice**

- The RMP for Gazyvaro (obinutuzumab) in the context of the variation procedure under evaluation by CHMP could be considered acceptable provided that an update to RMP version 11.1 is submitted.
- PRAC considered that long-term safety in lupus nephritis should be included in the RMP as missing information, and the long-term extension part of the REGENCY study should be included in the RMP as a category 3 study to evaluate this risk.

# 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. Enfortumab vedotin – PADCEV (CAP) – EMA/PSUR/0000257872

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00010989/202412)

**Background**

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Padcev, a centrally authorised medicine containing enfortumab vedotin 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 Padcev (enfortumab vedotin) in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add a warning on pneumonia and to include pneumonia and thrombocytopenia as undesirable effects with a frequency 'common'. Therefore, the current terms of the marketing authorisation(s) should be varied[10].
- In the next PSUR, the MAH should provide updated reviews including the new and followed-up cases of opportunistic infections and of pancytopenia. In addition, the MAH should provide a cumulative review of cases of leukopenia and lymphopenia, should closely monitor cases of urinary tract infections and pyelonephritis and present new cases or cases for which a significant safety follow-up information is obtained, including a causality assessment. The MAH should also present a cumulative number of cases of severe cutaneous adverse reaction (SCAR) cases, including data from literature and assess whether there is a need for an update of the PI.

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.

[10] 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.

### 6.1.2. Pegzilarginase – LOARGYS (CAP) – EMA/PSUR/0000257794

Applicant: Immedica Pharma AB

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000222/202412)

**Background**

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Loargys, a centrally authorised medicine containing pegzilarginase 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 Loargys (pegzilarginase) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing information regarding hypersensitivity reactions. PRAC also agreed to an additional change in SmPC section 4.2 to have 'once' explicitly stated in the context of weekly dosing. Therefore, the current terms of the marketing authorisation(s) should be varied[11].
- The MAH should reclassify 'severe hypersensitivity' to an important identified risk in the next RMP update.

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.

### 6.1.3. Ravulizumab – ULTOMIRIS (CAP) – EMA/PSUR/0000257874

Applicant: Alexion Europe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010787/202412)

**Background**

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

[11] Update of SmPC sections 4.2, 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion

- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide an integrated evaluation of controlled clinical trial data comparing lower respiratory tract infections in ravulizumab arm to comparator arm.
- The MAH should submit, as part of a post-authorisation measure, a cumulative review of all available data concerning liver injury and hepatic enzyme elevations (SMQ Drug related hepatic disorders–severe events only and SMQ Liver related investigations, signs and symptoms), including data from post-marketing sources, clinical trials and literature, as well as a discussion regarding the plausible mechanisms and causality assessments. The MAH should discuss whether an update of the product information is 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.

### 6.1.4. Roxadustat – EVRENZO (CAP) – EMA/PSUR/0000257864

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00010955/202412)

**Background**

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Evrenzo, a centrally authorised medicine containing roxadustat 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 Evrenzo (roxadustat) in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to amend a warning regarding thrombotic vascular events and to add cerebral infarction as an undesirable effect with a frequency 'uncommon'. Therefore, the current terms of the marketing authorisation(s) should be varied[12].
- In the next PSUR, the MAH should provide a cumulative review of all available data from clinical trials, post-marketing data and other sources based on the SMQ Myocardial infarction. The MAH should also provide a cumulative review of cases of vaso-occlusive crisis reported with roxadustat, including data from post marketing sources, clinical trials and literature and discuss whether an update of the PI is warranted. The MAH should also continue to monitor thrombocytopenia/platelet count decreased as a safety topic under monitoring focused on serious adverse reactions, in order to identify patient groups with higher risk of developing thrombocytopenia.

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

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

### 6.1.5. Sapropterin – KUVAN (CAP) – EMA/PSUR/0000257835

Applicant: Biomarin International Limited

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00002683/202412)

**Background**

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Kuvan, a centrally authorised medicine containing sapropterin 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 Kuvan (sapropterin) in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAH should provide cumulative reviews of cases of anaphylactic reaction, as well as of gastritis and oesophagitis, and discuss whether product information (PI) updates are warranted.
- The MAH should submit, as part of a post-authorisation measure, a cumulative review of use of Kuvan during pregnancy and discuss whether an update of the PI 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.

### 6.1.6. Sugemalimab – CEJEMLY (CAP) – EMA/PSUR/0000257890

Applicant: Cstone Pharmaceuticals Ireland Limited

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00011080/202412)

**Background**

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

- Nevertheless, the product information should be updated to add coeliac disease and exocrine pancreatic insufficiency as undesirable effects under Immune checkpoint inhibitor class effects subheading, mentioning that there have been cases of coeliac disease and pancreatic exocrine insufficiency reported during treatment with other immune checkpoint inhibitors which might also occur during treatment with sugemalimab. Therefore, the current terms of the marketing authorisation(s) should be varied[13].

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

### 6.1.7. Tislelizumab – TEVIMBRA (CAP) – EMA/PSUR/0000257798

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000136/202412)

**Background**

Based on the assessment of the PSUR, PRAC reviewed the benefit-risk balance of Tevimbra, a centrally authorised medicine containing tislelizumab 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 Tevimbra (tislelizumab) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add a warning regarding the safety in patients with pre-existing autoimmune disease. Therefore, the current terms of the marketing authorisation(s) should be varied[14].

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

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

See also Annex I 16.2.

[13] Update of SmPC section 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.
[14] 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.

### 6.2.1. Azathioprine – JAYEMPI (CAP); NAP – EMA/PSUR/0000257799

Applicants: Lipomed GmbH, various

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00000275/202412)

**Background**

Azathioprine is an immunosuppressant indicated in immunosuppressive regimens as an adjunct to immunosuppressive agents that form the mainstay of treatment (basis immunosuppression). It is indicated in combination with other immunosuppressive agents for the prophylaxis of transplant rejection in patients receiving allogenic kidney, liver, heart, lung, or pancreas transplants. It is also indicated either alone or in combination with corticosteroids and/or other drugs and procedures in severe cases of the following diseases, or in patients who are intolerant to steroids or who are dependent on steroids and in whom the therapeutic response is inadequate despite treatment with high doses of steroids: moderate to severe inflammatory bowel disease (IBD), severe rheumatoid arthritis, systemic lupus erythematosus (SLE), dermatomyositis and polymyositis, auto-immune chronic active hepatitis, pemphigus vulgaris and bullous pemphigoid, polyarteritis nodosa, auto-immune haemolytic anaemia, chronic refractory idiopathic thrombocytopenic purpura, relapsing remittent multiple sclerosis, Behcet's disease, pyoderma gangrenosum and generalised myasthenia.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Jayempi, (a) centrally authorised medicine(s) containing azathioprine, and nationally authorised medicines containing azathioprine 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 azathioprine-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add cardiac dysfunction as a clinical feature of hypersensitivity reactions and to add new information about the risk of cholestasis of pregnancy. In addition, the PI should be updated to add pellagra and posterior reversible encephalopathy syndrome as warnings and as undesirable effects with frequency 'not known'. The PI should also be updated to add sialadenitis and tremor as undesirable effects with frequency 'not known'. Finally, the PI should be updated to amend the existing information regarding the drug-drug interaction between azathioprine and allopurinol. Therefore, the current terms of the marketing authorisations should be varied[15].

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

[15] Update of SmPC sections 4.4, 4.5, 4.6 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.

### 6.2.2. Bosentan – STAYVEER (CAP); TRACLEER (CAP); NAP – EMA/PSUR/0000257801

Applicants: Janssen Cilag International, various

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00000425/202411)

**Background**

Bosentan is an endothelin receptor antagonist indicated in the treatment of pulmonary arterial hypertension (PAH), and to reduce the number of new digital ulcers in patients with systemic sclerosis and ongoing digital ulcer disease.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Stayveer and Tracleer, centrally authorised medicines containing bosentan, and nationally authorised medicines containing bosentan, and issued a recommendation on their marketing authorisations.

**Summary of recommendation(s) and conclusions**

- Based on the review of the data on safety and efficacy, the benefit-risk balance of bosentan-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add autoimmune hepatitis as a warning and as an undesirable effect with a frequency 'rare'. Therefore, the current terms of the marketing authorisations should be varied[16].
- In the next PSUR, the MAHs should continue to monitor cases of pulmonary oedema in patients with chronic thromboembolic pulmonary hypertension (CTEPH) or other post-capillary conditions than pulmonary veno-occlusive disease (PVOD), and discuss any new relevant information.
- The MAHs which have an RMP in place should remove from the list of safety concerns the important risks of decrease in haemoglobin concentration, decrease of sperm count, pulmonary oedema associated with PVOD, interactions with substrates, inducers or inhibitors of cytochrome P450 isoenzymes CYP3A4 and CYP2C9, testicular disorders and male infertility, and respiratory tract infection in children, as well as the missing information of use of bosentan with the addition of sildenafil in children and use in children with renal function impairment, in the next RMP update to be submitted within an upcoming regulatory procedure affecting the RMP.

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

### 6.2.3. Levetiracetam – KEPPRA (CAP); NAP – EMA/PSUR/0000257824

Applicants: UCB Pharma, various

PRAC Rapporteur: Jo Robays

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

Scope: Evaluation of a PSUSA procedure (PSUSA/00001846/202411)

**Background**

Levetiracetam is a pyrrolidone derivative and it is indicated in various epileptic disorders.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of Keppra, (a) centrally authorised medicine(s) containing levetiracetam, and nationally authorised medicines containing levetiracetam 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 levetiracetam-containing product(s) in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to amend the existing information on the risk of neurodevelopmental disorders in children exposed prenatally to levetiracetam. Therefore, the current terms of the marketing authorisations should be varied[17].
- In the next PSUR, the MAH(s) should provide a cumulative review regarding the association between levetiracetam exposure and the onset of urinary incontinence/enuresis, including data from all sources. In addition, the MAH(s) should present an update of cases of drug withdrawal syndrome neonatal, hypokalaemia, hyperammonaemia, renal dysfunction disorders, drug-drug interaction with temozolomide, drug-drug interaction with direct oral anticoagulants, ECG QT prolongation and torsade de Pointes associated with ECG QT prolongation.

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. Acetylsalicylic acid / bisoprolol (NAP) – EMA/PSUR/0000257841

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00010287/202411)

**Background**

Acetylsalicylic acid/bisoprolol fixed-dose combination products are indicated for the treatment of angina pectoris, coronary heart disease and in hypertension, or for patients that are on

[17] Update of SmPC section 4.6. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CHMP for adoption of an opinion.

stable treatment at the same dose level with bisoprolol for arterial hypertension or angina pectoris and with acetylsalicylic acid for unstable angina pectoris, secondary prevention of myocardial infarction, prevention of graft occlusion after coronary artery bypass grafting (CABG) or after coronary angioplasty for secondary prevention of transient ischaemic attacks and ischaemic cerebrovascular accidents.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing acetylsalicylic acid/bisoprolol and issued a recommendation on their marketing authorisations.

**Summary of recommendation(s) and conclusions**

- Based on the review of the data on safety and efficacy, the benefit-risk balance of acetylsalicylic acid / bisoprolol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add a warning regarding the risk of severe hypoglycaemia with the concomitant use of beta-blockers and sulfonylureas. Therefore, the current terms of the marketing authorisations should be varied[18].
- In the next PSUR, the MAHs of acetylsalicylic acid/bisoprolol fixed dose combination products should provide all available data related to DRESS, including data from spontaneous reports, clinical trials and scientific literature, and discuss whether an update of the PI is warranted.

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

### 6.3.2. Acetylsalicylic acid/ caffeine/ paracetamol (NAP) – EMA/PSUR/0000257831

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002291/202412)

**Background**

Acetylsalicylic acid/caffeine/paracetamol fixed dose combination products are indicated for the symptomatic treatment of mild and moderate pain (e.g. headache, toothache, cold-related sore throat, period pain, muscular and joint pain, back pain, minor arthritis pain), the treatment of headache and migraine attacks with or without aura, and for the symptomatic relief of pain and fever of common cold, subject to certain conditions.

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

**Summary of recommendation(s) and conclusions**

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of acetylsalicylic acid/caffeine/paracetamol-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisations should be maintained.

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

### 6.3.3. Bisoprolol / hydrochlorothiazide (NAP) – EMA/PSUR/0000257832

Applicant(s): various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00000420/202411)

**Background**

Bisoprolol/hydrochlorothiazide is a fixed dose combination indicated for the treatment of essential hypertension.

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

**Summary of recommendation(s) and conclusions**

- Based on the review of the data on safety and efficacy, the benefit-risk balance of bisoprolol / hydrochlorothiazide-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated add a warning regarding the risk of severe hypoglycaemia with the concomitant use of beta-blockers and sulfonylurea. Therefore, the current terms of the marketing authorisations should be varied[19].
- In the next PSUR, the MAH Viatris should provide a review of cases of skin melanoma, including data from literature, together with a thorough assessment and a discussion on whether an update the safety information for hydrochlorotiazide containing products is warranted. The MAH Teva should continue to monitor cases of tinnitus.

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

### 6.3.4. Diamorphine (NAP) – EMA/PSUR/0000257810

Applicant(s): various

PRAC Lead: Liana Martirosyan

[19] Update of SmPC sections 4.4 and 4.5. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

Scope: Evaluation of a PSUSA procedure (PSUSA/00001028/202411)

**Background**

Diacetylmorphine (diamorphine) is a pro-drug for the active metabolites morphine and morphine-6-glucuronide narcotic analgesic, which primarily exerts its effect on the opioid receptors of the central nervous system and smooth musculature, and is indicated for opiate dependence/abuse and for acute severe nociceptive pain in children and adolescents 2 to 15 years of age in a hospital setting, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing diamorphine 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 diamorphine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated in order to further minimise the risk of opioid use disorder (OUD), to add/amend the information regarding the risk of neonatal withdrawal syndrome and to add warnings about the risks of sleep-related breathing disorders and opioid-induced endocrinopathies. The PI should also be updated to reflect the drug-drug interaction with gabapentinoids, and to amend the drug-drug interaction with anticholinergic medicines. In addition, the PI should be updated to add a new black box warning about the risk of dependence and addiction in the package leaflet. Therefore, the current terms of the marketing authorisation(s) should be varied[20].
- In the next PSUR, the MAHs should continue to monitor cases of sphincter of Oddi dysfunction and pancreatitis, and discuss any new significant safety information, including whether update of the PI 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.

### 6.3.5. Diphenhydramine / paracetamol (NAP) – EMA/PSUR/0000257807

Applicant(s): various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00001110/202411)

**Background**

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

Diphenhydramine/paracetamol is a fixed dose combination indicated for the treatment of mild-to-moderate pain, fever, cough and cold, and allergic symptoms or difficulty getting to sleep due to these symptoms, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing diphenhydramine/paracetamol 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 diphenhydramine/paracetamol-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAHs should provide an updated cumulative review for the MedDRA preferred term (PT) 'tubulointerstitial nephritis', including data concerning paracetamol-associated tubulointerstitial nephritis from all sources, including clinical trials, literature and the MAH's global safety database. The MAHs should include a causality assessment, together with a discussion on a possible mechanism of action and discuss whether an update of the product information (PI) is warranted. The MAHs should also provide a cumulative review of cases of QT prolongation, including all cases at therapeutic doses identified using the SMQ 'Torsade de pointes/QT prolongation' associated with diphenhydramine, including cases identified from clinical trials, literature and the MAH's global safety database. In particular any risk factors for QT prolongation associated with diphenhydramine use should be evaluated and discussed, as well as whether an update of PI is warranted. Finally, the MAHs should include severe cutaneous adverse reactions (SCARs) as an important potential risk in the PSUR and monitored accordingly, and discuss any measures to mitigate this risk, (e.g. specific clinical actions advised in the PI) are 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.

### 6.3.6. Domperidone (NAP) – EMA/PSUR/0000257804

Applicant(s): various

PRAC Lead: Jo Robays

Scope: Evaluation of a PSUSA procedure (PSUSA/00001158/202411)

**Background**

Domperidone is a D2 antagonist with antiemetic properties and it is indicated for the relief of the symptoms of nausea and vomiting in adults and adolescents, subject to certain conditions.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing domperidone 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 domperidone-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated to add a contraindication regarding confirmed or suspected pheochromocytoma due to the risk of severe hypertension episodes. Therefore, the current terms of the marketing authorisation(s) should be varied[21].
- In the next PSUR, the MAHs should review and discuss all data available regarding the safety of domperidone used during pregnancy and to the newborn including outcomes of births, risk of extrapyramidal syndrome in newborn but also neurological adverse drug reactions (ADRs) more general, if domperidone is administered at the end of pregnancy. The MAHs should propose an update of the PI, as warranted.

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

### 6.3.7. Hydromorphone (NAP) – EMA/PSUR/0000257819

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure (PSUSA/00001686/202411)

**Background**

Hydromorphone is a semisynthetic indicated for the treatment of severe (malignant and sometime non-malignant) pain when not successfully controlled by other analgesics.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing hydromorphone 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 hydromorphone-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated in order to further minimise the risk of opioid use disorder (OUD). In addition, the PI should be updated to add a new black box warning about the risk of dependence and addiction in the package leaflet. Therefore, the current terms of the marketing authorisation(s) should be varied[22].
- In the next PSUR, the MAHs should provide a review of cases of drug-drug interaction between hydromorphone and anticholinergic medicines, including data from the literature and the post-marketing setting.

[21] Update of SmPC section 4.3. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position
[22] Update of SmPC sections 4.2, 4.4 and 4.8. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position

The 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.

### 6.3.8. Levamisole hydrochloride (NAP) – EMA/PSUR/0000268962

Applicant(s): various

PRAC Lead: Roxana Dondera

Scope: Evaluation of a PSUSA procedure (PSUSA/00001845/202501)

**Background**

Levamisole is an anti-helmintic and it is indicated for the treatment of infections by the following gastro-intestinal worm species: *Ascaris lumbricoides*, *Necator americanus*, *Ancylostoma duodenale*.

**Summary of conclusions**

- The PRAC Lead presented the conclusions based on the preliminary assessment report, indicating serious concerns in relation to the risk-benefit balance of levamisole-containing products in their authorised indications.
- The Lead Member State (LMS) considered that the MAH Gedeon Richter should submit additional data regarding the risk of leukoencephalopathy, including a succinct discussion of the impact of this risk on the benefit-risk balance of levamisole containing products, taking into consideration all available information, and to propose effective risk minimisation measures to reduce this risk in the authorised indications. In addition, the MAH Gedeon Richter should provide information on the magnitude of off-label use in the various therapeutic fields outside of the authorised indication and also on the misuse and the associated safety concerns.
- The LMS will assess the responses once submitted by the MAH. PRAC will adopt a recommendation to CMDh at the PRAC September 2025 plenary meeting.

### 6.3.9. Methocarbamol (NAP) - EMA/PSUR/0000257823

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002011/202412)

**Background**

Methocarbamol is a centrally acting muscle relaxant, indicated for the symptomatic treatment of painful muscular tension, particularly in the lower back (lumbago).

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing methocarbamol 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 methocarbamol-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAHs should remove the risks regarding interactions and use in special populations from the list of safety concerns. In addition, the MAHs should address the risk of 'fall and injury (including due to interaction with other medication and increased risk in the elderly)' as an important identified risk in future PSURs.

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

### 6.3.10. Methocarbamol / paracetamol (NAP) – EMA/PSUR/0000257826

Applicant(s): various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure (PSUSA/00002013/202412)

**Background**

Methocarbamol/paracetamol is a fixed dose combination indicated for the treatment of painful muscle spasms associated with short-term muscle disorders, such as spasms in the lower back.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing methocarbamol/paracetamol 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 methocarbamol/paracetamol-containing medicinal products in the approved indication(s) remains unchanged.
- The current terms of the marketing authorisation(s) should be maintained.
- In the next PSUR, the MAHs should provide a summary and discussion of the safety results of the MioPain study: Efficacy and safety of different dosage regimens of the combination methocarbamol/paracetamol in acute non-specific Low Back Pain (LBP).

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

### 6.3.11. Nicotine (NAP) - EMA/PSUR/0000257828

Applicant(s): various

PRAC Lead: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00002153/202412)

**Background**

Nicotine is a nicotinic acetylcholine receptor agonist, indicated for abrupt smoking cessation, gradual smoking cessation and an aid for smokers during temporary abstinence when smoking is not allowed.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing nicotine 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 nicotine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add atrial fibrillation as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[23].
- In the next PSUR, the MAHs should maintain or include the following safety concerns: cardiovascular events (including arrythmia and patients with prior cardiac history), pregnancy and lactation, and addiction/dependence.

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

### 6.3.12. Phosphocreatine (NAP) – EMA/PSUR/0000257837

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00002398/202411)

**Background**

Phosphocreatine is a high energy compound in the skeletal muscle, indicated for the treatment of disorders of myocardial metabolism in ischemic conditions or myocardial metabolic suffering in ischaemic conditions, as well as cardioprotection in cardiac surgery, as additive to cardioplegic solution or as protection of the heart muscle during cardiac surgery when it is added to cardioplegic solutions.

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

**Summary of recommendation(s) and conclusions**

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

- Based on the review of the data on safety and efficacy, the benefit-risk balance of phosphocreatine-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information should be updated to add urticaria as an undesirable effect with a frequency 'not known'. Therefore, the current terms of the marketing authorisation(s) should be varied[24].
- In the next PSUR, the MAHs should provide a critical assessment on cases of off label use and use in unapproved indication, and should keep monitoring any case of angioedema, including a critical assessment, if any. The MAHs should include 'serious skin reactions' as important potential risks and 'use in unapproved indication' as missing information in the list of safety concerns in the PSUR. Clarification on the method used for adverse drug reaction (ADR) causality assessment is also expected.

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.

### 6.3.13. Tapentadol (NAP) – EMA/PSUR/0000257836

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00002849/202411)

**Background**

Tapentadol is an opioid analgesic, indicated in adults only for the management of severe chronic pain that can be adequately managed only with opioid analgesics.

Based on the assessment of the PSUR(s), PRAC reviewed the benefit-risk balance of nationally authorised medicine(s) containing tapentadol 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 tapentadol-containing medicinal products in the approved indication(s) remains unchanged.
- Nevertheless, the product information (PI) should be updated in order to further minimise the risk of opioid use disorder (OUD): add information regarding treatment goals and discontinuation, add a reminder that the product should not be used longer than necessary and to amend the warning that repeated use of opioids can lead to OUD, as well as to add a warning that a higher dose and longer duration of opioid treatment can increase the risk of developing OUD. Moreover, the PI of immediate release formulations should be updated to add drug dependence as an undesirable effect with a frequency 'uncommon'. In addition, the PI should be updated to add a reminder that the

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

overdose can be fatal and to add the drug-drug interaction with anticholinergic medicines. The package leaflet should be updated to add a reminder that the product must be stored in a safe and secure place and to add a new black box warning about the risk of dependence and addiction. Therefore, the current terms of the marketing authorisation(s) should be varied[25].

- In the next PSUR, the MAHs should provide a cumulative review of cases of erectile dysfunction, including data from clinical trials, literature and post marketing setting, and considerations on a possible pathomechanism (e.g. opioid-receptor-based, noradrenaline-reuptake-inhibition-related, link to the important potential risk 'endocrine effects'). Suggestions for further measures including a proposal for an update of the PI should be presented if deemed appropriate. The MAHs should also provide a review of endocrine effects, including an assessment of the statement on exogenous opioids and the human endocrine system by the Endocrine Society (*Karavitaki et al. (2024)*) as well as other relevant publications, and a cumulative and interval analysis of case reports from studies and spontaneous reporting, and discuss whether an update of the PI is warranted.

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

## 6.4. Follow-up to PSUR/PSUSA procedures

See Annex I 16.4.

## 6.5. Variation procedure(s) resulting from PSUSA evaluation

None

## 6.6. Expedited summary safety reviews[26]

None

# 7. Post-authorisation safety studies (PASS)

## 7.1. Protocols of PASS imposed in the marketing authorisation(s)[27]

See also Annex I 17.1.

### 7.1.1. Lecanemab – LEQEMBI (CAP) – EMA/PASS/0000267311

Applicant: Eisai GmbH

PRAC Rapporteur: Eva Jirsová

[25] Update of SmPC sections 4.2, 4.4,4.5, 4.8, 4.9. The package leaflet is updated accordingly. The PRAC AR and PRAC recommendation are transmitted to CMDh for adoption of a position
[26] 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
[27] In accordance with Article 107n of Directive 2001/83/EC

Scope: PASS protocol [107n]: Study BAN2401-G000-505; A prospective observational registry study to evaluate the use and safety of LEQEMBI in routine clinical practice (EEA)

**Background**

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

In order to fulfil the obligation to conduct a PASS imposed in accordance with Article 107n(3) of Directive 2001/83/EC, the MAH Eisai GmbH submitted on 29 April 2025 a PASS protocol version 1.0 to the EMA for Leqembi (lecanemab).

**Endorsement/Refusal of the protocol**

- Having considered the draft protocol version 1.0 in accordance with Article 107n of Directive 2001/83/EC, PRAC objected to the draft protocol for the above listed medicinal product(s), as PRAC considered that that the study design did not fulfil the study objectives at this stage.
- PRAC therefore recommended that the MAH should explore existing registry initiatives with an aim to undertake this study leveraging on existing data sources. In addition, the MAH should propose comparator group for each study objective, particularly to address the concern regarding possible acceleration of disease progression due to amyloid-related imaging abnormalities (ARIA), and for a further general characterisation of the safety profile following long-term use. The MAH should also revise the plan for the evaluation of compliance and effectiveness of the risk minimisation measures accordingly.
- The MAH should submit a revised PASS protocol within 60 days to EMA. A 60 days-assessment timetable will be followed.

## 7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[28]

See also Annex I 17.2.

### 7.2.1. Netarsudil – RHOKIINSA (CAP) – EMA/PAM/0000272898

Applicant: Santen Oy

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of information with supportive rationale and justification with annexes to withdraw the protocol and non-interventional post-authorisation safety study (PASS), Study number STN1013900-SA01 (previously submitted as original PASS Protocol designed by Aerie Pharmaceuticals Ireland Limited: AR-13324-OBS02), for netarsudil mesylate (Rhokiinsa)

[28] 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

**Background**

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

As part of the RMP for Rhokiinsa (netarsudil), the MAH was required to conduct a PASS in order to further characterise the long-term safety profile of Rhokiinsa in the real-world setting and in comparison with long-term treatment of non-Rhokiinsa ocular hypotensive agent(s) in patients with elevated intraocular pressure (IOP) due to primary open angle glaucoma (POAG) or ocular hypertension (OHT). In this procedure, the MAH has submitted to EMA a notification letter for the withdrawal of this PASS. PRAC was requested to provide advice to CHMP on this submission.

**Summary of advice**

- PRAC considered that the STN1013900-SA01 PASS could be removed from the RMP, based on the justification provided by the MAH. No further additional pharmacovigilance activities are considered necessary to address the safety concerns 'long-term safety of netarsudil (beyond 12 months)' and 'use in patients with compromised corneal epithelium'. PRAC considered that routine pharmacovigilance is sufficient to identify and characterise the risks of netarsudil. Therefore, the MAH should submit to EMA, within 60 days, a variation procedure to update the RMP and in accordance with the GVP module V (Rev. 2).

## 7.3. Results of PASS imposed in the marketing authorisation(s)[29]

None

## 7.4. Results of PASS non-imposed in the marketing authorisation(s)[30]

See also Annex I 17.4.

### 7.4.1. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) - EMA/VR/0000263592

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Sonja Radowan

Scope: Update of sections 4.4 and 4.8 of the SmPC to add "Guillain-Barre syndrome" (GBS) to the list of adverse drug reactions with frequency "very rare" based on the results from study EPI-ZOSTER-032 VS US DB, listed as a category 3 study in the RMP. This is a non-interventional PASS study to evaluate the safety of Shingrix in adults ≥ 65 years of age in the United States. The Package Leaflet is updated accordingly. The RMP version 11.0 has also been submitted.

**Background**

[29] In accordance with Article 107p-q of Directive 2001/83/EC
[30] 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

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 Shingrix (herpes zoster vaccine (recombinant, adjuvanted)), the MAH conducted a non-imposed non-interventional PASS to assess safety of Shingrix in adults ≥ 65 years of age in the United States. The Rapporteur assessed the MAH's final study results.

**Summary of advice**

- Based on the available data 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 request for supplementary information (RSI).
- PRAC considered that there is sufficient evidence to indicate an increased risk of GBS following Shingrix exposure in individuals aged ⩾65 years, therefore, the inclusion in the product information[31] of GBS as an undesirable effect with a frequency 'very rare' is justified. Additionally, PRAC considered that a warning in the product information is not considered necessary in the absence of any specific actionable recommendation or preventive action. Also, PRAC did not agree with the proposed update to Part III of the RMP (Pharmacovigilance plan) and considered that GBS should remain as 'safety concern addressed' for study EPI-ZOSTER-030 VS US DB. Moreover, PRAC considered that GBS should remain in the list of safety concerns in the RMP and that it should be re-classified from an important potential risk to an important identified risk at this stage. The MAH should continue to closely monitor reports of GBS, and any new information that becomes available should be promptly assessed to determine whether additional regulatory actions are warranted.

## 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.

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

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

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

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

### 8.1. Annual reassessments of the marketing authorisation

See Annex I 18.1.

### 8.2. Conditional renewals of the marketing authorisation

See Annex I 18.2.

### 8.3. Renewals of the marketing authorisation

See Annex I 18.3.

## 9. Product related pharmacovigilance inspections

### 9.1. List of planned pharmacovigilance inspections

None

### 9.2. Ongoing or concluded pharmacovigilance inspections

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

### 9.3. Others

None

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

### 10.1. Safety related variations of the marketing authorisation

None

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

None

## 10.3. Other requests

None

## 10.4. Scientific Advice

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

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

## 11.1. Safety related variations of the marketing authorisation

### 11.1.1. Buprenorphine (NAP) - DK/H/1986/001-003/II/032; DK/H/0718/001007/II/060

Applicant(s): Mundipharma A/S (BuTrans, Norspan)

PRAC Lead: Karin Erneholm

Scope: PRAC consultation on variation procedures regarding an update of the product information to reflect the drug-drug interaction between buprenorphine and nalmefene, on request of Denmark

**Background**

Buprenorphine is an opioid partial agonist at the μ (mu) opioid receptor and an antagonist at the κ (kappa) opioid receptor administered sublingually or for injection (subcutaneous) for the treatment of opioid dependence. Buprenorphine is also utilised sublingually and intravenously/intramuscularly in low doses for the treatment of moderate to severe pain. Buprenorphine is also indicated for the treatment of moderate to severe cancer pain and severe pain which does not respond to non-opioid analgesics as transdermal patch.

In the context of the evaluation of a type II variation procedure regarding an update of the product information (PI) to reflect the drug-drug interaction between buprenorphine and nalmefene, Denmark requested PRAC advice on its assessment.

**Summary of advice**

- Based on the review of the available information, PRAC agreed with the RMS assessment that the main concern regarding the drug-drug interaction between buprenorphine and nalmefene is the potential for severe withdrawal syndrome, however PRAC noted that the potential for withdrawal symptoms occurrence is mainly relevant for the buprenorphine products in the treatment of the opioid dependence and that nalmefene (indicated for the treatment of alcohol dependence) has a contraindication of co-administration with those buprenorphine products. PRAC therefore agreed with the RMS position that the PI[32] changes for the buprenorphine transdermal patches should be accepted, with no contraindication with concomitant use of nalmefene included for buprenorphine-containing transdermal patches for pain treatment, as the risk in these products would rather be insufficient for pain

[32] Update of sections 4.4 and 4.5 of the SmPC. The package Leaflet is updated accordingly

management or potentially overdose, instead of a severe withdrawal syndrome. Additionally, buprenorphine transdermal patches for the treatment of pain are contraindicated in the opioid dependent patients and for narcotic withdrawal treatment.

### 11.1.2. Carbamazepine (NAP) - DE/H/xxxx/WS/1925

Applicant(s): Novartis Pharma GmbH (Tegretal, Tegretol)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a worksharing procedure regarding the update of the product information (PI) to reflect the risks for congenital malformations, microcephaly, and infants being small for gestational age (SGA) associated with *in utero* exposure to carbamazepine, on request of Germany

**Background**

Carbamazepine is an anticonvulsant indicated for the treatment of epilepsy and nerve pain.

In the context of the evaluation of a type II variation procedure on a worksharing procedure regarding the update of the PI to reflect the risks for congenital malformations, microcephaly, and infants being SGA associated with *in utero* exposure to carbamazepine, Germany requested PRAC advice on its assessment.

**Summary of advice**

- Based on the review of the available information, PRAC was of the view that the current wording in the relevant PI (SmPC section 4.6) informing of the increased risk of major congenital malformations is reflective of the available data and therefore remains valid without the need to be further updated. Furthermore, PRAC considered that the PI[33] of carbamazepine should be updated to reflect the increased risk for microcephaly infants being SGA associated with *in utero* exposure to carbamazepine. In addition, as regards neurodevelopmental disorders, PRAC noted that the MAH, despite requested so, has not conducted a cumulative review nor appropriately discussed the published findings of *Madley-Dowd P et al., 2024*[34]. PRAC therefore advised that the MAH should perform a comprehensive review within the ongoing variation procedure.

### 11.1.3. Modafinil (NAP) - DE/H/3259/001-002/II/042

Applicant(s): Teva GmbH (Vigil)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a variation procedure regarding the update of the product information and the RMP based on the final results of the PASS: Assessment of Pregnancy Outcomes in Women Exposed to Modafinil/Armodafinil: Pregnancy Database Study (C10953-CNS-40155) and of the US Nuvigil and Provigil pregnancy registry, on request of Germany

**Background**

[33] Update of section 4.6 of the SmPC. The package leaflet is updated accordingly
[34] Madley-Dowd P et al. Nat Commun. 2024; 15(1): 9640.

Modafinil and armodafinil are amphetamine derivates indicated in adults for the treatment of excessive sleepiness associated with narcolepsy with or without cataplexy.

In the context of the evaluation of a type II variation procedure to update the product information (PI) and RMP based on the final PASS pregnancy report for study C10953-CNS-40155, Germany requested PRAC advice on its assessment.

**Summary of advice**

- Based on the review of the available information, PRAC agreed that the current data does not justify the introduction of a contraindication in pregnancy and that the existing recommendation on use during pregnancy remains valid. Regarding the information on spontaneous abortions, PRAC noted the limitations of the available data but agreed that there is value in reflecting this finding in the PI[35] . In addition, PRAC agreed that an update of the RMP is needed as follows: maintain 'teratogenicity' as an important potential risk and remove of the direct healthcare professional communication (DHPC) sent in 2019/2020 from an updated RMP. Furthermore, PRAC noted that new scientific literature on breastfeeding during administration of modafinil have become available and advised that these should be reviewed by the MAH at the next regulatory opportunity together with a proposal to update the PI.

## 11.2. Other requests

None

# 12. Organisational, regulatory and methodological matters

## 12.1. Mandate and organisation of PRAC

### 12.1.1. PRAC membership

### 12.1.2. The Chair thanked Jana Lukacisinova for her contribution as an alternate representing Czechia, as well as Gudrun Þengilsdóttir for her contribution as an alternate representing Iceland.Vote by proxy

Annalisa Capuano gave a proxy to Maria Teresa Herdeiro, Elena Kaisis to Georgia Gkegka, Jan Neuhauser to Martin Huber, Maia Uuskula to Zane Neikena and Gudrun Stefansdottir to David Olsen, covering the entire meeting.

### 12.1.3. Scientific Committee Meetings – face to face schedule for 2026

The EMA Secretariat presented the face-to-face and virtual meetings schedule for 2026. PRAC noted the information.

## 12.2. Coordination with EMA Scientific Committees or CMDh-v

None

[35] Update of section 4.6 of the SmPC. The package leaflet is updated accordingly

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

None

## 12.4. Cooperation within the EU regulatory network

None

## 12.5. Cooperation with International Regulators

### 12.5.1. International Conference on Harmonisation (ICH) – Additional values for E2B codelists

The EMA Secretariat presented to PRAC the proposal to extend the codelist of the 'ICH(E2B(R3) C.5.4 Study Type Where Reaction(s) / Event(s) Were Observed' field included in the ICSRs, to add three values to support the revision of ICH E2D. EMA have identified three other fields where additions of values to the codelists could enhance data collection: F.r.3.1 Test result code, G.k.10.r Drug additional type, and G.k.4.r.6b Drug administration duration unit. The PharmacoVigilance Business Team (PhVBT) and the Eudravigilance-Expert Working Group (EV-EWG) were informed and did not raise any comments. PRAC noted the information and agreed with the proposal.

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

Following the review of the comments received through the Plenary Working Party consultation and the regional regulatory consultation in May 2025, the ICH E2D(R1) Expert Working Group is ready to progress into step 4 with endorsement of the revised ICH E2D Guideline by the ICH Management Committee. PRAC was informed that no major concerns were raised in the frame of this latest round of regulatory consultation and only editorial changes have been implemented compared to the version that was presented to PRAC in May 2025 (see PRAC minutes May 2025).

Post-meeting note: PRAC endorsed the final version of the revised guideline in writing on 5 August 2025.

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

None

## 12.7. PRAC work plan

None

## 12.8. Planning and reporting

None

## 12.9. Pharmacovigilance audits and inspections

### 12.9.1. Pharmacovigilance systems and their quality systems

None

### 12.9.2. Pharmacovigilance inspections

None

### 12.9.3. Pharmacovigilance audits

None

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

### 12.10.1. Periodic safety update reports

None

### 12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Jana Lukacisinova

The EMA Secretariat provided to PRAC an update on the work of the GPAG. PRAC also appointed Petar Mas as PRAC lead for GPAG.

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

## 12.11. Signal management

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

PRAC lead: Martin Huber

The EMA Secretariat presented to PRAC an update on the activities of the SMART working group – Methods Processes, including a topic related to the results of a DARWIN EU® study which leverages a federated network of real-world data sources across Europe to generate regulatory-grade evidence estimating background incidence rates of adverse events of special interest (AESIs) related to COVID-19 and other vaccines, with potential application to future vaccine safety monitoring. In addition, PRAC was informed on plans and discussions for rolling out Artificial Intelligence (AI) solutions, including the need for infrastructure, change management, and prioritisation of projects based on their potential impact and feasibility. Finally, PRAC was informed of the upcoming in-person meeting of the group in October 2025. PRAC noted the information.

## 12.12. Adverse drug reactions reporting and additional monitoring

### 12.12.1. Specific adverse drug reaction (ADR) follow-up questionnaire (FUQ) drafting group – update on the activities

PRAC lead: Tiphaine Vaillant

The PRAC lead presented to PRAC the drafting group proposals related to the next step activities following the publication of the Specific ADR FUQ guideline, clarifying issues regarding the pregnancy FUQ, the question and answer (Q&A) tool/explanatory notes and further steps on the repository set up. PRAC noted the information and supported a further revision on the process regarding the repository.

### 12.12.2. Management and reporting of adverse reactions to medicinal products

None

### 12.12.3. Additional monitoring

None

### 12.12.4. 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. Good Pharmacovigilance Practice (GVP) Guideline on product or population specific considerations III: pregnancy and breastfeeding

PRAC lead: Ulla Wändel LimingaThe EMA Secretariat presented to PRAC the final proposal on the update of GVP Module P.III taking into consideration previously received comments via the public consultation. For further background information, refer to PRAC minutes February 2025. PRAC noted the information, and the members were asked to review and provide any final comments to the document by 10 September 2025 before its adoption by PRAC.

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

PRAC lead: Ulla Wändel LimingaThe EMA Secretariat updated PRAC on the final text as agreed in the author team and outlined the implementation of the comments received in May 2025. For further information, refer to PRAC minutes May 2025. PRAC adopted the document and the regular consultation of GVP documents with other EMA committees and the PhVIWG will follow.

### 12.21.3. Real world study to evaluate the safety of aliskiren by assessing the risk of cardiac events in patients with resistant hypertension DARWIN EU® - PRAC Sponsor's critical appraisal

PRAC lead: Amelia CupelliFollowing the conclusion on the PSUSA of aliskiren (see PRAC minutes May 2025), PRAC discussed the PRAC Sponsor's proposal of a DARWIN EU® Study 'Risk of cardiac events in users of aliskiren'. The proposed stepwise approach will include first a study to characterise users of aliskiren, including their demographics, indication of use, co-medication use prior to and following initiation, as well as presence of comorbidities. Results from the first step will inform the second step, the conduct of a self-controlled-case-series study to investigate the association of aliskiren use with cardiovascular events (including sudden death). PRAC agreed with this approach, emphasizing that the following aspects should be considered: further investigate if additional data sources can be added which have access to inpatient data, provide stratification of outcomes by gender for the association study, investigate if absolute risks can be provided based on findings from the characterisation study.

# 13. Any other business

None

# 14. Annex I – Signals assessment and prioritisation[36]

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[37].

## 14.1. New signals detected from EU spontaneous reporting systems

### 14.1.1. Bosutinib – BOSULIF (CAP); NAP

Applicant: Pfizer Europe MA EEIG (Bosulif), various

PRAC Rapporteur: Martin Huber

Scope: Signal of cutaneous vasculitis

EPITT 20184 – New signal

### 14.1.2. Datopotamab deruxtecan – DATROWAY (CAP)

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Mari Thorn

Scope: Signal of anaphylactic reaction

EPITT 20181 – New signal

### 14.1.3. Sulfasalazine (NAP)

Applicant(s): various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Signal of idiopathic intracranial hypertension (Pseudotumor cerebri)

EPITT 20188 – New signal

## 14.2. New signals detected from other sources

None

[36] 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

[37] 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

# 15. Annex I – Risk management plans

## 15.1. Medicines in the pre-authorisation phase

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

### 15.1.1. Denosumab - (CAP MAA) - EMEA/H/C/006239

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

### 15.1.2. Enzalutamide - (CAP MAA) - EMEA/H/C/006612

Scope (pre D-180 phase): Treatment of prostate cancer

### 15.1.3. Rivaroxaban - (CAP MAA) - EMEA/H/C/006643

Scope (pre D-180 phase): Prevention of atherothrombotic events

### 15.1.4. Teduglutide - (CAP MAA) - EMEA/H/C/006564

Scope (pre D-180 phase): Treatment of Short Bowel Syndrome

### 15.1.5. Ustekinumab - (CAP MAA) - EMEA/H/C/006794

Scope (pre D-210 phase): Treatment of Crohn's Disease, treatment of plaque psoriasis and paediatric plaque psoriasis, Treatment of Psoriatic arthritis (PsA)

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

Applicants: Bristol-Myers Squibb, Pfizer EEIG

PRAC Rapporteur: Bianca Mulder

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

### 15.2.2. COVID-19 mRNA vaccine – COMIRNATY (CAP) – EMA/VR/0000262269

Applicant: BioNTech Manufacturing GmbH

PRAC Lead: Liana Martirosyan

Scope: A grouped application consisting of:

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

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

### 15.2.3. Darbepoetin alfa – ARANESP (CAP) – EMA/VR/0000267359

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 10.0 in order to remove the safety concern and risk minimisation measures regarding the 'Incorrect Use of the Pre-filled Pen Device Associated with Adverse Reactions, Including Underdose and Drug Dose Omission'. The Annex II is updated accordingly.

### 15.2.4. Leflunomide – ARAVA (CAP) – EMA/VR/0000264105

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Liana Martirosyan

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

### 15.2.5. Levetiracetam – LEVETIRACETAM ACCORD (CAP) – EMA/VR/0000268045

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Jo Robays

Scope: C.I.11.z - To update Risk Management Plan (v7.0) for Levetiracetam Accord to update safety concerns in line with EPAR for Risk-management-plan of reference product Keppra (Version 10.2, dated 07-Oct-2024) published on 6 January 2025.

### 15.2.6. Odevixibat – BYLVAY (CAP); KAYFANDA (CAP) – EMA/VR/0000268240

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: C.I.11.z - to submit, for both Kayfanda and Bylvay, the consolidated version (version 7.0) of odevixibat's EU RMP combining all the approved changes from EU RMP versions 6.2 and 6.3.

### 15.2.7. Pemetrexed – ARMISARTE (CAP); NAP – EMA/VR/0000246752

Applicant: Actavis Group Ptc ehf.

PRAC Rapporteur: Tiphaine Vaillant

Scope: To update of the Risk Management Plan in order to remove the Important potential risk of 'Medication errors' in line with PRAC PSUR assessment report.

### 15.2.8. Rituximab – RIXATHON (CAP); RIXIMYO (CAP) – EMA/VR/0000249103

Applicant: Sandoz GmbH

PRAC Rapporteur: Karin Erneholm

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

### 15.2.9. Sodium zirconium cyclosilicate – LOKELMA (CAP) – EMA/VR/0000264628

Applicant: AstraZeneca AB

PRAC Rapporteur: Terhi Lehtinen

Scope: Submission of an updated RMP version 3.1 in order to include 'new onset cardiac failure' as an important potential risk.

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

Applicant: Fresenius Kabi Deutschland GmbH

PRAC Rapporteur: Karin Bolin

Scope: Quality

### 15.3.2. Aflibercept – EYLEA (CAP) – EMA/VR/0000264981

Applicant: Bayer AG

PRAC Rapporteur: Zoubida Amimour

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

C.I.6: Extension of indication to include the treatment of visual impairment due to macular oedema secondary to retinal vein occlusion (branch, central and hemiretinal RVO) for EYLEA, based on results from study 22153 (QUASAR); this is a randomized, double-masked, active-controlled Phase 3 study of the efficacy and safety of aflibercept 8 mg in macular edema secondary to retinal vein occlusion. 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 accordingly. The RMP version 36.1 has also been submitted.

C.I.4: Update of section 4.2 of the SmPC in order to change posology recommendations of the approved indications nAMD and DME based on the results from study 22153 (QUASAR) and post-hoc analysis of the pivotal studies 20968 (PULSAR), 21091 (PHOTON) and Phase II study 21086 (CANDELA).

### 15.3.3. Asciminib – SCEMBLIX (CAP) – EMA/VR/0000265010

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: A grouped application consisting of:

C.I.6.a: Extension of indication to include treatment of adult patients with newly diagnosed or previously treated Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP) for SCEMBLIX, based on primary and key secondary analysis results from study CABL001J12301 (ASC4FIRST, J12301); this is an ongoing Phase III, multi-center, open-label, randomized study of oral asciminib (80 mg once daily, q.d.) versus Investigator selected tyrosine kinase inhibitor (TKI) in patients with newly diagnosed Ph+ CML-CP, with the primary and key secondary objectives to compare the major molecular response (MMR) rates at Week 48 and Week 96, respectively. As a consequence, sections 4.1, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated accordingly. RMP version 4.0 has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection.

C.I.4: Update of sections 4.2, 4.5, 5.1, 5.2 and 5.3 of the SmPC in order to introduction of a new posology regimen based on results from studies CABL001J12301 and CABL001A2302 (ASC4OPT, A2302). CABL001A2302 is an ongoing Phase IIIb, multi-center, open-label, treatment optimization study of oral asciminib (80 mg daily, randomized to 40 mg b.i.d. or 80 mg q.d.) in patients with Ph+ CML-CP previously treated with two or more TKIs, with the primary objective to estimate the MMR rate at Week 48 of all the patients (40 mg b.i.d. and 80 mg q.d.) with no evidence of MMR at baseline. The Package Leaflet is updated accordingly. RMP version 4.0 has also been submitted.

### 15.3.4. Asciminib – SCEMBLIX (CAP) – EMA/X/0000256688

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Jirsová

Scope: Extension application to introduce a new strength (100 mg film-coated tablets) grouped with a type II variation (C.I.6.a) to add a new indication (treatment of adult patients with Philadelphia chromosome-positive chronic myeloid leukaemia in chronic phase (Ph+ CML-CP) harbouring the T315I mutation), based on final results from study CABL001X2101 and study CABL001A2004. Study CABL001X2101 is a Phase I, multicenter, open-label, dose escalation FIH study to define the MTD/RDEs, to characterize safety and tolerability, and to assess the PK profile and preliminary evidence of efficacy of asciminib given as single agent or in combination with either nilotinib or imatinib or dasatinib in patients with Ph+ CML or Ph+ ALL.

Study CABL001A2004 assessed the real-world effectiveness of asciminib and treatment patterns in patients with Chronic Myeloid Leukemia with T315I mutation. As a consequence, sections 1, 2, 3, 4, 5, 6 and 8 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 3.0 of the RMP has also been submitted. As part of the application the MAH is requesting a 1-year extension of the market protection.

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

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Bianca Mulder

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

### 15.3.6. Baricitinib – OLUMIANT (CAP) – EMA/X/0000257923

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new pharmaceutical form (oral suspension) associated with a new strength (2 mg/ml).

## 15.3.7. Budesonide – JORVEZA (CAP) – EMA/X/0000257468

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (0.2 mg/ml oral suspension). The new presentation is indicated for paediatric patients 2 to 17 years of age.

## 15.3.8. Cemiplimab – LIBTAYO (CAP) – EMA/VR/0000264999

Applicant: Regeneron Ireland Designated Activity Company

PRAC Rapporteur: Bianca Mulder

Scope: Extension of indication to include treatment of adjuvant treatment of adult patients with Cutaneous Squamous Cell Carcinoma (CSCC) at high risk of recurrence after surgery and radiation for LIBTAYO, based on interim results from study R2810-ONC-1788; this is a phase 3, randomized, placebo-controlled, double-blind study of adjuvant cemiplimab versus placebo after surgery and radiation therapy in patients with high risk CSCC;  As a consequence, sections 4.1, 4.2, 4.8, 5.1, and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.2 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the warnings for the excipients proline and polysorbate to reflect EU guidance (Section 4.4), and also updated Annex IID of the PI in line with the updates made to the RMPv4.2 to consolidate the aRMMs.

## 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. COVID-19 mRNA vaccine – SPIKEVAX (CAP) – EMA/VR/0000278795

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Quality

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

Applicant: Viatris Limited

PRAC Rapporteur: Maria del Pilar Rayon

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

## 15.3.12. Florbetaben (18F) – 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.

## 15.3.13. Fosnetupitant / Netupitant / Palonosetron – AKYNZEO (CAP) – EMA/X/0000258060

Applicant: Helsinn Birex Pharmaceuticals Limited

PRAC Rapporteur: Amelia Cupelli

Scope: Extension application to introduce a new pharmaceutical form (300 mg / 0.5 ml oral suspension).

## 15.3.14. Gadopiclenol – ELUCIREM (CAP); VUEWAY (CAP) – EMA/VR/0000249008

Applicants: Bracco Imaging S.p.A., Guerbet

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of new population (0 to 2 years of age patients) for ELUCIREM / VUEWAY, based on final results from study GDX-44-015; this is a phase ii clinical study concerning gadopiclenol pharmacokinetics, safety and efficacy in pediatric patients < 2 years of age undergoing contrast-enhanced MRI; extension of indication is also supported with the non-clinical data. 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 0.4 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to remove Annex IV from the PI. As part of the application, the MAH is requesting a 1-year extension of the market protection.

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

Applicant: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

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

C.I.13: Submission of the final report from non-clinical study 1022-9241 listed as a category 3 study in the RMP. This is a 26-Week Toxicity Study of Ganaxolone Metabolite, M2, by Oral Gavage in the Sprague-Dawley rat with a 2-Week Recovery Period. The RMP version 3 has also been submitted.
C.I.13: Submission of the final report from non-clinical study 20447815 listed as a category 3 study in the RMP. This is a An Oral (Gavage) Study of the Effects of M2 (Ganaxolone Metabolite) Administration on Embryo/Fetal Development in CD (Sprague Dawley) IGS Rat. The RMP version 3 has also been submitted.
C.I.13: Submission of the final report from Weight of Evidence (WoE) assessment to evaluate the need for a 2-year carcinogenicity study in rats with GNX, listed as a category 3 study in the RMP.
C.I.13: Submission of the final report from WoE assessment to evaluate the need for a 2-year carcinogenicity study in rats with M2, listed as a category 3 study in the RMP.
C.I.13: Submission of the final report from WoE assessment to evaluate the need for a juvenile toxicity study with M2, listed as a category 3 study in the RMP.

## 15.3.16. Ganaxolone – ZTALMY (CAP) – EMA/VR/0000263646

Applicant: Immedica Pharma AB

PRAC Rapporteur: Adam Przybylkowski

Scope: A grouped application consisting of:

C.I.4: Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from a transgenic mouse carcinogenicity study listed as a category 3 study in the RMP; this is a 26-week Oral Gavage Carcinogenicity Study of Ganaxolone in Hemizygous CByB6F1-Tg(HRAS)2Jic Mice; The RMP version 3.2 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI.

C.I.4: Update of section 5.3 of the SmPC in order to update non-clinical information based on final results from non-clinical study for juvenile toxicity in M2 (metabolite) listed as a category 3 study in the RMP; this is an Oral (Gavage) administration juvenile toxicity study of M2 (Ganaxolone Metabolite) in CD (Sprague Dawley) IGS Rats.

## 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. Herpes zoster vaccine (recombinant, adjuvanted) – SHINGRIX (CAP) – EMA/VR/0000267360

Applicant: GlaxoSmithKline Biologicals

PRAC Rapporteur: Sonja Radowan

Scope: Update of section 5.1 of the SmPC to include the final results of study ZOSTER-073, listed as a category 3 study in the RMP. This is a phase IIIB, open label, long term follow-up study to assess persistence of immune responses to GSK's HZ/su vaccine 4-7 years after primary vaccination; and immunogenicity and safety assessment of revaccination with 2 additional doses of HZ/su vaccine, administered 1-2 months apart, 6-8 years after primary vaccination of adults with renal transplant from study ZOSTER-041. The RMP version 12.0 has also been included.

### 15.3.19. Imipenem / Cilastatin / Relebactam – RECARBRIO (CAP) – EMA/VR/0000265089

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to extend the approved adult indications for RECARBRIO to include treatment of paediatric population from birth to <18 years of age, based on final results from two paediatric studies (MK-7655A-021 and MK-7655A-020); phase 2/3 study MK-7655A-021 addressed safety, tolerability, efficacy and PK, and phase 1b study MK-7655A-020 addressed PK, safety, and tolerability of MK-7655A in paediatric subjects from birth to less than 18 years of age with confirmed or suspected gram-negative infections. 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 2.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and implement minor editorial corrections.

### 15.3.20. Inotuzumab ozogamicin – BESPONSA (CAP) – EMA/VR/0000257310

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of paediatric patients 1 year and older with relapsed or refractory CD22-positive B-cell precursor acute lymphoblastic leukaemia

(ALL) for BESPONSA, based on final results from studies ITCC-059 (WI203581) and INO-Ped-ALL-1 (WI235086).

Study WI203581 is a Phase 1/2, multicenter, European, multi-cohort, open-label study in pediatric patients (≥1 and <18 years of age) with R/R CD22-positive ALL; Study WI235086 is an open-label, Phase 1 study to assess safety and tolerability of InO in Japanese pediatric patients with R/R CD22-positive AL.

As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 6.6 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet.

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

Applicant: Eli Lilly and Co (Ireland) Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment of juvenile idiopathic arthritis for TALTZ, based on week 16 results from study I1F-MC-RHCG; this is a multicenter, open-label, efficacy, safety, tolerability, and pharmacokinetic study (COSPIRIT-JIA) of subcutaneous ixekizumab with adalimumab reference arm, in children from 2 to less than 18 years of age with juvenile idiopathic arthritis subtypes of enthesitis-related arthritis (including juvenile-onset ankylosing spondylitis) and juvenile psoriatic arthritis was performed to evaluate the efficacy and safety of ixekizumab for 16 weeks after treatment initiation. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.1 of the RMP has also been submitted. Furthermore, the PI is in line with the latest QRD template version 10.4.

### 15.3.22. Leuprorelin – CAMCEVI (CAP) – EMA/X/0000258054

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Amelia Cupelli

Scope: Extension application to add a new strength of 21 mg for Leuproelin prolonged-release suspension for injection pre-filled syringe, for subcutaneous (SC) administration.

### 15.3.23. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/VR/0000265024

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

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

Type II (C.I.6): Extension of indication to include the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a Bruton’s tyrosine kinase (BTK) inhibitor for BREYANZI, based on results

from the pivotal Study 017001 MCL Cohort (TRANSCEND-NHL-001); this is a Phase 1, Multicenter, Open-Label Study of JCAR017, CD19-targeted Chimeric Antigen Receptor (CAR) T Cells, for Relapsed and Refractory (R/R) B-cell Non-Hodgkin Lymphoma (NHL). As a consequence, sections 4.1, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package leaflet is updated in accordance. Version 7.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI and to update the list of local representatives in the Package Leaflet.

## 15.3.24. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/VR/0000272242

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2, 4.4, 4.7 and 4.8 of the SmPC in order to update the post-treatment safety monitoring information based on clinical trials and real-world data. The Package leaflet section is updated in accordance. Version 8.0 of the RMP has also been submitted. In addition, the MAH the opportunity to update Annex II.

## 15.3.25. Lomitapide – LOJUXTA (CAP) – EMA/X/0000258068

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Bianca Mulder

Scope: Extension application to add a new strength of 2 mg hard capsules.

This application is grouped with

- type II variation (C.I.6.a): an Extension of Indication to include treatment of paediatric patients aged 5 years and older with homozygous familial hypercholesterolaemia (HoFH) for LOJUXTA, based on final results from the pivotal paediatric study APH-19; this is a phase 3, single-arm, open-label, international, multi-centre study to evaluate the efficacy and safety of lomitapide in paediatric patients with homozygous familial hypercholesterolaemia (HOFH) on stable lipid-lowering therapy. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The Annex II and Package Leaflet are updated accordingly. The RMP version 7.1 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.

- 3 x type IB variations (C.I.7.b): to delete the 30 mg, 40 mg and 60 mg strengths from the Lojuxta marketing authorisation (EU/1/13/851/004 - 006).

## 15.3.26. Maralixibat - LIVMARLI (CAP) - EMEA/H/C/005857/X/0015, Orphan

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new pharmaceutical form (tablet) associated

with new strengths 10 mg, 15mg, 20 mg and 30 mg.
The RMP (version 5.0) is updated in accordance.

## 15.3.27. Methylthioninium chloride – METHYLTHIONINIUM CHLORIDE PROVEBLUE (CAP) – EMA/VR/0000265559

Applicant: Provepharm

PRAC Rapporteur: Karin Bolin

Scope: Submission of the final report from study PVP-2016005; this is an Open-label, Parallel group, Population-matched, Single-Dose Study to Investigate the Influence of Hepatic Impairment on the Pharmacokinetics and safety of ProvayBlue (methylene blue). The RMP version 3.4 has also been submitted.

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

Applicant: Agios Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

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

## 15.3.29. 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.

## 15.3.30. Ponatinib – ICLUSIG (CAP) – EMA/VR/0000263550

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of adult patients with newly-diagnosed Ph+ ALL for ICLUSIG, based on interim results from study Ponatinib-3001 (PhALLCON); this is a phase 3, randomized, open-label, multicenter study comparing ponatinib versus imatinib, administered in combination with reduced intensity chemotherapy, in patients with newly diagnosed Ph+ ALL; supportive data were derived from two single-arm, open-label clinical studies (AP24534 11 001 in combination with chemotherapy and INCB 84344-201 as monotherapy). 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 23.2 of the RMP has also been submitted. In addition, earlier approved updates were incorporated to the PI.

## 15.3.31. Posaconazole – NOXAFIL (CAP) – EMA/VR/0000263360

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Extension of indication for NOXAFIL to include treatment of patients two years of age and older for invasive aspergillosis (IA) based on final results from study MK-5592-104 (P104); this is a Phase 2, open-label, noncomparative clinical study that evaluated the safety, efficacy, and PK of POS in pediatric participants aged 2 to <18 years with IA. 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 18.1 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement editorial changes to the PI.

## 15.3.32. Ranibizumab – RIMMYRAH (CAP) – EMA/VR/0000246182

Applicant: QILU Pharma Spain S.L.

PRAC Rapporteur: Karin Bolin

Scope: Quality

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

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

Scope: To modify the approved therapeutic indication to include active immunisation for the prevention of lower respiratory tract disease (LRTD) caused by Respiratory Syncytial Virus in individuals 18 through 59 years of age who are at increased risk for LRTD caused by RSV for

mRESVIA, based on results from Study mRNA-1345-P303 (Part A) - A Phase 3 Study to Evaluate the Immunogenicity and Safety of mRNA-1345, an mRNA Vaccine Targeting Respiratory Syncytial Virus, in High-risk Adults. As a consequence, sections 4.1, 4.6, 4.8 and 5.1 of the SmPC and the corresponding sections of the Package Leaflet are updated accordingly. The updated RMP Version 1.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the PI. As part of the application, the MAH also requests an extension of the market protection by one additional year.

## 15.3.34. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – MRESVIA (CAP) – EMA/VR/0000263124

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

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

C.I.4: Update of section 4.5 of the SmPC in order to add drug-drug interaction information of co-administration of mRESVIA (mRNA-1345) dispersion for injection, in its all-registered presentations, with a Standard dose, Seasonal Influenza Vaccine, based on data forthcoming from mRNA-1345-P302 part A clinical study. It is a Phase 3 study to evaluate safety and immunogenicity of mRNA-1345 for RSV when given alone or co-administered with a Seasonal Influenza vaccine or COVID-19 vaccine. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted.

C.I.4: Update of section 4.5 of the SmPC in order to add drug-drug interaction information of co-administration of mRESVIA (mRNA-1345) dispersion for injection, in its all-registered presentations, with COVID-19 Vaccine, based on data forthcoming from mRNA-1345-P302 part B clinical study. It is a Phase 3 study to evaluate safety and immunogenicity of mRNA-1345 for RSV when given alone or co- administered with a Seasonal Influenza vaccine or COVID-19 vaccine. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted.

C.I.4: Update of section 4.5 of the SmPC in order to add drug-drug interaction information of co-administration of mRESVIA (mRNA 1345) dispersion for injection, in its all-registered presentations, with a High-dose, Quadrivalent Seasonal Influenza vaccine in Adults ≥65 Years of Age, based on data forthcoming from mRNA-1345-P304 clinical study. It is a Phase 3 Study to evaluate the safety and immune response of mRNA-1345, when co-administered with a High-dose, Quadrivalent Seasonal Influenza vaccine. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted.

## 15.3.35. Rurioctocog alfa pegol – ADYNOVI (CAP) – EMA/VR/0000268348

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Update of sections 4.2, 4.4, 4.8, 5.1, and 5.2 of the SmPC in order to update clinical pharmacokinetic, efficacy, and safety information based on final results from study 261203, listed as a category 3 study in the RMP; this is a phase 3, prospective, multi-center, open

label study to investigate safety, immunogenicity, and hemostatic efficacy of PEGylated Factor VIII (BAX 855) in previously untreated patients (PUPs); the Package Leaflet is updated accordingly. The RMP version 5.0 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to introduce editorial changes, and to bring the PI in line with the latest QRD template.

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

Applicant: Atnahs Pharma Netherlands B.V.

PRAC Rapporteur: Julia Pallos

Scope: Update of sections 4.6 and 5.2 of the SmPC in order to update information on lactation and breastfeeding based on results from the post-marketing lactation study JZP110-401 listed as a category 3 study in the RMP. This was a Phase 4, open-label, single-dose study to evaluate the PK of solriamfetol in the breast milk and plasma of healthy postpartum women following oral administration of a 150 mg solriamfetol tablet. The Package Leaflet is updated accordingly. The RMP version 1.3 has also been submitted.

## 15.3.37. Secukinumab – COSENTYX (CAP) – EMA/VR/0000267996

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Monica Martinez Redondo

Scope: Submission of the final report from study CAIN457F2304E1, listed as a category 3 study in the RMP. This is a phase 3, long-term, open-label, efficacy, safety and tolerability in JPsA and ERA subtypes of JIA up to 4 years in patients with active JPsA and ERA subtypes of JIA and who completed the Phase III study CAIN457F2304. The RMP version 12.0 has also been submitted.

## 15.3.38. Somapacitan – SOGROYA (CAP) – EMA/VR/0000264734

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Grouped extension of indication application to include treatment of children born small for gestational age (SGA), Noonan syndrome (NS) and idiopathic short stature (ISS) for SOGROYA, based on interim results from the pivotal, confirmatory phase 3 study NN8640-4467 supported by the phase 3 study NN8640-4469 and the phase 2 study NN8640-4245. Study 4467 is a study comparing the effect and safety of once weekly dosing of somapacitan with daily Norditropin as well as evaluating long-term safety of somapacitan in a basket study design in children with short stature either born small for gestational age or with Turner syndrome, Noonan syndrome, or idiopathic short stature. Study 4469 is a study evaluating the safety and efficacy of once-weekly dosing of somapacitan in a basket study design in paediatric participants with short stature either born small for gestational age or with turner syndrome, Noonan syndrome or idiopathic short stature. Study 4245 is a dose-finding trial evaluating the effect and safety of once-weekly treatment of somapacitan

compared to daily Norditropin in children with short stature born small for gestational age with no catch-up growth by 2 years of age or older. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 4.0 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template version 10.4. As part of the application, the MAH is requesting a 1-year extension of the market protection.

## 15.3.39. Sonidegib – ODOMZO (CAP) – EMA/VR/0000268112

Applicant: Sun Pharmaceutical Industries (Europe) B.V.

PRAC Rapporteur: Petar Mas

Scope: Update of sections 5.3, and 6.6 of the SmPC in order to update non-clinical safety information on carcinogenicity based on final results from studies 8371102, and BRT_17_037G_TN; this is a 26-Week Oral Gavage Carcinogenicity Study with LDE225 in Transgenic Mice (RasH2 [001178-T (hemizigous), CByB6F1-Tg(HRAS)2Jic]), and a 104-Week Carcinogenicity Study of LDE225 in Wistar Rats by Oral Route, respectively. Sections 5.3 and 6.6 of the SmPC were also updated to include a statement on risk to the environment in line with the commitment following EMEA/H/C/002839/IB/0056. The RMP version 8.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to introduce editorial changes, and to bring the PI in line with the latest QRD template.

## 15.3.40. Sugemalimab – CEJEMLY (CAP) – EMA/VR/0000261157

Applicant: Cstone Pharmaceuticals Ireland Limited

PRAC Rapporteur: Petar Mas

Scope: Extension of indication to include the treatment of unresectable stage III non-small-cell lung cancer (NSCLC) with no sensitising EGFR mutations, or ALK, ROS1 genomic tumour aberrations in adults whose disease has not progressed following concurrent or sequential platinum-based chemoradiotherapy for CEJEMLY, based on final results from study CS1001-301; this is a Phase III, multicentre, randomised, double-blind, placebo-controlled study assessing the efficacy and safety of sugemalimab as consolidation therapy versus placebo in participants with locally advanced or unresectable stage III NSCLC who have not progressed after concurrent or sequential chemoradiotherapy. 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 2.0 of the RMP has also been submitted.

## 15.3.41. Talquetamab – TALVEY (CAP) – EMA/VR/0000264615

Applicant: Janssen Cilag International

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Submission of the interim report from study 64407564MMY1001 listed as a Specific Obligation in the Annex II of the Product Information. This is a phase 1/2, first-in-human, open-label, dose escalation study of talquetamab, a humanized GPRC5D x CD3 bispecific antibody, in subjects with relapsed or refractory multiple myeloma. Safety data were revised based on the 2-year follow-up analysis for the pivotal RP2D population The Annex II and the RMP version 3.2 are updated accordingly.

## 15.3.42. Tasimelteon - HETLIOZ (CAP) - EMEA/H/C/003870/X/0039, Orphan

Applicant: Vanda Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new pharmaceutical form associated with new strength (4 mg/ml oral solution). The new formulation is indicated for the treatment of night time sleep disturbances in Smith-Magenis Syndrome (SMS) in paediatric patients 3 to 15 years of age. The RMP (version 5.0) is updated in accordance.

## 15.3.43. 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.

## 15.3.44. Tezepelumab – TEZSPIRE (CAP) – EMA/VR/0000262075

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

Scope: Submission of the final report from study D5180C00021 listed as a category 3 study in the RMP. This is a Regional, Multicentre, Randomized, Double-Blind, Placebo Controlled, Parallel Group, Phase 3 Study to Evaluate the Efficacy and Safety of Tezepelumab in Adults with Severe Uncontrolled Asthma (DIRECTION). The RMP version 5 has also been submitted.

## 15.3.45. Tislelizumab – TEVIMBRA (CAP) – EMA/VR/0000269879

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: A grouped application consisting of:

C.I.4: Update of sections 4.2, 5.1, 5.2, and 6.6 of the SmPC in order to introduce an alternative dosing regimen of 400 mg every 6 weeks (Q6W) based on POP-PK and exposure-response analyses, and observed clinical data, and update safety information based on data collected in studies BGB-A317-315 and BGB-A317-212 (400 mg Q6W), and study BGB-A317-001; the Package Leaflet is updated accordingly. The RMP version 4.1 has also been submitted.

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

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

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

## 15.3.47. 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.

## 15.3.48. Vonicog alfa – VEYVONDI (CAP) – EMA/VR/0000264863

Applicant: BAXALTA INNOVATIONS GmbH

PRAC Rapporteur: Mari Thorn

Scope: Extension of indication to include treatment of haemorrhage in children aged less than 18 years for VEYVONDI, based on results from studies 071102 and SHP677-304. Study 071102 is a phase 3, prospective, multicenter, uncontrolled, open-label clinical study to

determine the efficacy, safety, and tolerability of rVWF with or without ADVATE in the treatment and control of bleeding episodes, the efficacy and safety of rVWF in elective and emergency surgeries, and the pharmacokinetics (PK) of rVWF in children diagnosed with severe VWD; study SHP677-304 is a phase 3B, prospective, open-label, uncontrolled, multicenter study on long term safety and efficacy of vonicog alfa in pediatric and adult subjects with severe VWD.

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 accordingly. Version 6.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.4, to update the PI in accordance with the latest EMA excipients guideline, and to implement editorial changes to the PI.

# 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. Adagrasib – KRAZATI (CAP) – EMA/PSUR/0000257790

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00000214/202412)

### 16.1.2. Arpraziquantel - ARPRAZIQUANTEL (Art 58) - EMEA/H/W/004252/PSUV/0004

Applicant: Merck Europe B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUR procedure

### 16.1.3. Atidarsagene autotemcel – LIBMELDY (CAP) – EMA/PSUR/0000257860

Applicant: Orchard Therapeutics (Netherlands) B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010899/202412)

### 16.1.4. Berotralstat – ORLADEYO (CAP) – EMA/PSUR/0000257866

Applicant: Biocryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure (PSUSA/00010930/202412)

### 16.1.5. Bevacizumab gamma – LYTENAVA (CAP) – EMA/PSUR/0000257885

Applicant: Outlook Therapeutics Limited

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00011065/202411)

### 16.1.6. Budesonide – KINPEYGO (CAP) – EMA/PSUR/0000257894

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011007/202412)

### 16.1.7. Buprenorphine – SIXMO (CAP) – EMA/PSUR/0000257873

Applicant: L. Molteni & C. Dei Fratelli Alitti Societa' Di Esercizio S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00010778/202411)

### 16.1.8. COVID-19 mRNA vaccine – COMIRNATY (CAP) – EMA/PSUR/0000257861

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00010898/202412)

### 16.1.9. COVID-19 mRNA vaccine – SPIKEVAX (CAP) – EMA/PSUR/0000257883

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010897/202412)

### 16.1.10. COVID-19 vaccine (recombinant, adjuvanted) – NUVAXOVID (CAP) – EMA/PSUR/0000257887

Applicant: Novavax CZ a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010972/202412)

### 16.1.11. Cabozantinib – CABOMETYX (CAP); COMETRIQ (CAP) – EMA/PSUR/0000257853

Applicant: Ipsen Pharma

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010180/202411)

### 16.1.12. Cefepime / Enmetazobactam – EXBLIFEP (CAP) – EMA/PSUR/0000257800

Applicant: Advanz Pharma Limited

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000305/202412)

### 16.1.13. Dantrolene sodium hemiheptahydrate – AGILUS (CAP) – EMA/PSUR/0000257902

Applicant: Norgine B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00011063/202411)

### 16.1.14. Daratumumab – DARZALEX (CAP) – EMA/PSUR/0000257879

Applicant: Janssen Cilag International

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010498/202411)

### 16.1.15. Dopamine hydrochloride – NEOATRICON (CAP) – EMA/PSUR/0000257893

Applicant: BrePco Biopharma Limited

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure (PSUSA/00011066/202411)

### 16.1.16. Efgartigimod alfa – VYVGART (CAP) – EMA/PSUR/0000257895

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00011014/202412)

### 16.1.17. Elacestrant – ORSERDU (CAP) – EMA/PSUR/0000257797

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Sonja Radowan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000120/202412)

### 16.1.18. Eladocagene exuparvovec – UPSTAZA (CAP) – EMA/PSUR/0000257869

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00011004/202412)

### 16.1.19. Elafibranor – IQIRVO (CAP) – EMA/PSUR/0000257878

Applicant: Ipsen Pharma

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00011092/202412)

### 16.1.20. Elotuzumab – EMPLICITI (CAP) – EMA/PSUR/0000257854

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010500/202411)

## 16.1.21. Entrectinib – ROZLYTREK (CAP) – EMA/PSUR/0000257876

Applicant: Roche Registration GmbH

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00010874/202412)

## 16.1.22. Etelcalcetide – PARSABIV (CAP) – EMA/PSUR/0000257856

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010533/202411)

## 16.1.23. Ethinylestradiol / Norelgestromin – EVRA (CAP) – EMA/PSUR/0000257812

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001311/202411)

## 16.1.24. Fidanacogene elaparvovec – BEQVEZ (SRD[38]) – EMA/PSUR/0000257889

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00011079/202412)

## 16.1.25. Flortaucipir ($^{18}$F) – TAUVID (CAP) – EMA/PSUR/0000257881

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011073/202411)

## 16.1.26. Fondaparinux sodium – ARIXTRA (CAP) – EMA/PSUR/0000257813

Applicant: Viatris Healthcare Limited

PRAC Rapporteur: Mari Thorn

[38] European Commission implementing decision for the withdrawal of Beqvez (fidanacogene elaparvovec), at the holder's request: 15 May 2025

Scope: Evaluation of a PSUSA procedure (PSUSA/00001467/202412)

### 16.1.27. Formoterol / Glycopyrronium bromide / Budesonide – RILTRAVA AEROSPHERE (CAP); TRIXEO AEROSPHERE (CAP) – EMA/PSUR/0000257877

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure (PSUSA/00010908/202412)

### 16.1.28. Inclisiran – LEQVIO (CAP) – EMA/PSUR/0000257862

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010904/202412)

### 16.1.29. Inebilizumab – UPLIZNA (CAP) – EMA/PSUR/0000257868

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010996/202412)

### 16.1.30. Inotuzumab ozogamicin – BESPONSA (CAP) – EMA/PSUR/0000257859

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00010659/202412)

### 16.1.31. Iptacopan – FABHALTA (CAP) – EMA/PSUR/0000257901

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Lina Seibokiene

Scope: Evaluation of a PSUSA procedure (PSUSA/00011054/202412)

### 16.1.32. Iron – VELPHORO (CAP) – EMA/PSUR/0000257848

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010296/202411)

### 16.1.33. Ketoconazole – KETOCONAZOLE ESTEVE (CAP) – EMA/PSUR/0000257850

Applicant: Esteve Pharmaceuticals S.A.

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00010316/202411)

### 16.1.34. Lamivudine - EPIVIR (CAP); Lamivudine / Zidovudine - COMBIVIR (CAP) – EMA/PSUR/0000257847

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00009207/202411)

### 16.1.35. Larotrectinib – VITRAKVI (CAP) – EMA/PSUR/0000257875

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure (PSUSA/00010799/202411)

### 16.1.36. Levodopa – INBRIJA (CAP) – EMA/PSUR/0000257892

Applicant: Acorda Therapeutics Ireland Limited

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Evaluation of a PSUSA procedure (PSUSA/00107800/202412)

### 16.1.37. Maribavir – LIVTENCITY (CAP) – EMA/PSUR/0000257897

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00011024/202411)

### 16.1.38. Mosunetuzumab – LUNSUMIO (CAP) – EMA/PSUR/0000257870

Applicant: Roche Registration GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure (PSUSA/00010999/202412)

### 16.1.39. Nirmatrelvir / Ritonavir – PAXLOVID (CAP) – EMA/PSUR/0000257871

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00010984/202412)

### 16.1.40. Octreotide – MYCAPSSA (SRD[39])– EMA/PSUR/0000257899

Applicant: Amryt Pharmaceuticals Designated Activity Company

PRAC Rapporteur: Eamon O Murchu

Scope: Evaluation of a PSUSA procedure (PSUSA/00011036/202412)

### 16.1.41. Olaparib – LYNPARZA (CAP) – EMA/PSUR/0000257846

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010322/202412)

### 16.1.42. Piflufolastat ($^{18}$F) – PYLCLARI (CAP) – EMA/PSUR/0000257788

Applicant: Curium Pet France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00000097/202411)

### 16.1.43. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) – PREVENAR 20 (CAP) – EMA/PSUR/0000257867

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00010981/202412)

[39] European Commission implementing decision for the withdrawal of Mycapssa (octreotide), at the holder's request: 27 February 2025

## 16.1.44. Quizartinib – VANFLYTA (CAP) – EMA/PSUR/0000257791

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00000176/202412)

## 16.1.45. Respiratory syncytial virus mRNA vaccine (nucleoside modified) – MRESVIA (CAP) – EMA/PSUR/0000257880

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00011075/202411)

## 16.1.46. Respiratory syncytial virus vaccine (bivalent, recombinant) – ABRYSVO (CAP) – EMA/PSUR/0000257789

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000102/202411)

## 16.1.47. Ritlecitinib – LITFULO (CAP) – EMA/PSUR/0000257795

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00000133/202412)

## 16.1.48. Rozanolixizumab – RYSTIGGO (CAP) – EMA/PSUR/0000257792

Applicant: UCB Pharma

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure (PSUSA/00000216/202412)

## 16.1.49. Setmelanotide – IMCIVREE (CAP) – EMA/PSUR/0000257865

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00010941/202411)

### 16.1.50. Sofosbuvir – SOVALDI (CAP) – EMA/PSUR/0000257852

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00010134/202412)

### 16.1.51. Sotorasib – LUMYKRAS (CAP) – EMA/PSUR/0000257886

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure (PSUSA/00010970/202411)

### 16.1.52. Sugemalimab – CEJEMLY (CAP) – EMA/PSUR/0000257890

Applicant: Cstone Pharmaceuticals Ireland Limited

PRAC Rapporteur: Petar Mas

Scope: Evaluation of a PSUSA procedure (PSUSA/00011080/202412)

### 16.1.53. Tabelecleucel – EBVALLO (CAP) – EMA/PSUR/0000257898

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00011028/202412)

### 16.1.54. Tenofovir alafenamide – VEMLIDY (CAP) – EMA/PSUR/0000257857

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010575/202411)

### 16.1.55. Tezepelumab – TEZSPIRE (CAP) – EMA/PSUR/0000257896

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00011015/202412)

## 16.1.56. Thyrotropin alfa – THYROGEN (CAP) – EMA/PSUR/0000257839

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00002940/202411)

## 16.1.57. Tirbanibulin – KLISYRI (CAP) – EMA/PSUR/0000257888

Applicant: Almirall S.A.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00010943/202412)

## 16.1.58. Tislelizumab – TEVIMBRA (CAP) – EMA/PSUR/0000257798

Applicant: Beone Medicines Ireland Limited

PRAC Rapporteur: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00000136/202412)

## 16.1.59. Toripalimab – LOQTORZI (CAP) – EMA/PSUR/0000257891

Applicant: Topalliance Biosciences Europe Limited

PRAC Rapporteur: Karin Erneholm

Scope: Evaluation of a PSUSA procedure (PSUSA/00011094/202412)

## 16.1.60. Tralokinumab – ADTRALZA (CAP) – EMA/PSUR/0000257863

Applicant: LEO PHARMA A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure (PSUSA/00010937/202412)

## 16.1.61. Trastuzumab deruxtecan – ENHERTU (CAP) – EMA/PSUR/0000257882

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00010894/202412)

### 16.1.62. Ublituximab – BRIUMVI (CAP) – EMA/PSUR/0000257796

Applicant: Neuraxpharm Pharmaceuticals S.L.

PRAC Rapporteur: Liana Martirosyan

Scope: Evaluation of a PSUSA procedure (PSUSA/00000045/202412)

### 16.1.63. Vadadustat – VAFSEO (CAP) – EMA/PSUR/0000257900

Applicant: Medice Arzneimittel Puetter GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00011050/202412)

### 16.1.64. Venetoclax – VENCLYXTO (CAP) – EMA/PSUR/0000257855

Applicant: Abbvie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure (PSUSA/00010556/202412)

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

### 16.2.1. Sufentanil – DZUVEO (CAP); NAP – EMA/PSUR/0000257838

Applicants: Laboratoire Aguettant, various

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00002798/202411)

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

### 16.3.1. Acrivastine , acrivastine / pseudoephedrine (NAP) – EMA/PSUR/0000257787

Applicant(s): various

PRAC Lead: Terhi Lehtinen

Scope: Evaluation of a PSUSA procedure (PSUSA/00000054/202412)

### 16.3.2. Antazoline / tetryzoline (NAP) – EMA/PSUR/0000257793

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00000219/202412)

### 16.3.3. Ceftobiprole (NAP) – EMA/PSUR/0000257858

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00010734/202411)

### 16.3.4. Chlorphenamine / dextromethorphan hydrobromide / paracetamol (NAP) – EMA/PSUR/0000257817

Applicant(s): various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure (PSUSA/00000699/202411)

### 16.3.5. Cinolazepam (NAP) – EMA/PSUR/0000257808

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00000769/202412)

### 16.3.6. Clotrimazole / dexamethasone (NAP) – EMA/PSUR/0000257805

Applicant(s): various

PRAC Lead: Carla Torre

Scope: Evaluation of a PSUSA procedure (PSUSA/00000830/202411)

### 16.3.7. Clotrimazole / hydrocortisone (NAP) – EMA/PSUR/0000257806

Applicant(s): various

PRAC Lead: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure (PSUSA/00000831/202411)

### 16.3.8. Clotrimazole / metronidazole (NAP) – EMA/PSUR/0000257815

Applicant(s): various

PRAC Lead: Roxana Dondera

Scope: Evaluation of a PSUSA procedure (PSUSA/00000832/202411)

### 16.3.9. Cyanocobalamin / folic acid / pyridoxine (NAP) – EMA/PSUR/0000257803

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure (PSUSA/00000893/202411)

### 16.3.10. Dermatan sulfate (NAP) – EMA/PSUR/0000257818

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00000957/202411)

### 16.3.11. Dextromethorphan / paracetamol / phenylephrine (NAP) – EMA/PSUR/0000257849

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00009247/202411)

### 16.3.12. Dextromethorphan hydrobromide / diphenhydramine hydrochloride / levomenthol (NAP) – EMA/PSUR/0000257802

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00001013/202411)

## 16.3.13. Dextromethorphan hydrobromide / paracetamol / promethazine hydrochloride (NAP) – EMA/PSUR/0000257833

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00002300/202411)

## 16.3.14. Dextromethorphan hydrobromide / pseudoephedrine hydrochloride / triprolidine hydrochloride (NAP) – EMA/PSUR/0000257809

Applicant(s): various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure (PSUSA/00001021/202411)

## 16.3.15. Dihydroxyaluminum sodium carbonate, dihydroxyaluminum sodium carbonate / dimeticone (NAP) – EMA/PSUR/0000257816

Applicant(s): various

PRAC Lead: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure (PSUSA/00001098/202411)

## 16.3.16. Drospirenone / estradiol (NAP) – EMA/PSUR/0000257811

Applicant(s): various

PRAC Lead: Bianca Mulder

Scope: Evaluation of a PSUSA procedure (PSUSA/00001184/202412)

## 16.3.17. Estradiol (17-beta) / progesterone (NAP) – EMA/PSUR/0000257845

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00009145/202412)

## 16.3.18. Human coagulation factor VIII (antihemophilic factor A) (NAP) – EMA/PSUR/0000257822

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure (PSUSA/00001620/202411)

## 16.3.19. Ketamine (NAP) – EMA/PSUR/0000257820

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure (PSUSA/00001804/202412)

## 16.3.20. Lornoxicam (NAP) – EMA/PSUR/0000257821

Applicant(s): various

PRAC Lead: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure (PSUSA/00001911/202412)

## 16.3.21. Metamizole sodium / pitofenone hydrochloride (NAP) – EMA/PSUR/0000257834

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure (PSUSA/00002443/202412)

## 16.3.22. Metoclopramide (NAP) - EMA/PSUR/0000257825

Applicant(s): various

PRAC Lead: Pernille Harg

Scope: Evaluation of a PSUSA procedure (PSUSA/00002036/202411)

## 16.3.23. Mexazolam (NAP) – EMA/PSUR/0000257830

Applicant(s): various

PRAC Lead: John Joseph Borg

Scope: Evaluation of a PSUSA procedure (PSUSA/00002047/202412)

## 16.3.24. Natamycin (NAP) – EMA/PSUR/0000257843

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure (PSUSA/00003179/202411)

## 16.3.25. Neomycin sulfate / nystatin / polymyxin b sulfate (NAP) – EMA/PSUR/0000257827

Applicant(s): various

PRAC Lead: Zoubida Amimour

Scope: Evaluation of a PSUSA procedure (PSUSA/00002139/202411)

## 16.3.26. Oxygen (NAP) – EMA/PSUR/0000257829

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00002257/202412)

## 16.3.27. Paracetamol / pseudoephedrine hydrochloride / triprolidine hydrochloride (NAP) – EMA/PSUR/0000257840

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure (PSUSA/00010270/202411)

## 16.3.28. Tibolone (NAP) – EMA/PSUR/0000257844

Applicant(s): various

PRAC Lead: Karin Bolin

Scope: Evaluation of a PSUSA procedure (PSUSA/00002947/202412)

## 16.3.29. Undecylenic acid (NAP) – EMA/PSUR/0000257842

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure (PSUSA/00003076/202411)

### 16.3.30. Urea hydrogen peroxide (NAP) – EMA/PSUR/0000257851

Applicant(s): various

PRAC Lead: Melinda Palfi

Scope: Evaluation of a PSUSA procedure (PSUSA/00009326/202411)

## 16.4. Follow-up to PSUR/PSUSA procedures

### 16.4.1. Dapagliflozin – FORXIGA (CAP) – EMA/PAM/0000278022

Applicant: AstraZeneca AB

PRAC Rapporteur: Mari Thorn

Scope: Follow-up LEG (from EMEA/H/C/PSUSA/00010029/202410): Review of all cases related to the potential association between dapagliflozin exposure and Drug reaction with eosinophilia and systemic symptoms (DRESS)

### 16.4.2. Dolutegravir – TIVICAY (CAP) – EMA/PAM/0000268716

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Responses to request for supplementary information on PAM/LEG submission for Tivicay, Dovato, Triumeq regarding diabetes and hypertension evaluation.

### 16.4.3. Dolutegravir / Abacavir / Lamivudine - TRIUMEQ (CAP) – EMA/PAM/0000268721

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Responses to request for supplementary information on PAM/LEG submission for Tivicay, Dovato, Triumeq regarding diabetes and hypertension evaluation.

### 16.4.4. Dolutegravir / Lamivudine - DOVATO (CAP) – EMA/PAM/0000268725

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: David Olsen

Scope: Responses to request for supplementary information on PAM/LEG submission for Tivicay, Dovato, Triumeq regarding diabetes and hypertension evaluation.

## 16.5. Variation procedure(s) resulting from PSUSA evaluation

None

## 16.6. Expedited summary safety reviews[40]

None

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

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

## 17.1. Protocols of PASS imposed in the marketing authorisation(s)[41]

### 17.1.1. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/PASS/0000269320

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: PASS amendment [107o]: Substantial amendment to a protocol for a non-interventional PASS of patients treated with commercially available liso-cel (lisocabtagene maraleucel) for relapsed/refractory diffuse large B-cell lymphoma, primary mediastinal B-cell lymphoma, and follicular lymphoma Grade 3B after 2 or more lines of systemic therapy in the postmarketing setting

### 17.1.2. Teduglutide – REVESTIVE (CAP) – EMA/PASS/0000269314

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: PASS amendment [107o]: Substantial amendment to a prospective, multi-center registry for patients with Short Bowel Syndrome (TED-R13-002)

### 17.1.3. Valproate (NAP) and related substances[42] – EMA/PASS/0000272975

Applicant: Sanofi S.r.l. (on behalf of a consortium)

PRAC Rapporteur: Liana Martirosyan

[40] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC
[41] In accordance with Article 107n of Directive 2001/83/EC
[42] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpromide, valproate bismuth, calcium valproate, valproate magnesium

Scope: Valproate PASS protocol (107n): MAH's response to EMEA/H/N/PSP/J/0108.1 [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 RSI adopted in Oct 2024.]

## 17.2. Protocols of PASS non-imposed in the marketing authorisation(s)[43]

### 17.2.1. Cannabidiol - EPIDYOLEX (CAP) – EMA/PAM/0000269446

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: PASS GWEP21042: Proposal for change in data collection. A Prospective, Observational Cohort Study to Assess Long-Term Safety in Patients Prescribed Epidyolex with a Focus on Drug-induced Liver Injury (DILI).

### 17.2.2. Efgartigimod alfa – VYVGART (CAP) – EMA/PAM/0000268754

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Revised protocol for PASS: Evaluation of long-term risk of malignancies in patients with myasthenia gravis (MG) treated with efgartigimod compared to MG patients on any other MG therapy and who do not have malignancy history in the lookback period.

### 17.2.3. Exagamglogene autotemcel - CASGEVY (CAP) – EMA/PAM/0000268688

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Bianca Mulder

Scope: On 7 April 2025, the MAH submitted responses to the PRAC Rapporteur's requests and an updated study protocol (version 3.0) of study Healthcare Professional Survey (HCP) to Assess the Effectiveness of the Additional Risk Minimization Measures (aRMM) for Casgevy® (exagamglogene autotemcel)

### 17.2.4. Fenfluramine – FINTEPLA (CAP) – EMA/PAM/0000268726

Applicant: UCB Pharma

PRAC Rapporteur: Martin Huber

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

Scope: PASS EP0219 (former ZX008-2102) protocol: A Drug Utilisation Study of Fenfluramine In Europe (DUS).

### 17.2.5. Garadacimab – ANDEMBRY (CAP) – EMA/PAM/0000267718

Applicant: CSL Behring GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Feasibility and protocol assessment of the Non-Interventional Post Authorisation Safety Study CSL312_5006 to assess the long-term safety in adults and adolescents.

### 17.2.6. Golimumab – SIMPONI (CAP) – EMA/PAM/0000268768

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. Lebrikizumab – EBGLYSS (CAP) – EMA/PAM/0000267190

Applicant: Almirall S.A.

PRAC Rapporteur: Liana Martirosyan

Scope: Protocol for PASS J2T-MC-B003: an Observational Database Study of Pregnancy and Infant Outcomes among Women Exposed to Lebrikizumab During Pregnancy

### 17.2.8. Linzagolix choline – YSELTY (CAP) – EMA/PAM/0000268672

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Protocol amendment (version 0.6): a multinational PASS on real-world treatment in patients receiving YSELTY (linzagolix choline) for moderate to severe symptoms of uterine fibroids, to evaluate routinely collected data on bone mineral density and to assess safety during long term (>12 months) use for linzagolix 200mg (with ABT) and 100mg (with and without ABT) dosing regimen. This is study DAISY (Bone Mineral Density Appraisal and other Important long-term Safety endpoints of Yselty).

### 17.2.9. Mogamulizumab – POTELIGEO (CAP) – EMA/PAM/0000264422

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Post-authorisation safety study (PASS) of allogeneic haematopoietic cell transplantation in patients treated with mogamulizumab (Poteligeo)".- observational CIBMTR cohort to collect real-world data with the aim to evaluate non-relapse mortality (NRM) and toxicities in patients with cutaneous T-cell lymphoma (CTCL) or adult T-cell leukemia/lymphoma (ATLL) treated with mogamulizumab pre- or post- allogeneic hematopoietic cell transplantation (alloHCT)

### 17.2.10. Nemolizumab - NEMLUVIO (CAP) – EMA/PAM/0000269409

Applicant: Galderma International

PRAC Rapporteur: Liana Martirosyan

Scope: First study protocol for a non-imposed non-interventional PASS to evaluate fetal and infant outcomes following maternal exposure to nemolizumab for treatment of moderate to severe AD or PN during pregnancy.

### 17.2.11. Rimegepant – VYDURA (CAP) – EMA/PAM/0000267777

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the fourth annual interim report of category 3 PASS C4951006
Responses to RSI raised in the EMEA/H/C/005725/MEA/002.3
An updated study protocol version 7.0

### 17.2.12. Rimegepant – VYDURA (CAP) – EMA/PAM/0000267781

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Karin Erneholm

Scope: Submission of the fourth annual interim report of category 3 PASS C4951005, including an updated study protocol version 6.0.

### 17.2.13. Ustekinumab – STELARA (CAP) – EMA/PAM/0000264394

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Updated Study Protocol (PCSIMM002807, Version 7.0, Amendment 2); SWIBREG - An Observational Postauthorization Safety Study to Describe The Safety of Ustekinumab and

Other Biologic Treatments in a Cohort of Patients With Ulcerative Colitis or Crohn's Disease Using Compulsory Swedish Nationwide Healthcare Registers and the Independent Swedish National Quality Register for Inflammatory Bowel Disease. Response to Issues adopted by CHMP on 30 January 2025 for MEA 047.5

### 17.2.14. Ustekinumab – STELARA (CAP) – EMA/PAM/0000264398

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Second Progress Report and updated study protocol (Version 6.0, Amendment 2) for An Observational Post-authorization Safety Study to Describe the Safety of Ustekinumab and Other Treatments of Ulcerative Colitis in a Cohort of Patients with Ulcerative Colitis Using the French Nationwide Claims Database (SNDS); Responses to the RSI adopted by the CHMP on 30 January 2025 (MEA 48.5)

## 17.3. Results of PASS imposed in the marketing authorisation(s)[44]

None

## 17.4. Results of PASS non-imposed in the marketing authorisation(s)[45]

### 17.4.1. Baricitinib – OLUMIANT (CAP) – EMA/VR/0000266452

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from the non-interventional Study I4V-MC-B025 listed as a category 3 study in the RMP. This is a rheumatologist and dermatologist survey to assess the effectiveness of the risk minimisation measures (RMM) for Olumiant, a JAK1/2 inhibitor. The RMP version 25.1 has also been submitted. In addition, the MAH took the opportunity to request an extension to the PASS commitment date for non-interventional Study I4V-MC-B038 (B038).

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

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

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

[44] In accordance with Article 107p-q of Directive 2001/83/EC
[45] 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

### 17.4.3. Conestat alfa – RUCONEST (CAP) – EMA/VR/0000263304

Applicant: Pharming Group N.V.

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of the final report from Ruconest EU registry listed as a category 3 study in the RMP. This is a non-imposed non-interventional PASS (phase IV) of C1 inhibitor Treatment Registry to assess the Safety and Immunological Profile of Ruconest in the treatment of HAE Attacks.

### 17.4.4. COVID-19 mRNA vaccine – SPIKEVAX (CAP) – EMA/VR/0000264109

Applicant: Moderna Biotech Spain S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: A grouped application consisting of:

C.I.4 Update of section 4.8 of the SmPC in order to update the frequency of the adverse reactions ''Anaphylaxis'' and ''Erythema multiforme" from ''Not known'' to ''Rare'', based on final results from study mRNA-1273-P904 listed as a category 3 study in the RMP. This is a Non-Interventional, Post-Authorisation Active Surveillance Safety Study Using Secondary Data to Monitor Real-World Safety of the mRNA-1273 Vaccine in the EU. The Package leaflet is updated accordingly. An updated RMP (version 11.0) is also included.

C.I.13: Submission of the final report from study mRNA-1273-P905 (Monitoring safety of COVID-19 Vaccine Moderna in pregnancy: an observational study using routinely collected health data in five European countries) listed as a category 3 study in the RMP.

### 17.4.5. Elosulfase alfa - VIMIZIM (CAP) – EMA/VR/0000268096

Applicant: Biomarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.6, 4.8 and 5.1 of the SmPC based on final results from Morquio A Registry Study (MARS, Study 110-504) listed as a category 1 study in the RMP; this is an observational registry study to evaluate long-term safety and effectiveness of elosulfase alfa. The RMP version 7.0 has also been submitted. In addition, the MAH took the opportunity to update Annex II and to update the PI in accordance with the latest EMA excipients guideline.

### 17.4.6. Etanercept – BENEPALI (CAP) – EMA/VR/0000263971

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Monica Martinez Redondo

Scope: A grouped application consisting of:

C.I.13: Submission of the final report from study (ARTIS) listed as a category 3 study in the RMP. This is a national prospective, observational, uncontrolled cohort study whose objectives are to evaluate the risk of selected AEs in RA, juvenile idiopathic arthritis, and other rheumatic disease patients treated with etanercept. The RMP version 10.0 has also been submitted.

C.I.13: Submission of the final report from study (BSRBR-RA) listed as a category 3 study in the RMP. This is an established nationwide register for patients with rheumatological disorders treated with biologic agents.

### 17.4.7. Erenumab - AIMOVIG (CAP) – EMA/VR/0000267640

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Terhi Lehtinen

Scope: Submission of the final study report for the non-interventional (NIS) study CAMG334A2023; this is a non-interventional study to examine patient characteristics and drug utilization patterns in migraine patients treated with prophylactic drugs in Nordic countries, listed as a category 3 PASS in the RMP. The RMP version 5.0 has also been submitted.

### 17.4.8. 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 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.

### 17.4.9. 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 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. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human ADA cDNA sequence (CAP) – STRIMVELIS - EMA/PAM/0000264435

Applicant: Fondazione Telethon Ets

PRAC Rapporteur: Liana Martirosyan

Scope: The Marketing Authorisation Holder (MAH), Fondazione Telethon ETS, submitted version 4.0 of the interim study report of study STRIM-003, dated 20 March 2025: Adenosine Deaminase Severe Combined Immunodeficiency (ADA-SCID) Registry for Patients Treated with Strimvelis (or GSK2696273) Gene Therapy: Long-Term Prospective, Non- Interventional Follow-up of Safety and Effectiveness (EUPAS15795). The date of previous version of the interim study report (Version 3.0) was 21 March 2023. The list of milestones continues with 2-yearly interim study reports up to the final clinical study report

### 17.5.2. Brexucabtagene autoleucel – TECARTUS (CAP) – EMA/PAM/0000267756

Applicant: Kite Pharma EU B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Second Annual Interim Safety Report for the Category 1 (ANX) Non-interventional Post Authorisation Efficacy and Safety Study (PAES/PASS) for Tecartus (Study KT-EU-472-6036) for the MCL indication

### 17.5.3. Cabotegravir - VOCABRIA (CAP) – EMA/PAM/0000263322

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: 3rd interim report from the DUS study (study 215161, Cat. 1 study): Drug Utilization, Adherence, Effectiveness and Resistance: A Prospective Observational Cohort Study in People Living with HIV (PLWH) initiating ARV regimen CAB+RPV LA in Collaboration with EuroSIDA

### 17.5.4. Difelikefalin - KAPRUVIA (CAP) - EMA/PAM/0000265268

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: Responses to the CHMP's request for information on three Cat 3 studies raised during assessment of the post-authorisation measures MEA/002.2, MEA/003.2, MEA/004.2 (adopted in January 2025).

This report covers the following post-authorisation commitments undertaken by the MAH:

- CR845-310501 A Two-part, Multicenter, Randomized, Double-blind Study to Evaluate the Efficacy and Safety of Oral Difelikefalin as Adjunct Therapy to a Topical Corticosteroid for Moderate-to- Severe Pruritus in Adult Subjects with Atopic Dermatitis (AD).
- CR845-310301 A Multicenter, Randomized, Double-blind, Placebo-controlled 12-Week Study to Evaluate the Safety and Efficacy of Oral Difelikefalin in Advanced Chronic Kidney Disease Subjects with Moderate-to-Severe Pruritus with an up to 52-Week Long-term Extension.
- CR845-310302 A Multicenter, Randomized, Double-blind, Placebo-controlled 12-Week Study to Evaluate the Safety and Efficacy of Oral Difelikefalin in Advanced Chronic Kidney Disease Subjects with Moderate-to-Severe Pruritus with an up to 52-Week Long-term Extension.

### 17.5.5. Inotersen - TEGSEDI (CAP) – EMA/PAM/0000263490

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: The first interim report of 'A prospective, non-interventional, long-term, multinational cohort safety study of patients with hereditary transthyretin amyloidosis with polyneuropathy (hATTR-PN)

### 17.5.6. Rilpivirine - REKAMBYS (CAP) – EMA/PAM/0000263320

Applicant: Janssen Cilag International

PRAC Rapporteur: Liana Martirosyan

Scope: 3rd interim report from the DUS study (study 215161, Cat. 1 study): Drug Utilization, Adherence, Effectiveness and Resistance: A Prospective Observational Cohort Study in People Living with HIV (PLWH) initiating ARV regimen CAB+RPV LA in Collaboration with EuroSIDA

### 17.5.7. Ustekinumab - STELARA (CAP) – EMA/PAM/0000264405

Applicant: Janssen Cilag International

PRAC Rapporteur: Rhea Fitzgerald

Scope: 7th Annual Report for An Observational Post-authorization Safety Study of Ustekinumab in the Treatment of Pediatric Patients Aged 6 Years and Older With Moderate to Severe Plaque Psoriasis; Protocol No.: CNTO1275PSO4056 (MEA 44.20)

## 17.6. Others

### 17.6.1. Buprenorphine – SIXMO (CAP)– EMA/PAM/0000268762

Applicant: L. Molteni & C. Dei Fratelli Alitti Societa' Di Esercizio S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: First progress report of an observational cohort study to evaluate the incidence of breakages and insertion/removal complications of buprenorphine implants in routine clinical care in Europe, in adult patients with a diagnosis of opioid dependence (RE-START study - MOLTeNI-2019-01).

### 17.6.2. Nivolumab / Relatlimab - OPDUALAG (CAP) – EMA/PAM/0000263880

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Gabriele Maurer

Scope: Statistical analysis plan (SAP) for study CA224122, an observational cohort study of adolescent patients (≥ 12 to < 18 years of age) treated with nivolumab + relatlimab FDC for the approved indications in the EU, using secondary data from the DMTR registry.

### 17.6.3. Odevixibat - KAYFANDA (CAP) – EMA/PAM/0000262851

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: PASS CLIN-60240-034: Prospective Registry-Based Study of the Long-Term Safety of Odevixibat in Patients with Alagille syndrome (ALGS).

SOB - Feasibility assessment of a Specific Obligation (PASS in ALGS) -

EMEA/H/C/006462/SOB/001

### 17.6.4. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) – MOSQUIRIX (CAP) – EMA/PAM/0000268751

Applicant(s): various

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the statistical analysis plan (SAP) for EPI-MAL-003 final analysis. EPI-MAL-003. EPI-MAL-003 is a category 3, prospective surveillance study to evaluate the safety, effectiveness and impact of Mosquirix in infants and young children in Sub-Saharan Africa.

### 17.6.5. Tezepelumab - TEZSPIRE (CAP) – EMA/PAM/0000268702

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

Scope: Progress report of the post-authorisation safety study on the risk of congenital malformations, adverse pregnancy outcomes, and adverse birth outcomes in pregnancies and offspring of women who received tezepelumab for severe asthma during pregnancy and women who received other SOC treatments for severe asthma during pregnancy.

### 17.6.6. Tezepelumab - TEZSPIRE (CAP) – EMA/PAM/0000268709

Applicant: AstraZeneca AB

PRAC Rapporteur: Eva Jirsová

Scope: Progress report of the observational multi-country Post-Authorisation Safety Study to evaluate the risk of serious adverse cardiovascular events in adolescent and adult patients with severe asthma taking Tezepelumab (TRESPASS)

## 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. Chenodeoxycholic acid – CHENODEOXYCHOLIC ACID LEADIANT (CAP) – EMA/S/0000264995

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

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

Applicant: Serb

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

### 18.1.3. Idursulfase – ELAPRASE (CAP) – EMA/S/0000263922

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Liana Martirosyan

Scope: Annual reassessment of the marketing authorisation

### 18.1.4. Maralixibat - LIVMARLI (CAP) - EMEA/H/C/005857/S/0019

Applicant: Mirum Pharmaceuticals International B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

### 18.1.5. Pegzilarginase – LOARGYS (CAP) – EMA/S/0000247405

Applicant: Immedica Pharma AB

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

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

Applicant: Siga Technologies Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Annual reassessment of the marketing authorisation

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

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Annual reassessment of the marketing authorisation

### 18.1.8. Zanamivir – DECTOVA (CAP) – EMA/S/0000265004

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Karin Bolin

Scope: Annual reassessment of the marketing authorisation

## 18.2. Conditional renewals of the marketing authorisation

### 18.2.1. Elranatamab – ELREXFIO (CAP) – EMA/R/0000269600

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Barbara Kovacic Bytyqi

Scope: Conditional renewal of the marketing authorisation

### 18.2.2. Pirtobrutinib – JAYPIRCA (CAP) – EMA/R/0000264598

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

### 18.2.3. Tafasitamab – MINJUVI (CAP) – EMA/R/0000256675

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Mari Thorn

Scope: Conditional renewal of the marketing authorisation

### 18.2.4. Valoctocogene roxaparvovec – ROCTAVIAN (CAP) – EMA/R/0000250212

Applicant: Biomarin International Limited

PRAC Rapporteur: Bianca Mulder

Scope: Conditional renewal of the marketing authorisation

## 18.3. Renewals of the marketing authorisation

### 18.3.1. Baloxavir marboxil – XOFLUZA (CAP) – EMA/R/0000265299

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Radowan

Scope: 5-year renewal of the marketing authorisation

### 18.3.2. Defatted powder of Arachis hypogaea L., semen (peanuts) – PALFORZIA (CAP) – EMA/R/0000264359

Applicant: Stallergenes

PRAC Rapporteur: Terhi Lehtinen

Scope: 5-year renewal of the marketing authorisation

### 18.3.3. Fedratinib – INREBIC (CAP) – EMA/R/0000264185

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Radowan

Scope: 5-year renewal of the marketing authorisation

### 18.3.4. Fostemsavir – RUKOBIA (CAP) – EMA/R/0000264656

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

### 18.3.5. Lumacaftor / Ivacaftor – ORKAMBI (CAP) – EMA/R/0000249341

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Eamon O Murchu

Scope: 5-year renewal of the marketing authorisation

### 18.3.6. Pertuzumab / Trastuzumab – PHESGO (CAP) – EMA/R/0000258704

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: 5-year renewal of the marketing authorisation

### 18.3.7. RECOMBINANT VESICULAR STOMATITIS VIRUS (STRAIN INDIANA) WITH A DELETION OF THE ENVELOPE GLYCOPROTEIN, REPLACED WITH THE ZAIRE EBOLAVIRUS (STRAIN KIKWIT-1995) SURFACE GLYCOPROTEIN – ERVEBO (CAP) – EMA/R/0000265014

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Liana Martirosyan

Scope: 5-year renewal of the marketing authorisation

### 18.3.8. Tagraxofusp – ELZONRIS (CAP) – EMA/R/0000261300

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Bianca Mulder

Scope: 5-year renewal of the marketing authorisation

### 18.3.9. Tucatinib – TUKYSA (CAP) – EMA/R/0000262094

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

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 July 2025 PRAC meeting, which was held in-person. Participants marked with "a" attended the plenary session while those marked with "b" attended the Extraordinary PRAC plenary meeting held on 31 July 2025.

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

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

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| | | | in discussion, final deliberations and voting on: | autoleucel – CARVYKTI (CAP) - EMEA/H/C/005095/SDA/021; idecabtagene vicleucel – ABECMA (CAP) - EMEA/H/C/004662/SDA/024; tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/SDA/026<br><br>15.2.1. Apixaban – ELIQUIS (CAP) – EMA/VR/0000262422<br><br>15.3.23. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/VR/0000265024<br><br>15.3.24. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/VR/0000272242<br><br>16.1.1. Adagrasib – KRAZATI (CAP) – EMA/PSUR/00000257790<br><br>16.1.20. Elotuzumab – EMPLICITI (CAP) – |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| | | | | EMA/PSUR/00 00257854<br><br>17.1.1. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/PASS/000 0269320<br><br>17.6.2. Nivolumab / Relatlimab - OPDUALAG (CAP) – EMA/PAM/000 0263880<br><br>18.3.3. Fedratinib – INREBIC (CAP) – EMA/R/000026 4185 |
| Martin Huber [a],[b] | Member | Germany | No interests declared | |
| Gabriele Maurer [a] | Alternate | Germany | No interests declared | |
| Georgia Gkegka [a],[b] | Member | Greece | No interests declared | |
| Maria Poulianiti [a] | Alternate* | Greece | No participation in discussion, final deliberations and voting on: | 4.1.1. Valproate (NAP) and related substances 6.2.2. Bosentan – STAYVEER (CAP); TRACLEER (CAP); NAP – EMA/PSUR/00 00257801 |
| Julia Pallos [a],[b] | Member | Hungary | No participation in discussion, final deliberations and voting on: | 4.2.1. Ciltacabtagene autoleucel – CARVYKTI (CAP) - EMEA/H/C/005 095/SDA/021; idecabtagene |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| | | | | vicleucel – ABECMA (CAP) - EMEA/H/C/004662/SDA/024; tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/SDA/026<br><br>15.2.1. Apixaban – ELIQUIS (CAP) – EMA/VR/0000262422<br><br>15.3.23. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/VR/0000265024<br><br>15.3.24. Lisocabtagene maraleucel / Lisocabtagene maraleucel – BREYANZI (CAP) – EMA/VR/0000272242<br><br>16.1.1. Adagrasib – KRAZATI (CAP) – EMA/PSUR/00000257790<br><br>16.1.20. Elotuzumab – EMPLICITI (CAP) – EMA/PSUR/00000257854<br><br>17.1.1. Lisocabtagene maraleucel / Lisocabtagene |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| | | | | maraleucel – BREYANZI (CAP) – EMA/PASS/0000269320<br><br>17.6.2. Nivolumab / Relatlimab - OPDUALAG (CAP) – EMA/PAM/0000263880<br><br>18.3.3. Fedratinib – INREBIC (CAP) – EMA/R/0000264185 |
| Melinda Palfi [a] | Alternate* | Hungary | No interests declared | |
| Guðrún Stefánsdóttir [a] | Member* | Iceland | No restrictions applicable to this meeting | |
| Rhea Fitzgerald [a,b] | Member | Ireland | No interests declared | |
| Eamon O Murchu [a,b] | Alternate | Ireland | No interests declared | |
| Amelia Cupelli [a,b] | Member | Italy | No interests declared | |
| Zane Neikena [a,b] | Member | Latvia | No interests declared | |
| Diana Litenboka [a] | Alternate* | Latvia | No interests declared | |
| Rugile Pilviniene [a] | Member | Lithuania | No restrictions applicable to this meeting | |
| Lina Seibokiene [a,b] | Alternate | Lithuania | No interests declared | |
| Anne-Cecile Vuillemin [b] | Member | Luxembourg | No interests declared | |
| Magdalena Wielowieyska [a,b] | Alternate | Luxembourg | No participation in discussion, final deliberations | 16.3.20. Lornoxicam (NAP) – EMA/PSUR/00000257821<br><br>16.1.37. |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| | | | and voting on: | Maribavir – LIVTENCITY (CAP) – EMA/PSUR/00000257897<br><br>16.1.42. Piflufolastat (18F) – PYLCLARI (CAP) – EMA/PSUR/00000257788<br><br>17.1.2. Teduglutide – REVESTIVE (CAP) – EMA/PASS/0000269314<br><br>18.1.3. Idursulfase – ELAPRASE (CAP) – EMA/S/0000263922 |
| John Joseph Borg [a],[b] | Member | Malta | No restrictions applicable to this meeting | |
| Benjamin Micallef [b] | Alternate | Malta | No interests declared | |
| Liana Martirosyan [a],[b] | Member (Vice-Chair) | Netherlands | No interests declared | |
| Bianca Mulder [a] | Alternate | Netherlands | No interests declared | |
| David Olsen [a] | Member | Norway | No participation in discussion, final deliberations and voting on: | 5.1.7. Elinzanetant - LYNKUET (CAP MAA) - EMEA/H/C/006298<br><br>15.3.2. Aflibercept – EYLEA (CAP) – EMA/VR/0000264981<br><br>16.1.35. Larotrectinib – VITRAKVI |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| | | | | (CAP) – EMA/PSUR/00 00257875<br><br>6.3.2. Acetylsalicylic acid/ caffeine/ paracetamol (NAP) – EMA/PSUR/00 00257831<br><br>16.3.6. Clotrimazole / dexamethason e (NAP) – EMA/PSUR/00 00257805<br>6.3.10. Clotrimazole / hydrocortisone (NAP) – EMA/PSUR/00 00257806<br><br>16.3.16. Drospirenone / estradiol (NAP) – EMA/PSUR/00 00257811 |
| Pernille Harg [a,b] | Alternate | Norway | No interests declared | |
| Adam Przybylkowski [b] | Member | Poland | No restrictions applicable to this meeting | |
| Katarzyna Ziolkowska [a] | Alternate | Poland | No interests declared | |
| Ana Sofia Diniz Martins [a] | Member | Portugal | No interests declared | |
| Carla Torre [a,b] | Alternate | Portugal | No restrictions applicable to this meeting | |
| Roxana Dondera [a] | Member | Romania | No interests declared | |

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Irina Sandu [a,b] | Alternate* | Romania | No interests declared | |
| Anna Mareková [a] | Member* | Slovakia | No interests declared | |
| Miroslava Gocova [a,b] | Alternate | Slovakia | No interests declared | |
| Polona Golmajer [a] | Member | Slovenia | No interests declared | |
| Marjetka Plementas [a,b] | Alternate* | Slovenia | No interests declared | |
| Maria del Pilar Rayon [a,b] | Member | Spain | No interests declared | |
| Monica Martinez Redondo [a,b] | Alternate | Spain | No interests declared | |
| Mari Thorn [a] | Member | Sweden | No restrictions applicable to this meeting | |
| Karin Bolin [a,b] | Alternate | Sweden | No restrictions applicable to this meeting | |
| Annalisa Capuano [a] | Member* | Independent scientific expert | No restrictions applicable to this meeting | |
| Milou-Daniel Drici [a,b] | Member | Independent scientific expert | No restrictions applicable to this meeting | |
| Maria Teresa Herdeiro [a,b] | Member | Independent scientific expert | No restrictions applicable to this meeting | |
| Patricia McGettigan [a,b] | Member | Independent scientific expert | No restrictions applicable to this meeting | |
| Hedvig Marie Egeland Nordeng [a,b] | Member | Independent scientific expert | 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 |
|---|---|---|---|---|
| Anette Kirstine Stark [a,b] | Member | Independent scientific expert | No restrictions applicable to this meeting | |
| Roberto Frontini [a,b] | Member | Healthcare Professionals' Representative | No restrictions applicable to this meeting[46] | |
| Martin Votava [a,b] | Alternate | Healthcare Professionals' Representative | No restrictions applicable to this meeting | |
| Yiannoula Koulla [a,b] | Member | Patients' Organisation Representative | No interests declared | |
| Christelle Bizimungu [a] | Expert | Belgium | | |
| Evelien De Clercq [a] | Expert | Belgium | | |
| Laurence de Fays [b] | Expert | Belgium | | |
| Fabrice Moore [a] | Expert | Belgium | | |
| Flora Musuamba Tshinanu [a] | Expert | Belgium | | |
| Charlotte Selvais [a] | Expert | Belgium | | |
| Chloé Wyndham-Thomas [a] | Expert | Belgium | | |
| Nina Lalić [a] | Expert | Croatia | | |
| Ivana Ljubičić [a] | Expert | Croatia | | |
| Michaela Skorepova [a] | Expert | Czech Republic | | |
| Marian Hjortlund Allon [a] | Expert | Denmark | | |
| Kristina Laursen [a] | Expert | Denmark | | |
| Line Michan [a] | Expert | Denmark | | |
| Thadeus Bao Quan Nguyen [a] | Expert | Denmark | | |
| Lærke Nilausen [a] | Expert | Denmark | | |

[46] The outcome of the DoI evaluation for the plenary meeting for this member was 'no interests declared'.

| Name | Role | Member state or affiliation | Outcome restriction following evaluation of e-DoI | Topics on agenda for which restrictions apply |
|---|---|---|---|---|
| Helle Gerda Olsen [a] | Expert | Denmark | | |
| Moritz Sander [a] | Expert | Denmark | | |
| Emma Stadsbjerg [a] | Expert | Denmark | | |
| Karima Adamo [a] | Expert | France | | |
| Benjamin Burrus [a] | Expert | France | | |
| Nicolas Camhaji [b] | Expert | Expert | | |
| Samuel Crommelynck [a] | Expert | France | | |
| Camille De-Kervasdoue [a] | Expert | France | | |
| Nathalie Dumarcet [b] | Expert | France | | |
| Henning Brohmann [a] | Expert | Germany | | |
| Dennis Lex [a] | Expert | Germany | | |
| Clare Foley [a] | Expert | Ireland | | |
| Melanie Murphy [a] | Expert | Ireland | | |
| Patrizia Felicetti [b] | Expert | Italy | | |
| Carmela Macchiarulo [b] | Expert | Italy | | |
| Pasquale Marchione [b] | Expert | Italy | | |
| Inge Zomerdijk [a] | Expert | Netherlands | | |
| Kristina Nadrah [a] | Expert | Slovenia | | |
| Maria Martinez Gonzalez [a] | Expert | Spain | | |
| Elena Martinez [a] | Expert | Spain | | |
| Sol Ruiz [a] | Expert | Spain | | |
| Annika Andersson [b] | Expert | Sweden | | |
| Bernice Aronsson [a] | Expert | Sweden | | |
| Charlotte Backman [a] | Expert | Sweden | | |
| Helena Back [a] | Expert | Sweden | | |
| A representative from the European Commission attended the meeting | | | | |
| Observers from Health Canada attended the meeting. | | | | |
| Meeting run with support from relevant EMA staff | | | | |

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

# 20. Annex III - List of acronyms and abbreviations

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

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

# 21. Explanatory notes

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