Pharmacovigilance Risk Assessment Committee (PRAC)
Draft agenda for the meeting on 09-12 January 2023

Chair: Sabine Straus – Vice-Chair: Martin Huber

09 January 2023, 10:30 – 19:30, via teleconference
10 January 2023, 08:30 – 19:30, via teleconference
11 January 2023, 08:30 – 19:30, via teleconference
12 January 2023, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)
23 January 2023, 09:00 – 12:00, via teleconference

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Of note, this agenda is a working document primarily designed for PRAC members and the work the Committee undertakes.

Note on access to documents
Some documents mentioned in the agenda 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 ongoing procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006 Rev.1).
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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 09-12 January 2023. See January 2023 PRAC minutes (to be published post February 2023 PRAC meeting).

1.2. Agenda of the meeting on 09-12 January 2023

Action: For adoption

1.3. Minutes of the previous meeting on 28 November - 01 December 2022

Action: For adoption

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**

3.2.1. **Topiramate (NAP); topiramate, phentermine (NAP) - EMEA/H/A-31/1520**

Applicant(s): various

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur: Martin Huber

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

**Action:** For adoption of a list of questions (LoQ) for an expert group meeting

3.3. **Procedures for finalisation**

None

3.4. **Re-examination procedures\(^1\)**

None

3.5. **Others**

3.5.1. **Janus kinase (JAK) inhibitors\(^2\): abrocitinib - CIBINQO (CAP); baricitinib - OLUMIANT (CAP); filgotinib - JYSELECA (CAP); tofacitinib - XELJANZ (CAP); upadacitinib - RINVOQ (CAP) – EMEA/H/A-20/1517**

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Rinvoq), Eli Lilly Nederland B.V. (Olumiant), Galapagos N.V. (Jyseleca), Pfizer Europe MA EEIG (Cibinqo, Xeljanz)

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur(s): Liana Gross-Martirosyan (Olumiant, Xeljanz), Nikica Mirošević Skvrce (Cibinqo, Jyseleca, Rinvoq)

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

**Action:** For discussion on the need for a revised recommendation to CHMP

---

\(^1\) Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

\(^2\) Indicated for the treatment of inflammatory disorders
4. Signals assessment and prioritisation

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP)

Applicant: AstraZeneca AB
PRAC Rapporteur: Jean-Michel Dogné
Scope: Signal of myositis
Action: For adoption of PRAC recommendation
EPITT 19882 – New signal
Lead Member State(s): BE

4.1.2. Elasomeran - SPIKEVAX (CAP)

Applicant: Moderna Biotech Spain, S.L.
PRAC Rapporteur: Marie Louise Schougaard Christiansen
Scope: Signal of myositis
Action: For adoption of PRAC recommendation
EPITT 19884 – New signal
Lead Member State(s): DK

4.1.3. Lenvatinib – LENVIMA (CAP); KISPLYX (CAP)

Applicant: Eisai GmbH
PRAC Rapporteur: To be appointed
Scope: Signal of adrenal insufficiency
Action: For adoption of PRAC recommendation
EPITT 19870 – New signal
Lead Member State(s): SE

4.1.4. Progesterone (NAP)

Applicant: various
PRAC Rapporteur: To be appointed
Scope: Signal of meningioma

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.
Action: For adoption of PRAC recommendation
EPITT 19871 – New signal
Lead Member State(s): SE

4.1.5. **Tozinameran - COMIRNATY (CAP)**

Applicant: BioNTech Manufacturing GmbH
PRAC Rapporteur: Menno van der Elst
Scope: Signal of myositis
Action: For adoption of PRAC recommendation
EPITT 19883 – New signal
Lead Member State(s): NL

4.2. **New signals detected from other sources**

4.2.1. Glucagon-like peptide-1 (GLP-1) receptor agonists: dulaglutide – TRULICITY (CAP); exenatide – BYDUREON (CAP), BYETTA (CAP); insulin degludec, liraglutide – XULTOPHY (CAP); liraglutide – SAXENDA (CAP), VICTOZA (CAP); lixisenatide – LYXUMIA (CAP); semaglutide – OZEMPIC (CAP), RYBELSUS (CAP), WEGOVY (CAP)

Applicant: AstraZeneca AB (Bydureon, Byetta), Eli Lilly Nederland B.V. (Trulicity), Novo Nordisk A/S (Ozempic, Rybelsus, Saxenda, Victoza, Wegovy, Xultophy), sanofi-aventis groupe (Lyxumia)
PRAC Rapporteur: To be appointed
Scope: Signal of thyroid cancer
Action: For adoption of PRAC recommendation
EPITT 18292 – New signal
Lead Member State(s): NL

4.3. **Signals follow-up and prioritisation**

4.3.1. 3-hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins): atorvastatin (NAP); fluvastatin (NAP);Lovastatin (NAP); pitavastatin (NAP); pravastatin (NAP); rosuvastatin (NAP); simvastatin (NAP) and other relevant fixed dose combinations; pravastatin, fenofibrate – PRAVAFENIX (CAP); simvastatin, fenofibrate – CHOLIB (CAP)

Applicant(s): Laboratoires SMB s.a. (Pravafenix), Mylan IRE Healthcare Limited (Cholib); various
PRAC Rapporteur: Nathalie Gault
Scope: Signal of myasthenia gravis
Action: For adoption of PRAC recommendation
4.3.2. Dabrafenib - TAFINLAR (CAP) - EMEA/H/C/002604/SDA/020; trametinib - MEKINIST (CAP) - EMEA/H/C/002643/SDA/015

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Signal of haemophagocytic lymphohistiocytosis
Action: For adoption of PRAC recommendation
EPITT 19824 – Follow-up to September 2022
Lead Member State(s): SE

4.3.3. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/SDA/013

Applicant: Bayer AG
PRAC Rapporteur: Menno van der Elst
Scope: Signal of thrombotic microangiopathy
Action: For adoption of PRAC recommendation
EPITT 19832 – Follow-up to September 2022

4.3.4. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/056

Applicant: BioNTech Manufacturing GmbH
PRAC Rapporteur: Menno van der Elst
Scope: Signal of vulval ulceration
Action: For adoption of PRAC recommendation
EPITT 19840 – Follow-up to September 2022

4.4. Variation procedure(s) resulting from signal evaluation

None

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Aripiprazole - EMEA/H/C/005929

Scope: Indicated for the maintenance treatment of schizophrenia
Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP
5.1.2. **Coronavirus (COVID-19) vaccine (recombinant protein receptor binding domain fusion heterodimer) - EMEA/H/C/006058**

Scope: Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.3. **Ganaxolone - EMEA/H/C/005825, Orphan**

Applicant: Marinus Pharmaceuticals Emerald Limited

Scope: Treatment of epileptic seizures associated with cyclindependent kinase-like 5 deficiency disorder (CDD)

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.4. **Leniolisib - EMEA/H/C/005927, Orphan**

Applicant: Pharming Technologies B.V.

Scope (accelerated assessment): Treatment of activated phosphoinositide 3-kinase delta syndrome (APDS)

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.5. **Mirikizumab - EMEA/H/C/005122**

Scope: Treatment of moderately to severely active ulcerative colitis

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.6. **Recombinant respiratory syncytial virus pre-fusion F protein, adjuvanted with AS01E - EMEA/H/C/006054**

Scope (accelerated assessment): Active immunization or the prevention of lower respiratory tract disease (LRTD)

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.1.7. **Ublituximab - EMEA/H/C/005914**

Scope: Treatment of relapsing forms of multiple sclerosis (RMS)

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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

5.2.1. **Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/II/0044**

Applicant: Roche Registration GmbH
PRAC Rapporteur: Jana Lukacisinova

Scope: Submission of an updated RMP version 3.2 in order to remove the important identified risks of Interstitial Lung Disease (ILD)/Pneumonitis, Hepatotoxicity, Photosensitivity, Bradycardia, Severe myalgia and Creatine Phosphokinase (CPK) elevations as safety concerns. Furthermore template updates in line with the GVP Product or Population-Specific Considerations III: Pregnant and breastfeeding women are made

Action: For adoption of PRAC Assessment Report

5.2.2. Efavirenz - STOCRIN (CAP) - EMEA/H/C/000250/II/0130

Applicant: Merck Sharp & Dohme B.V.
PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP version 9.0 including removal of all safety concerns in line with revision 2 of GVP module V on `Risk management

Action: For adoption of PRAC Assessment Report

5.2.3. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0085/G

Applicant: Moderna Biotech Spain, S.L.
PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped application comprising of : 1) submission of RMP version 6.0 to add Spikevax bivalent Original / Omicron BA.4-5 vaccine (mRNA-1273.222), to update studies mRNA-1273-P904, mRNA-1273-P905 and mRNA-1273-P910 in the Pharmacovigilance Plan to include exposure to Spikevax bivalent vaccines, to update the INN to elasomeran/davesomeran, and to reclassify studies mRNA-1273-P205 from category 2 to category 3 studies in the Pharmacovigilance Plan; 2) submission of the final clinical study report (CSR) from study mRNA-1273-P201, a Phase 2a, Randomized, Observer-Blind, Placebo-Controlled, Dose-Confirmation Study to Evaluate the Safety, Reactogenicity, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults ≥= 18 Years listed as a category 3 study including addition of clinical trial exposure data for part C of the study mRNA-1273-P201

Action: For adoption of PRAC Assessment Report

5.2.4. Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil - STRIBILD (CAP) - EMEA/H/C/002574/WS2320/0120; emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/WS2320/0177

Applicant(s): Gilead Sciences Ireland UC
PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of Annex II and the RMP for Truvada and Stribild to version 18.1 and 14.1 to remove of the paediatric additional Risk Minimisation Measures (aRMMs) for HIV indication. In addition, the MAH took the opportunity to introduce changes to the PI

Action: For adoption of PRAC Assessment Report
5.2.5. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0017, Orphan

Applicant: Zogenix ROI Limited
PRAC Rapporteur: Martin Huber
Scope: Submission of an updated RMP version 2.10 in order to implement a targeted follow-up questionnaire (FUQ) to further improve the collection of follow-up information on cases of vascular heart disease (VHD) and pulmonary arterial hypertension (PAH) suggested by PRAC following PSUSA/00010907/2021122
Action: For adoption of PRAC Assessment Report

5.2.6. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/WS2369/0066; ZARZIO (CAP) - EMEA/H/C/000917/WS2369/0067

Applicant(s): Sandoz GmbH
PRAC Rapporteur: Menno van der Elst
Scope: Submission of an updated RMP version 13.0 to reduce the list of safety concerns and remove risks which are well characterised and already included in the product information, following PSUR single assessment (PSUSA) procedure (PSUSA/00001391/202109) concluded in May 2022. Additionally, the due date of the final study report EP06-501 (MEA007) has been updated from Q3 2025 to Q1 2025
Action: For adoption of PRAC Assessment Report

5.2.7. Glycopyrronium - SIALANAR (CAP) - EMEA/H/C/003883/II/0026

Applicant: Proveca Pharma Limited
PRAC Rapporteur: Zane Neikena
Scope: Submission of an updated RMP version 3.1 in order to remove study PRO/GLY/004: a drug utilisation study (DUS) to assess the efficacy of risk minimisation measures for Sialanar
Action: For adoption of PRAC Assessment Report

5.2.8. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/WS2378/0140; PROMETAX (CAP) - EMEA/H/C/000255/WS2378/0141

Applicant(s): Novartis Europharm Limited
PRAC Rapporteur: Tiphaine Vaillant
Scope: Submission of an updated RMP version 11.0 for Exelon/Prometax to remove the standalone multiple patch use annual report as an additional pharmacovigilance activity, which was endorsed by PRAC (EMA/CHMP/PRAC/342229/2021) on 22-Jul-2021 and to include the initial risks reviewed at the time of initial marketing authorisation that were agreed to within RMP Version 1.1 (final: 16-Jul-2007), as well as submission of the rationale for the removal of some safety concerns from the currently approved RMP Version 10.0, following the PRAC Assessment Report from the currently approved RMP (version 10.0) (EMEA/H/C/XXX/WS/1773). Furthermore, the MAH took the opportunity to introduce
editorial changes in the RMP

**Action:** For adoption of PRAC Assessment Report

### 5.2.9. Smallpox vaccine (live modified vaccinia virus Ankara) - IMVANEX (CAP) - EMEA/H/C/002596/II/0081

**Applicant:** Bavarian Nordic A/S  
**PRAC Rapporteur:** Brigitte Keller-Stanislawski  
**Scope:** Submission of an updated RMP version 9.1 in order to update the safety specifications in line with extension of the indication to "active immunisation against smallpox, monkeypox and disease caused by vaccinia virus in adults", update the missing information from the list of safety concerns, differentiate routine pharmacovigilance activities and additional pharmacovigilance activities, addition of non-BN (Bavarian Nordic) sponsored clinical study SEMVAc to additional pharmacovigilance activities and deletion of paediatric study POX-MVA-035 upon request by PRAC following the assessment of procedure EMEA/H/C/002596/II/0076 concluded at PRAC in July 2022  
**Action:** For adoption of PRAC Assessment Report

### 5.2.10. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS2356/0081; sofosbuvir, ledipasvir - HARVONI (CAP) - EMEA/H/C/003850/WS2356/0107; sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS2356/0068; sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP)-EMEA/H/C/004350/WS2356/0057

**Applicant(s):** Gilead Sciences Ireland UC  
**PRAC Rapporteur:** Ana Sofia Diniz Martins  
**Scope:** Submission of updated RMPs (version 8.1 – Epclusa, version 8.1 – Harvoni, version 6.1 – Vosevi, version 11.1- Sovaldi) following finalisation of procedure EMEA/H/C/WS2222 providing the final CSR for the non-imposed joint PASS study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals (DAA) for chronic hepatitis C (Study B20-146). In particular, the list of safety concerns has been updated to remove the important potential risks "recurrence of hepatocellular carcinoma (HCC)" and "emergence of HCC", and to remove "safety in patients with previous HCC" as an area of missing information. In addition, the completed PASS studies: DAA PASS and De Novo DAA PASS have been removed from the pharmacovigilance plan  
**Action:** For adoption of PRAC Assessment Report

### 5.2.11. Somatropin - NUTROPINAQ (CAP) - EMEA/H/C/000315/II/0077

**Applicant:** Ipsen Pharma  
**PRAC Rapporteur:** Anette Kirstine Stark  
**Scope:** Submission of an updated RMP version 4.0 in order to remove some of the safety concerns in compliance with GVP Module V Revision 2. In addition, the MAH took the opportunity to add data from final clinical study report of International Cooperative Growth Study (iNCGS) registry (non-interventional study) and exposure and safety information
**Action:** For adoption of PRAC Assessment Report

### 5.2.12. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0059

**Applicant:** Amgen Europe B.V., ATMP

**PRAC Rapporteur:** Brigitte Keller-Stanislawski

**EMA resources:** PL: Nikolaos Zafiropoulos; RMS: Aliki Mitropoulou

**Scope:** Submission of an updated RMP version 10 in order to update and reclassify identified risk of 'disseminated herpetic infection' based on the cumulative assessment of literature review and MAH Global Safety Database and to remove studies 20180062 and 20180099 from Planned and Ongoing Studies from the list of Pharmacovigilance Plan studies in the Annex II

**Action:** For adoption of PRAC Assessment Report

### 5.2.13. Voriconazole - VFEND (CAP); NAP - EMEA/H/C/000387/WS2270/0147

**Applicant:** Pfizer Europe MA EEIG

**PRAC Rapporteur:** Liana Gross-Martirosyan

**Scope:** Update of Annex II and RMP to version 6.0 to include the results from final clinical study report (CSR) following the completion of a non-interventional (NI) post-authorisation safety study (PASS) A1501103: an active safety surveillance program to monitor selected events in patients with long-term voriconazole use - MEA091. In addition, MAH is also taking this opportunity to introduce editorial changes [in fulfilment of MEA 091.5]

**Action:** For adoption of PRAC Assessment Report

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

#### 5.3.1. Agomelatine - VALDOXAN (CAP) - EMEA/H/C/000915/II/0051

**Applicant:** Les Laboratoires Servier

**PRAC Rapporteur:** Pernille Harg

**Scope:** Extension of indication to include new therapeutic indication in adolescents aged 12 to 17 years for the treatment of moderate to severe major depressive episodes, if depression is unresponsive to psychological therapy alone, for Valdoxan, further to the results of the phase 2 (CL2-20098-075) and phase 3 (CL3-20098-076) paediatric clinical studies included in the Paediatric Investigation Plan number EMEA-001181-PIP-11; As a consequence the sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly. The updated RMP version 25.1 has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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4 Advanced therapy medicinal product
5.3.2. Albutrepenonacog alfa - IDELVION (CAP) - EMEA/H/C/003955/II/0059, Orphan

Applicant: CSL Behring GmbH
PRAC Rapporteur: Menno van der Elst
Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update information and amend the frequencies of adverse drug reactions (ADRs) based on the final results from study CSL654_3003 (listed as a category 3 study in the RMP): an open-label, multicentre, uncontrolled study to evaluate the safety, pharmacokinetics and clinical response of recombinant factor IX albumin fusion protein (rIX-FP) with regard to the prevention and treatment of bleeding in previously untreated patients (PUPs) with haemophilia B. The package leaflet is updated accordingly. The RMP (version 4.0) has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and update the list of local representatives in the package leaflet

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.3. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/II/0033

Applicant: AstraZeneca AB
PRAC Rapporteur: Menno van der Elst
Scope: Update of section 5.1 of the SmPC based on interim results from pharmacokinetic (PK)/pharmacodynamic (PD) study (listed as a specific obligation in the Annex II in order to fulfil SOB 1 and SOB 3): a PK and PK/PD analysis of intravenously administered andexanet after dosing to steady state with a factor Xa inhibitor, rivaroxaban or Apixaban, in healthy subjects and patients who have acute major bleeding. In addition, the MAH took the opportunity implement editorial changes in Annex II of the SmPC. The RMP version 3.0 has also been submitted

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.4. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/II/0069, Orphan

Applicant: PTC Therapeutics International Limited
PRAC Rapporteur: Liana Gross-Martirosyan
Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information following results from study PTC124-GD-041-DMD, listed as a specific obligation in the Annex II; This is a Phase 3 multicentre, randomised, double-blind, 18-month, placebo-controlled study, followed by a 18-month open label extension to confirm the efficacy and safety of ataluren in the treatment of ambulant patients with mdDMD aged 5 years or older. Annex II, and Annex IIB are updated to delete the SOB and to reflect the switch from conditional to full marketing authorisation. The package leaflet is updated accordingly. The RMP version 11.0 has also been submitted. Minor corrections were done to align the PI with the latest QRD templates

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP
5.3.5. **Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0075**

Applicant: Roche Registration GmbH

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to add ‘pericardial disorders’ to the list of adverse drug reactions (ADRs) with frequency common in monotherapy and uncommon in combination therapy/based on final results from Drug Safety Report (DSR 1115896) including review of available clinical trial data, post-marketing data, and literature. In addition, the MAH took the opportunity to update Annex II section D of the SmPC and to implement editorial changes in the SmPC. The package leaflet was updated accordingly. The RMP version 23.1 has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.6. **Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/X/0035/G**

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to introduce a new strength (1 mg film-coated tablet), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment, as monotherapy or in combination with conventional synthetic disease modifying antirheumatic drugs (DMARDs), of active juvenile idiopathic arthritis (JIA) in patients 2 years of age and older who have had an inadequate response or intolerance to one or more prior conventional synthetic or biologic DMARDs, based on final results from the pivotal study JAHV (I4V-MC-JAHV); this is a multicentre, double-blind, randomised, placebo-controlled, medication-withdrawal Phase 3 study in children from 2 years to less than 18 years of age with JIA who have had an inadequate response or intolerance to treatment with at least 1 conventional DMARD (cDMARD) or biological (bDMARD). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 15.1 of the RMP has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.7. **Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0021**

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to change posology recommendation in including an additional dose regimen (q16w) for diabetic macular edema (DME) patients during the maintenance phase, update the frequency of adverse drug reactions, update pharmacokinetic, pharmacodynamic, efficacy and safety information, following the assessment of procedure II/10, based on final results from studies CRTH258B2301 (KESTREL) and CRTH258B2302 (KITE). The package leaflet is updated accordingly. The RMP version 10 has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP
5.3.8. **Caplacizumab - CABLIVI (CAP) - EMEA/H/C/004426/II/0040, Orphan**

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC in order to update information on long-term efficacy and safety based on final results from study ALX0681-C302/LTS16371 - Prospective Follow-up Study for Patients who Completed Study ALX0681-C301 (HERCULES) to Evaluate Long-term Safety and Efficacy of Caplacizumab (Post-HERCULES), listed as a category 3 study in the RMP. The Post-HERCULES study was a Phase III, 36-month follow-up study from HERCULES (parent study) to evaluate the long-term outcomes as well as the safety and efficacy of repeat use of caplacizumab in patients who experienced a recurrence of acquired thrombotic thrombocytopenic purpura (aTTP). The RMP version 3.0 has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.9. **Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0009**

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel, based on final results from study 17777 (ARASENS): a randomised, double-blind, placebo-controlled phase 3 study designed to demonstrate the superiority of darolutamide in combination with docetaxel over placebo in combination with docetaxel in overall survival (OS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC). As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated in accordance. The MAH also requested one additional year of market protection

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.10. **Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0012**

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of the final report of carcinogenicity study T104877-7 listed as a category 3 study in the RMP. This is a non-clinical study to assess the carcinogenic potential in mice. The study evaluates the effects of daily oral administration of darolutamide for a period of 6 months in tg-rash2 transgenic mouse model. The updated RMP version 3.1 has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.11. **Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/II/0065**

Applicant: Eli Lilly Nederland B.V.
PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of type 2 diabetes mellitus (T2DM) in children and adolescents aged 10 to less than 18 years based on final results from study H9X-MC-GBGC; this is a phase 3, double-blind, randomised, multi-centre, placebo-controlled superiority trial to evaluate PK, PD, safety and efficacy of dulaglutide in children from 10 to less than 18 years of age, with an open label extension to evaluate safety. 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 7.1 of the RMP has also been submitted.

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.12. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0060

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of atopic dermatitis in paediatric patients from 6 months to <6 years of age based on final results from study R668-AD-1539: a phase 2/3 study investigating the pharmacokinetics, safety, and efficacy of dupilumab in patients aged ≥6 months to <6 years with moderate-to-severe atopic dermatitis. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.0) are updated in accordance.

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.13. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/II/0014

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2 and 5.2 the SmPC in order to update pharmacokinetic information based on final results from study GP411174 listed as an additional pharmacovigilance activity in the RMP; this is a Phase I, non-randomised, single-dose, open-label study to investigate the effect of impaired hepatic function on the pharmacokinetics of entrectinib in volunteers with different levels of hepatic function. The RMP version 4.0 has also been submitted. In addition, the MAH took the opportunity to update in Annex II section C and to update the list of local representatives in the package leaflet.

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.14. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0015, Orphan

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.2 and 5.2 of the SmPC to update the safety information based on final results from study ZX008-1903 listed as a category 3 study in the RMP: a phase 1, open-label, single-dose study to evaluate the safety, tolerability, and pharmacokinetics of ZX008 (fenfluramine hydrochloride) in subjects with varying degrees of hepatic impairment.
The primary objective of this study was to compare the pharmacokinetics (PK) of a single dose of ZX008 (fenfluramine hydrochloride) in subjects with varying degrees of hepatic impairment with that of healthy matched control subjects. The RMP (version 2.7) was updated accordingly.

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.15. Givosiran - GIVLAARI (CAP) - EMEA/H/C/004775/II/0011/G, Orphan

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: 1) update of section 5.3 of the SmPC based on final results from study AS1-GLP18-007 listed as a category 3 study in the RMP: a 104-week subcutaneous injection carcinogenicity study in Sprague Dawley rats; 2) update of section 5.3 of the SmPC based on final results from study AS1-GLP18-004: a 26-week subcutaneous injection carcinogenicity study in TgRasH2 mice. The RMP version 2.1 has also been submitted. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet.

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.16. Human fibrinogen, human thrombin - EVICEL (CAP) - EMEA/H/C/000898/II/0099

Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of adverse drug reactions (ADRs), add Pseudomeningocele to the list of ADRs with frequency uncommon and to update efficacy and safety information on paediatric population, following P46/0030 based on the final results from paediatric clinical study BIOS-13-006. This is a Prospective Randomised Controlled Study Evaluating the Safety and Efficacy of EVICEL used for Suture- Line Sealing in Dura-Mater Closure during Paediatric Neurosurgical Cranial Procedures. The package leaflet is updated accordingly. Editorial changes are proposed to sections of the product information. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.3. The RMP version 15 has also been submitted.

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.17. Human thrombin, human fibrinogen - TACHOSIL (CAP) - EMEA/H/C/000505/II/0117

Applicant: Corza Medical GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of children aged 1 month to 18 years, based on available bibliographical data, results from study TC-2402-040-SP which compared TachoSil with Surgicel Original as adjunct to primary surgical treatment in both adult and paediatric subjects, and results from Study TC-019-IN: a prospective, uncontrolled study in paediatric subjects. As a consequence, sections 4.1, 4.2, and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to
implement minor editorial changes in the product information. Version 0.1 of the RMP has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.18. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/II/0009, Orphan

**Applicant:** Bristol-Myers Squibb Pharma EEIG  
**PRAC Rapporteur:** Jo Robays  
**Scope:** Extension of indication in β-thalassaemia to include adult patients with non-transfusion dependent β-thalassaemia (NTDT) for Reblozyl (luspatercept). 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 and the RMP (version 1.1) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.19. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0056

**Applicant:** Orexigen Therapeutics Ireland Limited  
**PRAC Rapporteur:** Martin Huber  
**Scope:** Submission of an updated study design and a protocol synopsis for study CVOT-2 (listed as a category 1 study in Annex II-D (ANX/001.7)): a multicentre, randomised, double-blind, placebo-controlled phase 4 study to assess the effect of naltrexone extended release (ER)/bupropion ER on the occurrence of major adverse cardiovascular events (MACE) in overweight and obese subjects with cardiovascular disease, as requested by CHMP in the conclusions of procedure ANX 001.6 adopted in April 2021. Annex II and the RMP (version 13) are updated accordingly

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.20. Nintedanib - OFEV (CAP) - EMEA/H/C/003821/X/0052/G

**Applicant:** Boehringer Ingelheim International GmbH  
**PRAC Rapporteur:** Nikica Mirošević Skvrce  
**Scope:** Extension application to add a new strength of 25 mg soft capsule grouped with a type II variation C.I.6.a to add a new indication of treatment of fibrosing Interstitial Lung Diseases (ILDs) in children and adolescents from 6 to 17 years of age, based on results from study 1199 0337 (InPedILD); a randomised, placebo-controlled, double-blind, multicentre, multinational, phase III clinical trial undertaken to evaluate dose-exposure and safety of nintedanib on top of standard of care in children and adolescents (6 to 17 years old) with clinically significant fibrosing ILD. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to implement minor editorial changes to the list of local representatives in the package leaflet. The updated RMP version 12.0 is also submitted
**5.3.21. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - EMEA/H/C/004750/II/0033/G, Orphan**

**Applicant:** Novartis Europharm Limited, ATMP

**PRAC Rapporteur:** Ulla Wändel Liminga

**Scope:** Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce additional guidance on liver function laboratory tests and monitoring before and after infusion and update information based on new safety information on the topic of acute liver failure (ALF) following two reports of fatal ALF. Update of sections 4.2 and 4.4 of the SmPC in order to provide additional guidance relevant to patient’s overall health status prior to dosing and to strengthen the existing description and guidance on systemic immune response. Update of the section 4.4 of the SmPC in order to indicate prompt attention to thrombotic microangiopathy (TMA) and to reflect the risk of life-threatening or fatal outcomes. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to update the Annex II

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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**5.3.22. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/II/0016**

**Applicant:** Bristol-Myers Squibb Pharma EEIG

**PRAC Rapporteur:** Maria del Pilar Rayon

**Scope:** Update of sections 4.2 and 5.2 of the SmPC in order to add a dose adjustment after completion of the dose escalation regimen in patients with mild or moderate chronic hepatic impairment (Child-Pugh class A or B) based on the final results from study RPC-1063-CP-004; this is a Phase I, multicenter, open-label study to evaluate the effect of mild or moderate hepatic impairment on the multiple-dose pharmacokinetics of ozanimod. The package leaflet is updated accordingly. The updated RMP version 5.0 has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

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**5.3.23. Pitolisant - WAKIX (CAP) - EMEA/H/C/002616/II/0030, Orphan**

**Applicant:** Bioprojet Pharma

**PRAC Rapporteur:** Kirsti Villikka

**Scope:** Extension of indication to include treatment of narcolepsy with or without cataplexy in adolescents and children from the age of 6 years, based on results from Study P11-06; an ongoing phase III, double-blind, multicentre, randomised, placebo-controlled trial undertaken to evaluate safety and efficacy of pitolisant in children from 6 to less than 18 years with narcolepsy with/without cataplexy. 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 7.0 of the RMP has also been submitted

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5 Advanced therapy medicinal product
**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.24. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - VAXNEUVANCE (CAP) - EMEA/H/C/005477/II/0013/G

Applicant: Merck Sharp & Dohme B.V.
PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped application comprising two type II variations as follows: 1) update sections 4.2, 4.4, 4.8, 5.1 of the SmPC in order to add safety data on recipients of haematopoietic stem cell transplant (HSCT) based on final results from study V114-022, listed as a category 3 study in the RMP; This is a Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of Vaxneuvance in Recipients of Allogeneic Hematopoietic Stem Cell Transplant; 2) update sections 4.2, 5.1 of the SmPC in order to update the information regarding a 3-dose regimen based on final results from study V114-026; a Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of a 3-dose Regimen of Vaxneuvance in Healthy Infants. The package leaflet is updated accordingly. The RMP version 2.1 has also been submitted.

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.25. Polatuzumab vedotin - POLIVY (CAP) - EMEA/H/C/004870/II/0018, Orphan

Applicant: Roche Registration GmbH
PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study GO29365 listed as a category 3 study in the RMP in order to address MEA/002. This is a phase Ib/II, multicenter, open-label study evaluating the safety, tolerability, and anti-tumor activity of polatuzumab vedotin in combination with rituximab or obinutuzumab plus bendamustine in patients with relapsed/refractory follicular lymphoma or relapsed/refractory diffuse large B-cell lymphoma. The RMP version 3.0 has also been submitted.

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.26. Remimazolam - BYFAVO (CAP) - EMEA/H/C/005246/X/0002

Applicant: Paion Deutschland GmbH
PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new pharmaceutical form associated with a new strength (50 mg powder for concentrate for solution for injection/infusion). The new presentation comes with a new indication to include the intravenous induction and maintenance of general anaesthesia (GA) in adults for Byfavo (remimazolam) 50 mg, based on final results from two pivotal trials: 1) study ONO-2745-05: a phase 2b/3, single-blind, randomised, parallel-group study assessing safety and efficacy in induction and maintenance of anaesthesia in American Society of Anesthesiologists (ASA) I/II patients (general surgery); 2) study CNS-7056-022: a phase 3, randomised, propofol controlled, parallel group, confirmatory single-blind efficacy and safety trial during induction and maintenance of anaesthesia in ASA III/IV patients. A new combined version of the SmPC,
labelling and package leaflet solely for the 50 mg strength and the GA indication is provided accordingly. The RMP (version 1.1) is updated accordingly. Finally, the MAH also requested an extension of the market protection by one additional year

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.27. Ripretinib - QINLOCK (CAP) - EMEA/H/C/005614/II/0004, Orphan

**Applicant:** Deciphera Pharmaceuticals (Netherlands) B.V.

**PRAC Rapporteur:** Željana Margan Koletić

**Scope:** Update of sections 4.2 and 5.2 of the SmPC in order to change posology recommendations in patients with hepatic impairment and update the description of pharmacokinetics based on final results from study DCC-2618-01-004: a phase 1 study of the pharmacokinetics, safety, and tolerability of ripretinib in subjects with hepatic impairment compared to healthy control subjects. The package leaflet and the RMP (version 2.0) are updated accordingly

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.28. Rituximab - RIXATHON (CAP) - EMEA/H/C/003903/WS2307/0062; RIXIMYO (CAP) - EMEA/H/C/004729/WS2307/0063

**Applicant(s):** Sandoz GmbH

**PRAC Rapporteur:** Anette Kirstine Stark

**Scope:** Update of section 4.1 of the SmPC in order to include the rapid infusion regimen (90 minutes) for second and subsequent infusions in the label for patients with non-Hodgkin’s lymphoma (NHL) or chronic lymphocytic leukaemia (CLL) based on non-interventional PASS CGP2013ES01R and scientific literature. The RMP version 7.0 has also been submitted

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

### 5.3.29. Tenofovir alafenamide - VEMLIDY (CAP) - EMEA/H/C/004169/II/0040

**Applicant:** Gilead Sciences Ireland UC

**PRAC Rapporteur:** Valentina Di Giovanni

**Scope:** Extension of indication to include treatment of chronic hepatitis B-infected children from 6 years and older and weighing at least 25 kilograms for Vemlidy, based on the interim results from Week 24 clinical study report (CSR) for Cohort 1 and Cohort 2 Group 1 and supporting modular summaries for the category 3 study GS-US-320-1092, ‘A randomised, double-blind evaluation of the pharmacokinetics, safety, and antiviral efficacy of tenofovir alafenamide (TAF) in children and adolescent subjects with chronic hepatitis B virus infection’. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. In addition, the MAH took the opportunity to update the wording in section 4.6 of the SmPC related to breastfeeding and pregnancies exposed to TAF, and to update the contact details of the local representative in Romania in the package leaflet. The RMP (version 8.2) is updated accordingly

**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP
5.3.30. **Tezepelumab - TEZSPIRE (CAP) - EMEA/H/C/005588/II/0001**

Applicant: AstraZeneca AB  
PRAC Rapporteur: Eva Jiřsová  
Scope: Addition of a new autoinjector (AI) presentation as an alternative method of administration, with consequential update to the product information. RMP (version 1.1) has been updated accordingly  
**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.31. **Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/II/0027**

Applicant: AbbVie Deutschland GmbH & Co. KG  
PRAC Rapporteur: Nikica Mirošević Skvrce  
Scope: Extension of indication to include treatment of moderately to severely active Crohn's disease in adult patients for RINVOQ, based on final results from three Phase III studies, two confirmatory placebo-controlled induction studies (Study M14 431/U-EXCEED/CD-1) and Study M14 433/U-EXCEL/CD-2) and a placebo-controlled maintenance/long-term extension study (Study M14-430/U-ENDURE/CD-3). M14-431 study is a Phase III, Multicenter, Randomised, Double-Blind, Placebo-Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Biologic Therapy. M14-433 study is a Phase III, Multicenter, Randomised, Double-Blind, Placebo Controlled Induction Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Moderately to Severely Active Crohn's Disease Who Have Inadequately Responded to or are Intolerant to Conventional and/or Biologic Therapies. M14-430 study is an ongoing Phase III, Multicenter, Randomised, Double-Blind, Placebo-Controlled Maintenance and Long-Term Extension Study of the Efficacy and Safety of Upadacitinib (ABT-494) in Subjects with Crohn's Disease Who Completed the Studies M14-431 or M14-433. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated in accordance. Version 11 of the RMP has also been submitted  
**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.32. **Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0096**

Applicant: Janssen-Cilag International N.V.  
PRAC Rapporteur: Rhea Fitzgerald  
Scope: Update of section 5.1 of the SmPC in order to update information with the 4-year clinical data in patients with ulcerative colitis based on the final report from study CNT01275UCO3001 listed as a category 3 study in the RMP; this is a phase 3, randomised, double blind, placebo-controlled, parallel-group, multicenter study to evaluate the safety and efficacy of ustekinumab induction and maintenance therapy in subjects with moderately to severely active ulcerative colitis. The RMP version 23.1 has also been submitted. In addition, the MAH took the opportunity to introduce a correction to the product information  
**Action:** For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to CHMP
6. Periodic safety update reports (PSURs)

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

6.1.1. Afamelanotide - SCENESSE (CAP) - PSUSA/00010314/202206

Applicant: Clinuvel Europe Limited
PRAC Rapporteur: Martin Huber
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

6.1.2. Alpelisib - PIQRAY (CAP) - PSUSA/00010871/202205

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

6.1.3. Amivantamab - RYBREVANT (CAP) - PSUSA/00010977/202205

Applicant: Janssen-Cilag International N.V.
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

6.1.4. Anakinra - KINERET (CAP) - PSUSA/00000209/202205 (with RMP)

Applicant: Swedish Orphan Biovitrum AB (publ)
PRAC Rapporteur: Anette Kirstine Stark
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

6.1.5. Artesunate - ARTESEinate AMIVAS (CAP) - PSUSA/00010958/202206

Applicant: Amivas Ireland Ltd
PRAC Rapporteur: Martin Huber
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP
6.1.6.  **Atidarsagene autotemcel - LIBMELDY (CAP) - PSUSA/00010899/202206**

Applicant: Orchard Therapeutics (Netherlands) B.V.
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

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6.1.7.  **Avatrombopag - DOPTELET (CAP) - PSUSA/00010779/202205**

Applicant: Swedish Orphan Biovitrum AB (publ)
PRAC Rapporteur: Monica Martinez Redondo
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

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6.1.8.  **Berotralstat - ORLADYO (CAP) - PSUSA/00010930/202206**

Applicant: BioCryst Ireland Limited
PRAC Rapporteur: Julia Pallos
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

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6.1.9.  **Binimetinib - MEKTOVI (CAP) - PSUSA/00010717/202206**

Applicant: Pierre Fabre Medicament
PRAC Rapporteur: Inês Ribeiro-Vaz
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

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6.1.10. **Buprenorphine ⁶ - SIXMO (CAP) - PSUSA/00010778/202205**

Applicant: L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A.
PRAC Rapporteur: Adam Przybylkowski
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

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6.1.11. **Cannabidiol ⁷ - EPIDYOLEX (CAP) - PSUSA/00010798/202206**

Applicant: GW Pharma (International) B.V.
PRAC Rapporteur: Ana Sofia Diniz Martins

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⁶ Implant(s) only
⁷ Centrally authorised product(s) only
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.12. Cholera vaccine, oral, live - VAXCHORA (CAP) - PSUSA/00010862/202206

Applicant: Emergent Netherlands B.V.
PRAC Rapporteur: Jean-Michel Dogné
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.13. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - PSUSA/00010912/202206

Applicant: AstraZeneca AB
PRAC Rapporteur: Jean-Michel Dogné
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP


Applicant: Novavax CZ, a.s.
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.15. Delafloxacin - QUOFENIX (CAP) - PSUSA/00010822/202206

Applicant: A. Menarini Industrie Farmaceutiche Riunite s.r.l.
PRAC Rapporteur: Željana Margan Koletić
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.16. Efmoroctocog alfa - ELOCTA (CAP) - PSUSA/00010451/202206

Applicant: Swedish Orphan Biovitrum AB (publ)
PRAC Rapporteur: Sonja Hrabcik
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP
6.1.17. Elasomeran - SPIKEVAX (CAP) - PSUSA/00010897/202206

Applicant: Moderna Biotech Spain, S.L.
PRAC Rapporteur: Marie Louise Schougaard Christiansen
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.18. Encorafenib - BRAFTOVI (CAP) - PSUSA/00010719/202206

Applicant: Pierre Fabre Medicament
PRAC Rapporteur: Rugile Pilviniene
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.19. Enfortumab vedotin - PADCEV (CAP) - PSUSA/00010989/202206

Applicant: Astellas Pharma Europe B.V.
PRAC Rapporteur: Eva Jirsová
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.20. Entrectinib - ROZLYTREK (CAP) - PSUSA/00010874/202206

Applicant: Roche Registration GmbH
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.21. Fenfluramine - FINTEPLA (CAP) - PSUSA/00010907/202206

Applicant: Zogenix ROI Limited
PRAC Rapporteur: Martin Huber
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.22. Formoterol fumarate dihydrate, glycopyrronium bromide, budesonide - RILTRAVA AEROSPHERE (CAP); TRIXEO AEROSPHERE (CAP) - PSUSA/00010908/202206

Applicant(s): AstraZeneca AB
PRAC Rapporteur: Jan Neuhauser
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.23. Galsulfase - NAGLAZYME (CAP) - PSUSA/00001515/202205

Applicant: BioMarin International Limited  
PRAC Rapporteur: Ana Sofia Diniz Martins  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

### 6.1.24. Glasdegib - DAURISMO (CAP) - PSUSA/00010859/202205

Applicant: Pfizer Europe MA EEIG  
PRAC Rapporteur: Menno van der Elst  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

### 6.1.25. Glibenclamide\(^8\) - AMGLIDIA (CAP) - PSUSA/00010690/202205

Applicant: Ammtek  
PRAC Rapporteur: Maria del Pilar Rayon  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

### 6.1.26. Human papillomavirus 9-valent vaccine (recombinant, adsorbed) - GARDASIL 9 (CAP) - PSUSA/00010389/202206

Applicant: Merck Sharp & Dohme B.V.  
PRAC Rapporteur: Jean-Michel Dogné  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

### 6.1.27. Human papillomavirus vaccine (rDNA\(^9\)) - 4-valent - GARDASIL (CAP) - PSUSA/00001634/202205

Applicant: Merck Sharp & Dohme B.V.  
PRAC Rapporteur: Ulla Wändel Liminga  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

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\(^8\) Centrally authorised product(s) only  
\(^9\) Ribosomal deoxyribonucleic acid
6.1.28. Hydroxycarbamide\(^{10}\) - SIKLOS (CAP); XROMI (CAP) - PSUSA/00001692/202206

**Applicant(s):** Addmedica S.A.S. (Siklos), Nova Laboratories Ireland Limited (Xromi)

**PRAC Rapporteur:** Jo Robays

**Scope:** Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.29. Imiglucerase - CEREZYME (CAP) - PSUSA/00001727/202205

**Applicant:** Genzyme Europe BV

**PRAC Rapporteur:** Liana Gross-Martirosyan

**Scope:** Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.30. Inclisiran - LEQVIO (CAP) - PSUSA/00010904/202206

**Applicant:** Novartis Europharm Limited

**PRAC Rapporteur:** Kimmo Jaakkola

**Scope:** Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.31. Indacaterol, mometasone furoate - ATECTURA BREEZHALER (CAP); BEMRIST BREEZHALER (CAP) - PSUSA/00010850/202205

**Applicant(s):** Novartis Europharm Limited

**PRAC Rapporteur:** Jan Neuhauser

**Scope:** Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.32. Inebilizumab - UPLIZNA (CAP) - PSUSA/00010996/202206

**Applicant:** Horizon Therapeutics Ireland DAC

**PRAC Rapporteur:** Amelia Cupelli

**Scope:** Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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6.1.33. Larotrectinib - VITRAKVI (CAP) - PSUSA/00010799/202205

**Applicant:** Bayer AG

**PRAC Rapporteur:** Rugile Pilviniene

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\(^{10}\) Centrally authorised product(s) only
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<tr>
<th>Scope: Evaluation of a PSUSA procedure</th>
<th>Action: For adoption of recommendation to CHMP</th>
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### 6.1.34. Latanoprost, netarsudil - ROCLANDA (CAP) - PSUSA/00010905/202206

Applicant: Santen Oy  
PRAC Rapporteur: Adam Przybyłkowski  
Scope: Evaluation of a PSUSA procedure  
Action: For adoption of recommendation to CHMP

### 6.1.35. Levodopa - INBRIJA (CAP) - PSUSA/00107800/202206

Applicant: Acorda Therapeutics Ireland Limited  
PRAC Rapporteur: Nikica Mirošević Skvrce  
Scope: Evaluation of a PSUSA procedure  
Action: For adoption of recommendation to CHMP

### 6.1.36. Levofloxacin\(^1\) - QUINSAIR (CAP) - PSUSA/00010429/202205

Applicant: Chiesi Farmaceutici S.p.A.  
PRAC Rapporteur: Maria del Pilar Rayon  
Scope: Evaluation of a PSUSA procedure  
Action: For adoption of recommendation to CHMP

### 6.1.37. Lidocaine, prilocaine\(^12\) - FORTACIN (CAP) - PSUSA/00010110/202205

Applicant: Recordati Ireland Ltd  
PRAC Rapporteur: Maria del Pilar Rayon  
Scope: Evaluation of a PSUSA procedure  
Action: For adoption of recommendation to CHMP

### 6.1.38. Luspatercept - REBLOZYL (CAP) - PSUSA/00010860/202206

Applicant: Bristol-Myers Squibb Pharma EEIG  
PRAC Rapporteur: Jo Robays  
Scope: Evaluation of a PSUSA procedure  
Action: For adoption of recommendation to CHMP

\(^1\) For inhalation use only  
\(^12\) Centrally authorised product(s) only
6.1.39. **Netarsudil - RHOKIINSA (CAP) - PSUSA/00107812/202206**

Applicant: Santen Oy  
PRAC Rapporteur: Maria del Pilar Rayon  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

6.1.40. **Nirmatrelvir, ritonavir - PAXLOVID (CAP) - PSUSA/00010984/202206**

Applicant: Pfizer Europe MA EEIG  
PRAC Rapporteur: Martin Huber  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

6.1.41. **Nonacog beta pegol - REFIXIA (CAP) - PSUSA/00010608/202205**

Applicant: Novo Nordisk A/S  
PRAC Rapporteur: Brigitte Keller-Stanislawski  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

6.1.42. **Nusinersen - SPINRAZA (CAP) - PSUSA/00010595/202205**

Applicant: Biogen Netherlands B.V.  
PRAC Rapporteur: Ulla Wändel Liminga  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

6.1.43. **Obeticholic acid - OCALIVA (CAP) - PSUSA/00010555/202205**

Applicant: Advanz Pharma Limited  
PRAC Rapporteur: Liana Gross-Martirosyan  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CHMP

6.1.44. **Onasemnogene abeparvovec - ZOLGENSMA (CAP) - PSUSA/00010848/202205**

Applicant: Novartis Europharm Limited, ATMP\(^{13}\)  
PRAC Rapporteur: Ulla Wändel Liminga

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\(^{13}\) Advanced therapy medicinal product
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CAT and CHMP

### 6.1.45. Pandemic influenza vaccine (H5N1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRazeneca (CAP) - PSUSA/00010501/202205

Applicant: AstraZeneca AB
PRAC Rapporteur: Sonja Hrabcik
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.46. Pegvaliase - PALYNZIQ (CAP) - PSUSA/00010761/202205

Applicant: BioMarin International Limited
PRAC Rapporteur: Rhea Fitzgerald
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.47. Pertuzumab, trastuzumab - PHESGO (CAP) - PSUSA/00010906/202206

Applicant: Roche Registration GmbH
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.48. Pixantrone - PIXUVRI (CAP) - PSUSA/00009261/202205

Applicant: Les Laboratoires Servier
PRAC Rapporteur: Kimmo Jaakkola
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.49. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - APEXXNAR (CAP) - PSUSA/00010981/202206

Applicant: Pfizer Europe MA EEIG
PRAC Rapporteur: Jean-Michel Dogné
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP
6.1.50. Polatuzumab vedotin - POLIVY (CAP) - PSUSA/00010817/202206

Applicant: Roche Registration GmbH
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.51. Relugolix, estradiol, norethisterone acetate - RYEQO (CAP) - PSUSA/00010942/202205

Applicant: Gedeon Richter Plc.
PRAC Rapporteur: Martin Huber
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.52. Roxadustat - EVRENZO (CAP) - PSUSA/00010955/202206

Applicant: Astellas Pharma Europe B.V.
PRAC Rapporteur: Anna Mareková
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.53. Rucaparib - RUBRACA (CAP) - PSUSA/00010694/202206

Applicant: Clovis Oncology Ireland Limited
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.54. Satralizumab - ENSPRYNG (CAP) - PSUSA/00010944/202205

Applicant: Roche Registration GmbH
PRAC Rapporteur: Jan Neuhauser
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.55. Semaglutide - OZEMPIC (CAP); RYBELSUS (CAP); WEGOVY (CAP) - PSUSA/00010671/202205

Applicant(s): Novo Nordisk A/S
PRAC Rapporteur: Mari Thorn
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.56. Setmelanotide - IMCIVREE (CAP) - PSUSA/00010941/202205

Applicant: Rhythm Pharmaceuticals Netherlands B.V.,
PRAC Rapporteur: Anna Mareková
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.57. Shingles (herpes zoster) vaccine (live) - ZOSTAVAX (CAP) - PSUSA/00009289/202205

Applicant: Merck Sharp & Dohme B.V.
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.58. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - PSUSA/00010524/202206

Applicant: Gilead Sciences Ireland UC
PRAC Rapporteur: Ana Sofia Diniz Martins
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.59. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/202206

Applicant: Sun Pharmaceutical Industries Europe B.V.
PRAC Rapporteur: Željana Margan Koletić
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.60. Sotorasib - LUMYKRAS (CAP) - PSUSA/00010970/202205

Applicant: Amgen Europe B.V.
PRAC Rapporteur: Marie Louise Schougaard Christiansen
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP
### 6.1.61. Tirbanibulin - KLISYRI (CAP) - PSUSA/00010943/202206

Applicant: Almirall, S.A.
PRAC Rapporteur: Anna Mareková
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.62. Tozinameran - COMIRNATY (CAP) - PSUSA/00010898/202206

Applicant: BioNTech Manufacturing GmbH
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.63. Tralokinumab - ADTRALZA (CAP) - PSUSA/00010937/202206

Applicant: LEO Pharma A/S
PRAC Rapporteur: Kimmo Jaakkola
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.64. Trametinib - MEKINIST (CAP) - PSUSA/00010262/202205

Applicant: Novartis Europharm Limited
PRAC Rapporteur: David Olsen
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.65. Trastuzumab deruxtecan - ENHERTU (CAP) - PSUSA/00010894/202206

Applicant: Daiichi Sankyo Europe GmbH
PRAC Rapporteur: Inês Ribeiro-Vaz
Scope: Evaluation of a PSUSA procedure
**Action:** For adoption of recommendation to CHMP

### 6.1.66. Treosulfan14 - TRECONDI (CAP) - PSUSA/00010777/202206

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH
PRAC Rapporteur: Julia Pallos

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14 Centrally authorised product(s) only
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

### 6.1.67. Turoctocog alfa pegol - ESPEROCT (CAP) - PSUSA/00010782/202206

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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

#### 6.2.1. Dasatinib - SPRYCEL (CAP); NAP - PSUSA/00000935/202206

Applicants: Bristol-Myers Squibb Pharma EEIG (Sprycel), various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.2.2. Naloxone\(^{15}\) - NYXOID (CAP); NAP - PSUSA/00010657/202205

Applicants: Mundipharma Corporation (Ireland) Limited (Nyxoid), various

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.2.3. Nepafenac - NEVANAC (CAP); NAP - PSUSA/00002143/202205

Applicants: Novartis Europharm Limited (Nevanac), various

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

#### 6.2.4. Treprostinil - TREPULMIX (CAP); NAP - PSUSA/00003013/202205

Applicants: SciPharm Sarl (Trepulmix), various

PRAC Rapporteur: Zane Neikena

\(^{15}\) For use in non-medical setting(s) only
Scope: Evaluation of a PSUSA procedure

**Action:** For adoption of recommendation to CHMP

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

#### 6.3.1. Alteplase (NAP) - PSUSA/00000112/202205

- **Applicant(s):** various
- **PRAC Lead:** Martin Huber
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

#### 6.3.2. Amikacin\(^{16}\) (NAP) - PSUSA/00000143/202206

- **Applicant(s):** various
- **PRAC Lead:** Maia Uusküla
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

#### 6.3.3. Bemiparin (NAP) - PSUSA/00000312/202204

- **Applicant(s):** various
- **PRAC Lead:** Monica Martinez Redondo
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

#### 6.3.4. Betaxolol (NAP) - PSUSA/00000401/202205

- **Applicant(s):** various
- **PRAC Lead:** Melinda Palfi
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

#### 6.3.5. Calcifediol (NAP) - PSUSA/00000491/202206

- **Applicant(s):** various
- **PRAC Lead:** Martin Huber
- **Scope:** Evaluation of a PSUSA procedure

\(^{16}\) Except for centrally authorised products
**Action:** For adoption of recommendation to CMDh

### 6.3.6. Diltiazem (NAP) - PSUSA/00001084/202205

- **Applicant(s):** various
- **PRAC Lead:** Anette Kirstine Stark
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

### 6.3.7. Eprosartan (NAP) - PSUSA/00001243/202204

- **Applicant(s):** various
- **PRAC Lead:** Martin Huber
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

### 6.3.8. Eprosartan, hydrochlorothiazide (NAP) - PSUSA/00001244/202204

- **Applicant(s):** various
- **PRAC Lead:** Martin Huber
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

### 6.3.9. Esomeprazole, naproxen (NAP) - PSUSA/00001270/202204

- **Applicant(s):** various
- **PRAC Lead:** Liana Gross-Martirosyan
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

### 6.3.10. Fusidic acid\(^{17}\) (NAP) - PSUSA/00010226/202205

- **Applicant(s):** various
- **PRAC Lead:** Melinda Palfi
- **Scope:** Evaluation of a PSUSA procedure
- **Action:** For adoption of recommendation to CMDh

### 6.3.11. Ibuprofen, pseudoephedrine (NAP) - PSUSA/00001711/202207

- **Applicant(s):** various

\(^{17}\) Systemic use
6.3.12. **Lanreotide (NAP) - PSUSA/00001826/202205**

Applicant(s): various  
PRAC Lead: Zane Neikena  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.13. **Latanoprost, timolol (NAP) - PSUSA/00001833/202206**

Applicant(s): various  
PRAC Lead: Ulla Wändel Liminga  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.14. **Levomethadone (NAP) - PSUSA/00001855/202205**

Applicant(s): various  
PRAC Lead: Jan Neuhauser  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.15. **Levonorgestrel**\(^\text{18}\) (NAP) - PSUSA/00010827/202205

Applicant(s): various  
PRAC Lead: Martin Huber  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.16. **Levofloxacin, dexamethasone**\(^\text{19}\) (NAP) - PSUSA/00010881/202206

Applicant(s): various  
PRAC Lead: Amelia Cupelli  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

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\(^{18}\) For emergency contraception only  
\(^{19}\) Ocular use
6.3.17.  **Macrogol 3350 (NAP) - PSUSA/00001924/202205**

Applicant(s): various  
PRAC Lead: Amelia Cupelli  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.18.  **Macrogol 4000, macrogol 4000 combinations\(^{20}\) (NAP) - PSUSA/00010392/202205**

Applicant(s): various  
PRAC Lead: Nathalie Gault  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.19.  **Methadone (NAP) - PSUSA/00002004/202205**

Applicant(s): various  
PRAC Lead: Ronan Grimes  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.20.  **Nicardipine (NAP) - PSUSA/00002149/202205**

Applicant(s): various  
PRAC Lead: Amelia Cupelli  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.21.  **Olsalazine (NAP) - PSUSA/00002213/202205**

Applicant(s): various  
PRAC Lead: Kirsti Villikka  
Scope: Evaluation of a PSUSA procedure  
**Action:** For adoption of recommendation to CMDh

6.3.22.  **Piracetam (NAP) - PSUSA/00002429/202204**

Applicant(s): various  
PRAC Lead: Kirsti Villikka
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.23. **Procyanidolic oligomers (NAP) - PSUSA/00002537/202205**

Applicant(s): various
PRAC Lead: Melinda Palfi
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.24. **Risperidone (NAP) - PSUSA/00002649/202205**

Applicant(s): various
PRAC Lead: Martin Huber
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.25. **Sodium tetradecyl sulphate (NAP) - PSUSA/00002767/202204**

Applicant(s): various
PRAC Lead: Ronan Grimes
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.26. **Tirofiban (NAP) - PSUSA/00002974/202205**

Applicant(s): various
PRAC Lead: Martin Huber
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.27. **Tolperisone (NAP) - PSUSA/00002991/202206**

Applicant(s): various
PRAC Lead: Melinda Palfi
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.28. **Valsartan (NAP), hydrochlorothiazide, valsartan (NAP) - PSUSA/00010396/202204**

Applicant(s): various
PRAC Lead: Mari Thorn
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

6.3.29. **Venlafaxine (NAP) - PSUSA/00003104/202205**

Applicant(s): various
PRAC Lead: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CMDh

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

6.4.1. **Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/LEG 008**

Applicant: Sanofi Winthrop Industrie
PRAC Rapporteur: Kimmo Jaakkola
Scope: Submission of an update of the Safety Evaluation Report (SER), addressing cutaneous T-cell lymphoma (CTCL) and dupilumab presented in the PSUR process 2021 and a discussion on the reasons for the higher than anticipated number of CTCL cases reported and whether conclusions of the SER are still valid (following PSUSA/00010645/2022203 concluded in November 2022)
Action: For adoption of advice to CHMP

6.4.2. **Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 028.6**

Applicant: Takeda Pharma A/S
PRAC Rapporteur: Tiphaine Vaillant
Scope: Sixth six-monthly update on the development of the child-resistant multi-dose nasal spray DoseGuard as requested in the conclusions of procedure R/0049 finalised in April 2019
Action: For adoption of advice to CHMP

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

6.5.1. **Baricitinib - OLMIANT (CAP) - EMEA/H/C/004085/II/0031**

Applicant: Eli Lilly Nederland B.V.
PRAC Rapporteur: Adam Przybylkowski
Scope: Update of section 4.4 of the SmPC in order to add new warnings on major adverse cardiac events (MACE) and amend an existing warning on malignancy and venous
thromboembolism (VTE) as requested in the conclusions of the last PSUR single assessment (PSUSA) procedure (PSUSA/00010578/202102) adopted in September 2021 and based on interim results from study I4V-MC-B023: a retrospective observational study to compare baricitinib relative to the standard of care. The package leaflet and the RMP (version 13.1) are updated accordingly. In addition, the MAH submitted a proposal for a direct healthcare professional communication (DHPC) and a communication plan.

**Action:** For adoption of PRAC Assessment Report

### 6.5.2. Erlotinib - TARCEVA (CAP) - EMEA/H/C/000618/II/0071

**Applicant:** Roche Registration GmbH  
**PRAC Rapporteur:** Marie Louise Schougaard Christiansen  
**EMA resources:** PL: Andrada Armasu; RMS: Andrada Armasu  
**Scope:** Update of section 4.8 of the SmPC in order to provide a single table listing all ADRs following PSUSA/00001255/202111. The package leaflet is updated accordingly

**Action:** For adoption of PRAC Assessment Report

### 6.5.3. Nirmatrelvir, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/II/0032

**Applicant:** Pfizer Europe MA EEIG  
**PRAC Rapporteur:** Martin Huber  
**Scope:** Update of section 4.8 of the SmPC in order to add ‘hypertension’ to the list of adverse drug reactions (ADRs) with frequency ‘uncommon’, following procedure EMEA/H/C/005973/LEG 006 (LEG assessed by PRAC), based on review of aggregated post-marketing data. The package leaflet is updated accordingly

**Action:** For adoption of PRAC Assessment Report

### 6.5.4. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/II/0152

**Applicant:** BioNTech Manufacturing GmbH  
**PRAC Rapporteur:** Menno van der Elst  
**Scope:** Update of section 4.8 of the SmPC, upon request by PRAC following the assessment of EMEA/H/C/PSUSA/00010898/202112, to add “dizziness” to the list of adverse drug reactions (ADRs) with frequency Uncommon. The package leaflet is updated accordingly

**Action:** For adoption of PRAC Assessment Report
6.6.  Expedited summary safety reviews

6.6.1.  Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 009.4

Applicant: Valneva Austria GmbH
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Fifth expedited summary safety report (SSR) for covid-19 vaccine (inactivated, adjuvanted) Valneva during the coronavirus disease (COVID-19) pandemic
Action: For adoption of PRAC Assessment Report

6.6.2.  Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 014.7

Applicant: Novavax CZ, a.s.
PRAC Rapporteur: Brigitte Keller-Stanislawski
Scope: Eighth expedited summary safety report (SSR) for Nuvaxovid (COVID-19 vaccine (recombinant, adjuvanted)) during the coronavirus disease (COVID-19) pandemic
Action: For adoption of PRAC Assessment Report

7.  Post-authorisation safety studies (PASS)

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

7.1.1.  Buprenorphine - SIXMO (CAP) - EMEA/H/C/PSA/S/0097

Applicant: L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A.
PRAC Rapporteur: Adam Przybylkowski
Scope: Substantial amendment to a protocol for a prospective, observational (non-interventional), post-authorisation safety cohort study to evaluate the incidence of the breakages and insertion/removal complications of buprenorphine implants (Sixmo) in routine clinical care
Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.2.  Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/PSA/S/0101

Applicant: Amgen Europe B.V.

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21 Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC
22 In accordance with Article 107n of Directive 2001/83/EC
PRAC Rapporteur: Eva Jirsová

Scope: Substantial amendment to a protocol for an observational study of blinatumomab safety and effectiveness, utilisation, and treatment practices

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.3. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/PSP/S/0099.1

Applicant: Janssen-Cilag International NV, ATMP23

PRAC Rapporteur: Jo Robays

Scope: MAH’s response to PSP/0099 [A Long-term Follow-up Study for Participants Previously Treated with Ciltacabtagene Autoleucel to collect data on delayed adverse events after administration of cilta-cel, and to characterize and understand the long-term safety profile of cilta-cel] as per the request to supplementary information (RSI) adopted in September 2022

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.4. Evinacumab - EVKEEZA (CAP) - EMEA/H/C/PSA/S/0098

Applicant: Regeneron Ireland DAC

PRAC Rapporteur: Mari Thorn

Scope: Substantial amendment to a protocol for an evaluation of the long-term effects of evinacumab treatment in patients with homozygous familial hypercholesterolemia (HoFH): safety outcomes in patients with HoFH who are ≥12 years old, frequency and outcomes of pregnancy in female patients with HoFH, atherosclerosis process over time in patients with HoFH who undergo cardiovascular imaging (as data allow), frequency of cardiovascular imaging of patients with HoFH

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.5. Methylphenidate hydrochloride (NAP) - EMEA/H/N/PSA/S/0074.2

Applicant: MEDICE Arzneimittel Pütter GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: MAH’s response to PSA/S/0074.1 [Interim study report for a protocol previously agreed in September 2021 (PSA/S/0074): a multicentre, observational, prospective PASS to evaluate the safety concerns of long-term cardiovascular and psychiatric risks within the adult attention deficit/hyperactivity disorder (ADHD) population taking Medikinet Retard (methylphenidate hydrochloride) according to normal standard clinical practice]

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

7.1.6. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/PSA/S/0099

Applicant: Novartis Europharm Limited, ATMP24

23 Advanced therapy medicinal product
PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Substantial amendment #05 to a protocol for a registry study to assess the long-term safety of patients with B lymphocyte malignancies treated with tisagenlecleucel

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

### 7.1.7. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/PSA/S/0100

Applicant: Novartis Europharm Limited, ATMP

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Substantial amendment #06 to a protocol for a registry study to assess the long-term safety of patients with B lymphocyte malignancies treated with tisagenlecleucel

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

### 7.1.8. Valproate (NAP) - EMEA/H/N/PSP/J/0075.9

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Fourth interim report and Statistical Analysis Plan v6.0 for drug utilisation study (DUS) extension (DUS ext.) to assess the effectiveness of the new risk minimisation measures and to further characterise the prescribing patterns for valproate and related substances

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

### 7.1.9. Valproate (NAP) - EMEA/H/N/PSP/J/0075.10

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Responses to the RSI of the third interim report and updated protocol (version 10) for drug utilisation study (DUS) extension (DUS ext.) to assess the effectiveness of the new risk minimisation measures and to further characterise the prescribing patterns for valproate and related substances

Action: For adoption of PRAC Assessment Report, PRAC outcome letter

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24 Advanced therapy medicinal product
25 Advanced therapy medicinal product
26 Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpromide, valproate bismuth, calcium valproate, valproate magnesium
27 Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpromide, valproate bismuth, calcium valproate, valproate magnesium
7.2. Protocols of PASS non-imposed in the marketing authorisation(s)28

7.2.1. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 002.1

Applicant: Pfizer Europe MA EEIG
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: MAH's response to MEA 002 [Protocol for study B7451084: an active surveillance study to monitor the real-world safety of abrocitinib among patients with atopic dermatitis (AD) in the EU. The objective of the study is to estimate the incidence rates of safety endpoints of interest among AD patients receiving abrocitinib and AD patients receiving appropriate systemic treatments including dupilumab for AD in a real-world setting] as per the request to supplementary information (RSI) as adopted in September 2022
Action: For adoption of advice to CHMP

7.2.2. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 003.1

Applicant: Pfizer Europe MA EEIG
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: MAH's responses to MEA 003 [Protocol for study B7451085: a drug utilisation study to evaluate the effectiveness of risk minimisation measures (RMMs) for abrocitinib in the EU using electronic healthcare data. The study objectives will be to evaluate indicators of HCP's adherence to the risk minimisation measures in accordance with the abrocitinib SmPC and prescriber brochure] as per the request to supplementary information (RSI) adopted in September 2022
Action: For adoption of advice to CHMP

7.2.3. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/MEA 004.1

Applicant: Pfizer Europe MA EEIG
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: MAH's response to MEA 004 [Protocol for study B7451015: an adolescent imaging substudy to evaluate if abrocitinib has any clinically meaningful effects on bone growth and development] as per the request to supplementary information (RSI) as adopted in September 2022
Action: For adoption of advice to CHMP

7.2.4. Avalglucosidase alfa - NEXVIADYME (CAP) - EMEA/H/C/005501/MEA 007

Applicant: Genzyme Europe BV
PRAC Rapporteur: Liana Gross-Martirosyan
Scope: Protocol for study OBS17445 (listed as category 3 study in the RMP): a PASS to

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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
assess long term safety in patients with Pompe disease treated with avalglucosidase alfa in the commercial setting

**Action:** For adoption of advice to CHMP

### 7.2.5. Beclometasone, formoterol, glycopyrronium bromide - TRIMBOW (CAP) - EMEA/H/C/004257/MEA 002.3

**Applicant:** Chiesi Farmaceutici S.p.A.

**PRAC Rapporteur:** Jan Neuhauser

**Scope:** Amendment to a previously agreed protocol for study CLI-05993BA1-05 (TRIBE) (listed as category 3 study in the RMP): a multinational database cohort study to assess adverse cardiovascular and cerebrovascular outcomes in patients with chronic obstructive pulmonary disease initiating a fixed triple therapy containing beclometasone dipropionate, formoterol fumarate and glycopyrronium administered via dry powder inhaler (DPI) compared to pressurised metered dose inhaler (pMDI)

**Action:** For adoption of advice to CHMP

### 7.2.6. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 007.7

**Applicant:** AstraZeneca AB

**PRAC Rapporteur:** Jean-Michel Dogné

**Scope:** Amendment to a previously agreed protocol (version 4) for study D8111R00006 (listed as category 3 study in the RMP): A post-authorisation/post-marketing observational study using existing secondary health data sources to evaluate the association between exposure to AZD1222 and safety concerns

**Action:** For adoption of advice to CHMP

### 7.2.7. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 008.1

**Applicant:** AstraZeneca AB

**PRAC Rapporteur:** Jean-Michel Dogné

**Scope:** Protocol for a systematic literature review for studies evaluating adverse events of Vaxzevria (AZD1222) in patients taking immunosuppressant medications and/or with primary immunodeficiency

**Action:** For adoption of advice to CHMP

### 7.2.8. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 004.2

**Applicant:** Novavax CZ, a.s.

**PRAC Rapporteur:** Brigitte Keller-Stanislawski

**Scope:** MAH’s response to MEA 004.1 [protocol for study 2019nCoV-402: UK Post-
Authorisation Safety Study Using the Clinical Practice Research Datalink (CPRD): A surveillance study to characterize the safety profile of Nuvaxovid in adults aged 18 years and older in the real-world setting using the UK CPRD] as per request for supplementary information (RSI) adopted in November 2022.

**Action:** For adoption of advice to CHMP

### 7.2.9. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 006.5

**Applicant:** Eli Lilly Nederland B.V.

**PRAC Rapporteur:** Amelia Cupelli

**Scope:** Amendment to a previously agreed protocol for study H9X-MC-B013 (listed as category 3 study in the RMP): a non-interventional retrospective study to estimate the incidence rates of events of interest among type 2 diabetes mellitus (T2DM) patients treated with dulaglutide compared to other glucagon-like peptide 1 (GLP-1) receptor agonists in order to better characterise the safety profile of dulaglutide in terms of acute pancreatitis, pancreatic and thyroid malignancies.

**Action:** For adoption of advice to CHMP

### 7.2.10. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 072

**Applicant:** Moderna Biotech Spain, S.L.

**PRAC Rapporteur:** Marie Louise Schougaard Christiansen

**Scope:** Protocol for study mRNA-1273-P919 (listed as category 3 study in the RMP): an observational study to assess maternal and infant outcomes following exposure to Spikevax during pregnancy and to assess whether the rate of pregnancy complications, adverse pregnancy outcomes, or adverse neonatal outcomes is associated with prenatal exposure to Spikevax.

**Action:** For adoption of advice to CHMP

### 7.2.11. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 034.5

**Applicant:** Moderna Biotech Spain, S.L.

**PRAC Rapporteur:** Marie Louise Schougaard Christiansen

**Scope:** MAH's response to MEA 034.4 [protocol for study mRNA-1273-P905 monitoring the safety of Spikevax (COVID-19 vaccine) in pregnancy: an observational study using routinely collected health data in five European countries] as per the request for supplementary information (RSI) adopted in September 2022 together with a revised protocol (v 1.2) and the second interim report.

**Action:** For adoption of advice to CHMP

### 7.2.12. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 005.4

**Applicant:** Zogenix ROI Limited

**PRAC Rapporteur:** Martin Huber
Scope: MAH's response to MEA 005.3 [Protocol for study ZX008-2102: a drug utilisation study (DUS) in Europe to describe fenfluramine use in routine clinical practice] as per the request for supplementary information (RSI) adopted in September 2022

**Action:** For adoption of advice to CHMP

### 7.2.13. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 004.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Amendment to a previously agreed protocol for study I5Q-MC-B001: galcanezumab US drug utilisation and safety outcomes study to describe, in real-world clinical practice, the utilisation of galcanezumab in the US, and the incidence of important safety outcomes such as serious hypersensitivity and long-term safety including serious cardiovascular events, and malignancies

**Action:** For adoption of advice to CHMP

### 7.2.14. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/MEA 001.6

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Amendment to a previously agreed protocol (v.1.6) for study P19-633: a post-marketing registry-based prospective cohort study of long-term safety of risankizumab in real world setting in Denmark and Sweden

**Action:** For adoption of advice to CHMP

### 7.2.15. Tixagevimab, cilgavimab - EVUSHELD (CAP) - EMEA/H/C/005788/MEA 012

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Protocol for study D8850R00006: a Non-interventional Multi-country Cohort Study to Assess the Safety of EVUSHELD (Tixagevimab/Cilgavimab) During Pregnancy

**Action:** For adoption of advice to CHMP

### 7.2.16. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 003.2

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Amendment to a previously agreed protocol for study P19-150: a long-term post-authorisation safety study (PASS) of upadacitinib use in rheumatoid arthritis (RA) patients in Europe to evaluate the safety of upadacitinib among patients with RA receiving routine clinical care to include additional study outcomes of bone fractures and add further clarification that the malignancy outcomes will be stratified for malignancies excluding NMSC and NMSC, separately (RMP version 6.2)
**Action:** For adoption of advice to CHMP

### 7.2.17. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 004.2

** Applicant:** AbbVie Deutschland GmbH & Co. KG  
**PRAC Rapporteur:** Nikica Mirošević Skvrce  
**Scope:** Amendment to a previously agreed protocol for study P19-141: a long-term post-authorisation safety study (PASS) of upadacitinib use in rheumatoid arthritis (RA) patients in the US in order to: 1) compare the incidence of malignancy, non-melanoma skin cancer (NMSC), major adverse cardiovascular events (MACE), venous thromboembolism (VTE) and serious infection events in adults with RA who receive upadacitinib in the course of routine clinical care relative to those who receive biologic therapy for the treatment of RA; 2) describe the incidence rates of herpes zoster, opportunistic infections and evidence of drug-induced liver injury (DILI); 3) describe the incidence of the above outcomes in very elderly patients (aged $\geq 75$ years); 4) characterise VTE clinical risk factors and baseline biomarkers in a sub-study of new initiators of upadacitinib and comparator biologic therapies  
**Action:** For adoption of advice to CHMP

### 7.2.18. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 012.2

** Applicant:** AbbVie Deutschland GmbH & Co. KG  
**PRAC Rapporteur:** Nikica Mirošević Skvrce  
**Scope:** MAH’s response to MEA 012.1 [protocol for study P21-825: an evaluation of the effectiveness of additional risk minimisation measures for upadacitinib in the treatment of atopic dermatitis] as per the request for supplementary information (RSI) adopted in September 2022  
**Action:** For adoption of advice to CHMP

### 7.2.19. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 014.2

** Applicant:** AbbVie Deutschland GmbH & Co. KG  
**PRAC Rapporteur:** Nikica Mirošević Skvrce  
**Scope:** MAH’s response to MEA 014.1 [protocol for study P21-824: a study of growth and development in adolescents with atopic dermatitis who receive upadacitinib] as per request for supplementary information (RSI) adopted in September 2022  
**Action:** For adoption of advice to CHMP

### 7.2.20. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 016

** Applicant:** AbbVie Deutschland GmbH & Co. KG  
**PRAC Rapporteur:** Nikica Mirošević Skvrce  
**Scope:** Protocol for study P23-479: Drug Utilization Study for Evaluation of the Effectiveness of Additional Risk Minimisation Measures for Upadacitinib in the Treatment of Ulcerative Colitis in Sweden and Denmark
**Action:** For adoption of advice to CHMP

### 7.2.21. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 017

**Applicant:** AbbVie Deutschland GmbH & Co. KG

**PRAC Rapporteur:** Nikica Mirošević Skvrce

**Scope:** Protocol for study P23-480: Comparative Cohort Study of Long-term Safety of Upadacitinib for the Treatment of Ulcerative Colitis in a Real-world Setting in Sweden and Denmark

**Action:** For adoption of advice to CHMP

### 7.2.22. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 053.2

**Applicant:** Janssen-Cilag International N.V.

**PRAC Rapporteur:** Rhea Fitzgerald

**Scope:** MAH’s response to MEA 053.1 [protocol for study CNTO1275PSO4005: a Nordic database initiative for exposure to ustekinumab - a review and analysis of major adverse cardiovascular events (MACE) from the Swedish and Danish national registry systems] as per the request for supplementary information (RSI) adopted in October 2022

**Action:** For adoption of advice to CHMP

### 7.2.23. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 054.2

**Applicant:** Janssen-Cilag International N.V.

**PRAC Rapporteur:** Rhea Fitzgerald

**Scope:** MAH’s response to MEA 054.1 [protocol for study PCSIMM004697: An Observational Longitudinal PASS of STELARA in the Treatment of Psoriasis and Psoriatic Arthritis: Analysis of Major Adverse Cardiovascular Events (MACE) using Swedish National Health Registers] as per the request for supplementary information (RSI) adopted in October 2022

**Action:** For adoption of advice to CHMP

### 7.3. Results of PASS imposed in the marketing authorisation(s)\(^{29}\)

#### 7.3.1. Valproate\(^{30}\) (NAP) - EMEA/H/N/PSR/J/0036

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

**PRAC Rapporteur:** Liana Gross-Martirosyan

**Scope:** Results for a joint survey among healthcare professionals (HCP) to assess knowledge of HCP and behaviour with regards to pregnancy prevention programme (PPP) as well as receipt/use of a direct healthcare professional communication (DHPC) and

\(^{29}\) In accordance with Article 107p-q of Directive 2001/83/EC

\(^{30}\) Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpromide, valproate bismuth, calcium valproate, valproate magnesium
 educational materials and survey among patients to assess knowledge of the patients with regards to PPP as well as receipt/use of educational materials, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMA/H/A-31/1454)]

**Action:** For adoption of list of questions (LoQ) for a stakeholder meeting

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

#### 7.4.1. Cobimetinib - COTELLIC (CAP) - EMEA/H/C/003960/II/0027

**Applicant:** Roche Registration Gmbh

**PRAC Rapporteur:** Menno van der Elst

**Scope:** Update of sections 4.4 and 5.1 of the SmPC in order to update information based on final results from study ML39302 listed as a category 3 study in the RMP in order to fulfil MEA/003.5; this is a non-interventional PASS study to investigate the effectiveness, safety and utilisation of cobimetinib and vemurafenib in patients with and without brain metastasis with BRAF V600 mutant melanoma under real world conditions. The RMP version 5.0 has also been submitted

**Action:** For adoption of PRAC Assessment Report

#### 7.4.2. Regorafenib - STIVARGA (CAP) - EMEA/H/C/002573/II/0039

**Applicant:** Bayer AG

**PRAC Rapporteur:** Menno van der Elst

**Scope:** Update of section 4.4 of the SmPC in order to remove the disease specific precaution for hepatocellular carcinoma based on final results from study REFINE (study number 19244) listed as a category 3 study in the RMP; this is an international, prospective, open-label, multi-center, observational study to describe the safety and effectiveness of treatment with regorafenib in real-world settings. The RMP version 6.1 has also been submitted

**Action:** For adoption of PRAC Assessment Report

#### 7.4.3. Siltuximab - SYLVANT (CAP) - EMEA/H/C/003708/II/0038, Orphan

**Applicant:** EUSA Pharma (Netherlands) B.V.

**PRAC Rapporteur:** Brigitte Keller-Stanislawski

**Scope:** Submission of the report from study ACCELERATE (Advancing Castleman Care with an Electronic Longitudinal Registry, E-Repository, And Treatment/Effectiveness Research): An International Registry for Patients with Castleman Disease - NCT02817997 listed as an obligation in the Annex II of the product information. This is a study Report to cover the data collected for 100 patients over a 5 year period in the ACCELERATE Registry study to collect information or patients with Castleman’s Disease who are candidates to receive

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31 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
Sylvant or are currently receiving treatment with Sylvant. The Annex II is updated accordingly.

**Action:** For adoption of PRAC Assessment Report

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

#### 7.5.1. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004.6

**Applicant:** AstraZeneca AB

**PRAC Rapporteur:** David Olsen

**Scope:** Second interim report for study D3250R00042: a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other therapies in real-world settings.

**Action:** For adoption of advice to CHMP

#### 7.5.2. Cabazitaxel - CABAZITAXEL ACCORD (CAP) - EMEA/H/C/005178/MEA 001.3

**Applicant:** Accord Healthcare S.L.U.

**PRAC Rapporteur:** Tiphaine Vaillant

**Scope:** Fourth six-monthly review of cases of 'medication error' for cabazitaxel reported during routine signal management activities.

**Action:** For adoption of advice to CHMP

#### 7.5.3. Damoctocog alfa pegol - JIVI (CAP) - EMEA/H/C/004054/ANX 001.1

**Applicant:** Bayer AG

**PRAC Rapporteur:** Menn van der Elst

**Scope:** First interim report for study 20904 (HA-SAFE): an observational study evaluating long-term safety of real-world treatment with damoctocog alfa pegol in previously treated patients with hemophilia A' (HA-SAFE). The HA-SAFE study is a post-authorisation measure defined in Annex II.D of the Jivi EU product information. The study protocol was agreed with EMA/PRAC in Nov 2019 (outcome letter); the date of FPFV was 14 May 2021 (impacted by the Covid-19 pandemic). As Annex to the first interim report also the statistical analysis plan is submitted.

**Action:** For adoption of advice to CHMP

#### 7.5.4. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 004.8

**Applicant:** Moderna Biotech Spain, S.L.

**PRAC Rapporteur:** Marie Louise Schougaard Christiansen

**Scope:** Third interim report for study mRNA-1273-P904 (study 1) (listed as a category 3
study in the RMP): a post-authorisation active surveillance safety study using secondary data to monitor real-world safety of Spikevax (COVID-19 mRNA-1273 vaccine) in Europe - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals in European populations and electronic database assessment of use in pregnant women and submission of MAH’s response to MEA 004.6 as per request for supplementary information (RSI) adopted in September 2022

**Action:** For adoption of advice to CHMP

### 7.5.5. Etanercept - NEPEXTO (CAP) - EMEA/H/C/004711/MEA 001.1

**Applicant:** Mylan IRE Healthcare Limited

**PRAC Rapporteur:** Monica Martinez Redondo

**Scope:** First interim report for a prospective, observational study using the German Biologics Register – Rheumatoid Arthritis (RABBIT): 1) to assess the long-term safety of etanercept in RA patients and 2) to describe the long-term effectiveness and response to treatment in patients using Nepexto in a real-life environment (listed as Category 3 study in the RMP)

**Action:** For adoption of advice to CHMP

### 7.5.6. Ketoconazole - KETOCONAZOLE HRA (CAP) - EMEA/H/C/003906/ANX 002.9

**Applicant:** HRA Pharma Rare Diseases

**PRAC Rapporteur:** Željana Margan Koletić

**Scope:** Fifth interim annual report for a prospective, multi-country, observational registry study to collect clinical information on patients with endogenous Cushing’s syndrome exposed to ketoconazole using the existing European registry on Cushing’s syndrome (ERCUSYN) to assess drug utilisation pattern and to document the safety (e.g. hepatotoxicity, QT prolongation) and effectiveness of ketoconazole

**Action:** For adoption of advice to CHMP

### 7.5.7. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 064.3

**Applicant:** Biogen Netherlands B.V.

**PRAC Rapporteur:** Brigitte Keller-Stanislawski

**Scope:** Sixth interim report for study 101MS411 (listed as a category 3 study in the RMP): an observational cohort study utilising the Tysabri outreach unified commitment to health (TOUCH) prescribing programme and certain EU multiple sclerosis (MS) registries to estimate the risk of progressive multifocal leukoencephalopathy (PML) and other serious opportunistic infections among patients who were exposed to an MS disease modifying therapies prior to treatment with Tysabri (natalizumab)

**Action:** For adoption of advice to CHMP
7.5.8.  **Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 066.4**

Applicant: Biogen Netherlands B.V.
PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual report of a retrospective analysis of extended interval dosing (EID) versus standard interval dosing (SID) to further investigate the efficacy and safety in terms of progressive multifocal leukoencephalopathy (PML) risk reduction with EID relative to SID (TOUCH database)

**Action:** For adoption of advice to CHMP

7.5.9.  **Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 067.1**

Applicant: Biogen Netherlands B.V.
PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual progress report for study: IMA-06-02: an open label, multinational, multi-center, prospective, observational study. Amendment is primarily to extend patient follow up from 10 to 15 years

**Action:** For adoption of advice to CHMP

7.5.10.  **Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 003.4**

Applicant: Alnylam Netherlands B.V.
PRAC Rapporteur: Rhea Fitzgerald

Scope: Second interim report for study ALN-TTR02-010: patisiran- lipid nanoparticle (LNP) pregnancy surveillance programme (PSP) to collect primary data on pregnant women from the US, the United Kingdom (UK), France, Spain, Italy, Portugal and Germany, and other potential countries, who have been exposed to patisiran during the exposure window, defined as 12 weeks prior to their last menstrual period (LMP), or at any time during pregnancy as well as to collect and analyse information pertaining to pregnancy complications and birth outcomes in women exposed to patisiran during pregnancy

**Action:** For adoption of advice to CHMP

7.5.11.  **Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/MEA 002.5**

Applicant: Novo Nordisk A/S
PRAC Rapporteur: Mari Thorn

Scope: Third study progress report for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus (T2DM) taking semaglutide - a cohort study based on Nordic registry data

**Action:** For adoption of advice to CHMP
7.5.12. Semaglutide - RYBELSUS (CAP) - EMEA/H/C/004953/MEA 002.3

**Applicant:** Novo Nordisk A/S  
**PRAC Rapporteur:** Mari Thorn  
**Scope:** Third study progress report for study NN9535-4447: an epidemiological database study to estimate the risk of pancreatic cancer in patients with type 2 diabetes mellitus (T2DM) taking semaglutide - a cohort study based on Nordic registry data  
**Action:** For adoption of advice to CHMP

7.5.13. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 017.5

**Applicant:** BioNTech Manufacturing GmbH  
**PRAC Rapporteur:** Menno van der Elst  
**Scope:** Second interim report for study C4591021 (former ACCESS/VAC4EU): an assessment of potential increased risk of adverse events of special interest (AESI), including myocarditis/pericarditis after being vaccinated with COVID-19 messenger ribonucleic acid (mRNA) vaccine estimating the time trend, in relation to DHPC letter dissemination, of the proportion of individuals who received real-world clinical assessments for myocarditis/pericarditis following Comirnaty (tozinameran) vaccination  
**Action:** For adoption of advice to CHMP

7.5.14. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 045.10

**Applicant:** Janssen-Cilag International N.V.  
**PRAC Rapporteur:** Rhea Fitzgerald  
**Scope:** MAH's response to MEA 045.9 [Third annual progress report for study RRA-20745: an observational PASS to describe the safety of ustekinumab and other Crohn's disease treatments in a cohort of patients with Crohn’s disease] as per the request for supplementary information (RSI) adopted in September 2022  
**Action:** For adoption of advice to CHMP

7.6. Others

7.6.1. Avapritinib - AYVAKYT (CAP) - EMEA/H/C/005208/SOB 008.1

**Applicant:** Blueprint Medicines (Netherlands) B.V.  
**PRAC Rapporteur:** Menno van der Elst  
**Scope:** Submission of statistical analysis plan for study BLU-285-1406: an imposed non-interventional PASS aiming to collect long-term safety and efficacy data for avapritinib in first-line patients with PDGFRA D842V-mutated gastrointestinal stromal tumour (GIST) given as specific obligation 3 (SOB3) of the conditional marketing authorisation for AYVAKYT  
**Action:** For adoption of advice to CHMP
7.6.2. **Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/MEA 002.5**

Applicant: Swedish Orphan Biovitrum AB (publ)
PRAC Rapporteur: Monica Martinez Redondo

**Scope:** MAH’s response to MEA 002.4 [feasibility assessment for study AVA-CLD-402: evaluation of the feasibility of conducting a PASS of Doptelet (avatrombopag) in patients with severe chronic liver disease (CLD) and of the use of potential European electronic health care databases] as per the request for supplementary information (RSI) adopted in May 2022

**Action:** For adoption of advice to CHMP

7.6.3. **Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 007.6**

Applicant: Biogen Netherlands B.V.
PRAC Rapporteur: Martin Huber

**Scope:** Submission of a clarification regarding the closure of the ESTEEM study 109MS401 (A Multicentre, Global, Observational Study to Collect Information on Safety and to Document the Drug Utilisation of BG00012 When Used in Routine Medical Practice in the Treatment of Relapsing Multiple Sclerosis). ESTEEM is a Category 3 PASS listed in the Risk Management Plan with a commitment to provide a yearly update. The MAH also submitted a clarification regarding the status of study 109MS401, together with a justification for proceeding with the closure of the study in October 2022, as previously agreed with the PRAC.

**Action:** For adoption of advice to CHMP

7.6.4. **Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.7**

Applicant: BioNTech Manufacturing GmbH
PRAC Rapporteur: Menno van der Elst

**Scope:** Response to Comirnaty BA.1 and BA.4.5 bivalent vaccine protocol amendments (following variation procedures II/0140 and II/0143): containing a combined justification not to amend the following post-authorisation safety studies (PASS): C4591010, C4591009, C4591021, and C4591022 regarding Omicron BA.1 and Omicron BA.4-5

**Action:** For adoption of advice to CHMP

7.7. **New Scientific Advice**

7.8. **Ongoing Scientific Advice**

7.9. **Final Scientific Advice (Reports and Scientific Advice letters)**
8. Renewals of the marketing authorisation, conditional renewal and annual reassessments

8.1. Annual reassessments of the marketing authorisation

8.1.1. Metreleptin - MYALEPTA (CAP) - EMEA/H/C/004218/S/0030 (without RMP)

Applicant: Amryt Pharmaceuticals DAC
PRAC Rapporteur: Adam Przybylkowski
Scope: Annual reassessment of the marketing authorisation
Action: For adoption of advice to CHMP

8.2. Conditional renewals of the marketing authorisation

8.2.1. Andexanet alfa - ONDEXXYA (CAP) - EMEA/H/C/004108/R/0034 (without RMP)

Applicant: AstraZeneca AB
PRAC Rapporteur: Menno van der Elst
Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.2.2. Ciltacabtagene autoleucel - CARVYKTI (CAP) - EMEA/H/C/005095/R/0008 (with RMP)

Applicant: Janssen-Cilag International NV, ATMP
PRAC Rapporteur: Jo Robays
Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP and CAT

8.2.3. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/R/0062 (without RMP)

Applicant: Otsuka Novel Products GmbH
PRAC Rapporteur: Jo Robays
Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.2.4. Lorlatinib - LORVIQUA (CAP) - EMEA/H/C/004646/R/0025 (without RMP)

Applicant: Pfizer Europe MA EEIG

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32 Advanced therapy medicinal product
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.2.5. Pandemic influenza vaccine (h5n1) (live attenuated, nasal) - PANDEMIC INFLUENZA VACCINE H5N1 ASTRazeneca (CAP) - EMEA/H/C/003963/R/0057 (without RMP)

Applicant: AstraZeneca AB
PRAC Rapporteur: Sonja Hrabcik
Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.2.6. VolanesorSen - WAYLIVRA (CAP) - EMEA/H/C/004538/R/0022 (without RMP)

Applicant: Akcea Therapeutics Ireland Limited
PRAC Rapporteur: Martin Huber
Scope: Conditional renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Blinatumomab - BLINCYTO (CAP) - EMEA/H/C/003731/R/0048 (with RMP)

Applicant: Amgen Europe B.V.
PRAC Rapporteur: Eva Jirsová
Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.2. Brexipiprazol - RXULTI (CAP) - EMEA/H/C/003841/R/0014 (with RMP)

Applicant: Otsuka Pharmaceutical Netherlands B.V.
PRAC Rapporteur: Lucia Kuráková
Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

8.3.3. Carmustine - CARMUSTINE OBIUS (CAP) - EMEA/H/C/004326/R/0009 (with RMP)

Applicant: Obvius Investment B.V
PRAC Rapporteur: Jan Neuhauser
Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

### 8.3.4. Ciclosporin - VERKAZIA (CAP) - EMEA/H/C/004411/R/0021 (with RMP)

Applicant: Santen Oy
PRAC Rapporteur: Jan Neuhauser
Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

### 8.3.5. Inotersen - TEGSEDI (CAP) - EMEA/H/C/004782/R/0035 (without RMP)

Applicant: Akcea Therapeutics Ireland Limited
PRAC Rapporteur: Rhea Fitzgerald
Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

### 8.3.6. Lipegfilgrastim - LONQUEX (CAP) - EMEA/H/C/002556/R/0077 (without RMP)

Applicant: Teva B.V.
PRAC Rapporteur: Kirsti Villikka
Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

### 8.3.7. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/R/0054 (without RMP)

Applicant: Amryt Pharmaceuticals DAC
PRAC Rapporteur: Menno van der Elst
Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

### 8.3.8. Metreleptin - MYALEPTA (CAP) - EMEA/H/C/004218/R/0031 (without RMP)

Applicant: Amryt Pharmaceuticals DAC
PRAC Rapporteur: Adam Przybylkowski
Scope: 5-year renewal of the marketing authorisation
Action: For adoption of advice to CHMP

### 8.3.9. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/R/0031 (with RMP)

Applicant: Pierre Fabre Medicament
PRAC Rapporteur: Menno van der Elst
Scope: 5-year renewal of the marketing authorisation

**Action:** For adoption of advice to CHMP

### 8.3.10. Nitisinone - NITYR (CAP) - EMEA/H/C/004582/R/0015 (with RMP)

- **Applicant:** Cycle Pharmaceuticals (Europe) Limited
- **PRAC Rapporteur:** Amelia Cupelli
- **Scope:** 5-year renewal of the marketing authorisation
- **Action:** For adoption of advice to CHMP

### 8.3.11. Prasugrel - PRASUGREL MYLAN (CAP) - EMEA/H/C/004644/R/0014 (without RMP)

- **Applicant:** Mylan Pharmaceuticals Limited
- **PRAC Rapporteur:** Anette Kirstine Stark
- **Scope:** 5-year renewal of the marketing authorisation
- **Action:** For adoption of advice to CHMP

### 8.3.12. Sufentanil - DZUVEO (CAP) - EMEA/H/C/004335/R/0009 (with RMP)

- **Applicant:** Laboratoire Aguettant
- **PRAC Rapporteur:** Adam Przybyłkowski
- **Scope:** 5-year renewal of the marketing authorisation
- **Action:** For adoption of advice to CHMP

### 8.3.13. Trastuzumab - TRAZIMERA (CAP) - EMEA/H/C/004463/R/0020 (without RMP)

- **Applicant:** Pfizer Europe MA EEIG
- **PRAC Rapporteur:** Brigitte Keller-Stanislawski
- **Scope:** 5-year renewal of the marketing authorisation
- **Action:** For adoption of advice to CHMP

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### 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 agenda.

9.3. **Others**

None

10. **Other safety issues for discussion requested by the CHMP or the 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. **Montelukast (NAP) - FI/H/xxxx/WS/112**

Applicant: Organon

PRAC Lead: Kimmo Jaakkola

Scope: PRAC consultation on a worksharing variation (WS) procedure evaluating the risk of severe and prolonged neuropsychiatric events/harms as well as the existing risk minimisation measures and the need for any further ones and/or labelling updates as per conclusions of the PSUSA procedure (PSUSA/00002087/202107) concluded in March 2022, on request of Finland
**Action:** For adoption of advice to Member States

### 11.2. Other requests

None

### 12. Organisational, regulatory and methodological matters

#### 12.1. Mandate and organisation of the PRAC

##### 12.1.1. PRAC membership

**Action:** For information

##### 12.1.2. Vote by proxy

None

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

None

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

##### 12.3.1. Methodology Working Party (MWP) – overview of scope and activities

**Action:** For discussion

##### 12.3.2. Scientific advice working party (SAWP) – re-nomination of PRAC representative(s)

**Action:** For discussion

#### 12.4. Cooperation within the EU regulatory network

##### 12.4.1. Coronavirus (COVID-19) pandemic - update

**Action:** For discussion

#### 12.5. Cooperation with International Regulators

None
12.6. Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee

None

12.7. PRAC work plan

12.7.1. PRAC work plan 2023

PRAC lead: Sabine Straus, Martin Huber

Action: For adoption

12.8. Planning and reporting

12.8.1. Marketing authorisation applications (MAA) forecast for 2022 – planning update dated Q4 2022

Action: For discussion

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: Menno van der Elst, Maia Uusküla

Action: For discussion
12.10.3. **PSURs repository**

None

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

*Action*: For adoption

### 12.11. **Signal management**


PRAC lead: Menno van der Elst

*Action*: For discussion

### 12.12. **Adverse drug reactions reporting and additional reporting**

12.12.1. **Management and reporting of adverse reactions to medicinal products**

None

12.12.2. **Additional monitoring**

None

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

*Action*: For adoption

12.12.4. **Specific adverse drug reaction (ADR) follow up questionnaire (FUQ) drafting group – update on the activities – next steps on Specific ADR FUQ repository**

PRAC lead: Tiphaine Vaillant

*Action*: For discussion

### 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 hearings – procedural and best practice guidance for PRAC members

**Action:** for discussion

#### 12.18.2. Safety communication

None
12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG)
Impact – revision of the process for prioritisation and follow-up of impact research

Action: For adoption

12.20.2. Study report on the impact of EU label changes for fluoroquinolone-containing medicinal products for systemic and inhalation use: post-referral prescribing trends

PRAC lead: Martin Huber, Eva Jirsová

Action: For adoption

12.21. Others

12.21.1. EMA-funded safety studies: analysis on Coronavirus (COVID-19) vaccines and myocarditis – updated study results

Action: For discussion

13. Any other business

Next meeting on: 06-09 February 2023
14. Explanatory notes

The Notes give a brief explanation of relevant agenda items and should be read in conjunction with the agenda.

EU Referral procedures for safety reasons: Urgent EU procedures and Other EU referral procedures
(Items 2 and 3 of the PRAC agenda)

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, the 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:

Signals assessment and prioritisation
(Item 4 of the PRAC agenda)

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 agenda)

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 agenda)

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 agenda)

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 agenda)

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: www.ema.europa.eu/