09 January 2023
EMA/PRAC/911454/2022 Human Medicines Division

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

Disclaimers

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

Of note, 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 on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006 Rev.1).

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1. Introduction

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

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[3]

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

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

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

EPITT 19822 – Follow-up to July 2022

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[4]

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

[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 mnDMD 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

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

5.3.21. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - EMEA/H/C/004750/II/0033/G, Orphan

Applicant: Novartis Europharm Limited, ATMP[5]

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 CAT and CHMP

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

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

[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 Jirsová

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 CNTO1275UCO3001 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 - ARTESUNATE 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

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

6.1.8. Berotralstat - ORLADEYO (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

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

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

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

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

[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

6.1.14. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - PSUSA/00010972/202206

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

[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

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

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

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

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

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

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

[10] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Latanoprost, netarsudil - ROCLANDA (CAP) - PSUSA/00010905/202206

Applicant: Santen Oy

PRAC Rapporteur: Adam Przybylkowski

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[11] - 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

[11] 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

[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. Treosulfan[14] - TRECONDI (CAP) - PSUSA/00010777/202206

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Julia Pallos

[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

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For discussion

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[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[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

[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

[20] Oral use

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/00010645/202203 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 - OLUMIANT (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[21]

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)[22]

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.

[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, ATMP[23]

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, ATMP[24]

[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[25]

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[26] (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[27] (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

[24] Advanced therapy medicinal product
[25] Advanced therapy medicinal product
[26] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium
[27] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, 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

[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 $\geqslant$ 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, valpriomide, 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 (EMEA/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)[31]

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

[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: Menno 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[32]

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

[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. Brexpiprazole - 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 OBVIUS (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 Przybylkowski

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

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

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

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:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000150.jsp&mid=WC0b01ac05800240d0

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/