13 March 2023
EMA/PRAC/60842/2023
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 13-16 March 2023

Chair: Sabine Straus – Vice-Chair: Martin Huber

13 March 2023, 10:30 – 19:30, via teleconference

14 March 2023, 08:30 – 19:30, via teleconference

15 March 2023, 08:30 – 19:30, via teleconference

16 March 2023, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

30 March 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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Table of contents

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 13-16 March 2023. See March 2023 PRAC minutes (to be published post April 2023 PRAC meeting).

1.2. Agenda of the meeting on 13-16 March 2023

Action: For adoption

1.3. Minutes of the previous meeting on 06-09 February 2023

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 outstanding issues (LoOI)

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Dupilumab – DUPIXENT (CAP)

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Kimmo Jaakkola

Scope: Signal of weight decreased, abnormal loss of weight, cachexia, body mass index decreased

Action: For adoption of PRAC recommendation

EPITT 19897 – New signal

Lead Member State(s): FI

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

4.1.2. Nusinersen – SPINRAZA (CAP)

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of arachnoiditis

Action: For adoption of PRAC recommendation

EPITT 19896 – New signal

Lead Member State(s): SE

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Ceftriaxone (NAP)

Applicant(s): various

PRAC Rapporteur: Zane Neikena

Scope: Signal of risk of factor V inhibition

Action: For adoption of PRAC recommendation

EPITT 19853 – Follow-up to November 2022

4.3.2. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/SDA 021

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Signal of hepatocellular damage and hepatitis (HLT)

Action: For adoption of PRAC recommendation

EPITT 19846 – Follow-up to November 2022

4.3.3. Propofol (NAP)

Applicant(s): various

PRAC Rapporteur: Karen Pernille Harg

Scope: Signal of medication errors that could potentially lead to life-threatening/fatal cases

Action: For adoption of PRAC recommendation

EPITT 19851 – Follow-up to November 2022

4.3.4. Voriconazole - VFEND (CAP) - EMEA/H/C/000387/SDA 092; VORICONAZOLE ACCORD (CAP); VORICONAZOLE HIKMA (CAP); NAP

Applicant: Accord Healthcare S.L.U. (Voriconazole Accord), Hikma Farmaceutica (Portugal), S.A. (Voriconazole Hikma), Pfizer Europe MA EEIG (Vfend), various

PRAC Rapporteur: Liana Gross-Martirosyan
Scope: Signal of drug interaction with flucloxacillin leading to subtherapeutic voriconazole levels

Action: For adoption of PRAC recommendation

EPITT 19849 – Follow-up to November 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. Alpelisib - EMEA/H/C/005468, Orphan

Applicant: Novartis Europharm Limited

Scope : Treatment of patients with severe manifestations of PIK3CA-related overgrowth spectrum

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

5.1.2. Atogepant monohydrate - EMEA/H/C/005871

Scope : Prophylaxis of migraine in adults who have at least 4 migraine days per month

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

5.1.3. Coronavirus (COVID-19) vaccine (recombinant protein receptor binding domain fusion heterodimer) – EMEA/H/C/006058

Scope : Booster for active immunisation to prevent COVID-19 in individuals 16 years of age and older who have previously received a messenger RNA (**mRNA**) COVID-19 vaccine

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

5.1.4. Dabigatran etexilate - EMEA/H/C/006023

Scope : Prevention of venous thromboembolic events

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

5.1.5. Piflufolastat (F 18) - EMEA/H/C/005520

Scope : Indicated in imaging in patients undergoing oncologic diagnostic procedures when increased expression of prostate specific membrane antigen is a diagnostic target

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

5.1.6. Sugammadex - EMEA/H/C/006083

Scope : Reversal of neuromuscular blockade induced by rocuronium or vecuronium in adults

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

5.1.7. Tislelizumab - EMEA/H/C/005919, Orphan

Applicant: Novartis Europharm Limited

Scope : Treatment of adult patients with unresectable, recurrent, locally advanced or metastatic oesophageal squamous cell carcinoma after prior chemotherapy

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

5.1.8. Tislelizumab - EMEA/H/C/005542

Scope : Treatment of locally advanced or metastatic non-squamous non-small cell lung cancer in adults, treatment of locally advanced or metastatic squamous non-small cell lung cancer in adults, locally advanced or metastatic non-small cell lung cancer after prior chemotherapy in adults

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. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS2430/0056; ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/WS2430/0068

Applicant(s): AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of an updated RMP version 7.1 for Viekirax and Exviera to include the completion of studies B16-959, B20-146, M14-423 (TOPAZ-I) and M14-222 (TOPAZ-II), following the outcome of EMEA/H/C/PSR/J/0038, EMEA/H/C/WS2216 and EMEA/H/C/WS2304, respectively. The MAH proposes to remove the emergence and recurrence of hepatocellular carcinoma as potential risks and update the related pharmacovigilance activities and other sections of the RMPs

Action: For adoption of PRAC Assessment Report

5.2.2. Dexamethasone - OZURDEX (CAP) - EMEA/H/C/001140/II/0044

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of an updated Annex II and RMP version 11 in order to remove additional risk minimisation measure: Patient guide, audio CD (where required)

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, Randomised, 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. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/II/0040, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP version 6.0 in order to correct the objectives of Morquio A registry study (MARS) in RMP to be consistent with version 6 of the protocol and to update the "Method used to calculate exposure" due to GDPR restrictions following the assessment of procedures PSA/S/0062 and PSUSA/00010218/202102

Action: For adoption of PRAC Assessment Report

5.2.5. 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

5.2.6. Miglustat - ZAVESCA (CAP) - EMEA/H/C/000435/II/0076

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Mari Thorn

Scope: Submission of an updated RMP version 15.1 in order to remove risks in line with GVP module V revision 2. The MAH has also taken the opportunity to introduce minor changes, such as update of the post marketing exposure data and alignment with the latest Company EU-RMP Template

Action: For adoption of PRAC Assessment Report

5.2.7. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/II/0039, Orphan

Applicant: Advanz Pharma Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP version 2.0 in order to change to EU Qualified Person for Pharmacovigilance (QPPV), update the list of safety concerns and include study data for 747-302 and 747-401

Action: For adoption of PRAC Assessment Report

5.2.8. Palivizumab - SYNAGIS (CAP) - EMEA/H/C/000257/II/0131

Applicant: AstraZeneca AB

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of an updated RMP version 2.0 in order to remove from the list of safety concerns "Anaphylaxis, Anaphylactic shock, and Hypersensitivity" and "Medication error of mixing lyophilised and liquid palivizumab before injection". In addition, the MAH took the opportunity to apply the revised template

Action: For adoption of PRAC Assessment Report

5.2.9. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2434/0049; NEPARVIS (CAP) - EMEA/H/C/004343/WS2434/0047

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP version 5.0 for Ernestro and its duplicate marketing authorisation Neparvis to update the milestones for MEA 002 (study CLCZ696B2014) and MEA 004 (study CLCZ696B2015) from 31 December 2022 to 30 June 2024

Action: For adoption of PRAC Assessment Report

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

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Gabriele Maurer

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

5.2.11. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/WS2402/0069; MODIGRAF (CAP) - EMEA/H/C/000954/WS2402/0045

Applicant(s): Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Submission of an updated RMP (version 4) to reflect the new Transplant Pregnancy Registry International (TPRI) final study submission milestone, related to procedure EMEA/H/C/000712/MEA030 and EMEA/H/C/000954/MEA022 (Study F506-PV-0001), from 21 December 2021 to 30 June 2023

Action: For adoption of PRAC Assessment Report

5.2.12. Zanubrutinib - BRUKINSA (CAP) - EMEA/H/C/004978/II/0008

Applicant: BeiGene Ireland Ltd

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the updated RMP (Version 3.0) in order to include changes on the dates of submission of information for the ongoing study BGB-3111-LTE1

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/II/0152

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include the prophylaxis of acute Graft versus Host Disease (aGvHD) in the adult and paediatric population for Orencia, based on final results from studies IM101311 - Abatacept Combined With a Calcineurin Inhibitor and Methotrexate for Graft Versus Host Disease Prophylaxis and IM101841 - Overall Survival In 7/8 HLA-Matched Hematopoietic Stem Cell Transplantation Patients Treated With Abatacept Combined With A Calcineurin Inhibitor And Methotrexate - An Analysis Of The Center For International Blood And Marrow Transplant Research (Cibmtr) Database. 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 Labelling are updated in

accordance. Version 28.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.2. Alpelisib - PIQRAY (CAP) - EMEA/H/C/004804/II/0018

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.5 and 5.2 of the SmPC in order to update drug-drug interaction information, based on final results from study BYL719A2111; this is a phase 1, open-label, fixed-sequence, two-period drug-drug interaction (DDI) study evaluating the PK probe substrates for CYP3A4, CYP2B6, CYP2C8, CYP2C9, and CYP2C19 when administered either alone or in combination with repeated doses of alpelisib. The Annex II and package leaflet are updated accordingly. The RMP version 6.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.3. Apalutamide - ERLEADA (CAP) - EMEA/H/C/004452/X/0028/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped application consisting of: 1) Extension application to add a new strength (240 mg) film-coated tablets. The RMP (version 6.1) has also been submitted; 2) Update of the SmPC/PL for Erleada 60 mg to align with the SmPC/PL proposed for the registration of the new Erleada film-coated tablet strength, 240 mg. The package leaflet for Erleada 60 mg is proposed to be updated to ensure consistency. In addition, few minor revisions are proposed to the SmPC for Erleada 60 mg, to align the SmPC proposed for the 240 mg strength: Sections 5.1 and 5.2: Orthographic corrections; Section 6.5: Further details on the description of the current packaging have been added, this change does not result from a change to the container; Section 6.6: The title of the section has been aligned with QRD template

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

5.3.4. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/X/0076

Applicant: Roche Registration GmbH

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with a new strength (1875 mg) and new route of administration (subcutaneous use). The RMP (version 24.0) is updated in accordance

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

5.3.5. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0037

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include the treatment of paediatric patients (from 2 years of age and older) with moderate to severe atopic dermatitis for OLUMIANT, based on the final results from study I4V-MC-JAIP; this is a Phase III, multicentre, randomised, double blind, placebo controlled, parallel-group, outpatient study evaluating the pharmacokinetics, efficacy, and safety of baricitinib in paediatric patients with moderate-to-severe atopic dermatitis. As a consequence sections 4.1, 4.2, 4.4, 4.5, 4.8, 4.9, 5.1, 5.2 of the SmPC are updated. The package leaflet has been updated accordingly. Version 17.1 of the RMP has also been submitted

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

5.3.6. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/II/0010

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of indication to include treatment of adults with active axial spondyloarthritis (axSpA), including non-radiographic axial spondyloarthritis (nr-axSpA) and ankylosing spondylitis (AS, radiographic axial spondyloarthritis), based on interim results from two interventional and controlled phase III clinical studies: AS0010 (BE MOBILE 1) and AS0011 (BE MOBILE 2), which provide evidence of the efficacy and safety of bimekizumab in axSpA (nr-axSpA and AS), both compared to placebo treatment. Further supportive data is provided by the results of a phase 2a exploratory study (AS0013), a phase 2b, dose-ranging study (AS0008) and its ongoing follow-on phase 2b open-label extension (OLE) study (AS0009). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 1.2 of the RMP has also been submitted. Furthermore, the product information is brought in line with the latest QRD template version 10.2 rev.1

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

5.3.7. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/II/0011

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of indication to include treatment of active psoriatic arthritis in adults patients who have had an inadequate response or who have been intolerant to one or more DMARDs for Bimzelx (bimekizumab), based on interim results of a Phase III study in biological DMARD naïve study participants (PA0010; BE OPTIMAL) and the final results of the Phase III study in study participants who are inadequate responders (inadequate response or intolerant) to ⩽2 prior TNF inhibitors (PA0011; BE COMPLETE). Both Phase III studies are interventional studies aimed to evaluate the efficacy and safety of bimekizumab. For PA0010, the Initial Treatment Period was placebo- and no inferential active reference (adalimumab)-controlled, while PA0011 was placebo-controlled. Further supportive data comprise the results of a Phase 1 study (PA0007), a Phase 2b dose-finding study (PA0008) and a Phase 2 open label extension study (PA0009). A Phase 3 open-label extension study is currently ongoing (PA0012). As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 to the SmPC have been updated. The package leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. Furthermore, the product information is brought in line with the latest QRD template version

10.2 rev.1. As part of the application the MAH is requesting a 1-year extension of the market protection

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

5.3.8. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0018

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Gabriele Maurer

Scope: Update of sections 4.2 and 5.1 of the SmPC in order to introduce an alternative posology regimen for wet age-related macular degeneration and update information based on modelling and simulation studies; the package leaflet is updated accordingly. The RMP version 9.0 has also been submitted

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

5.3.9. Budesonide, formoterol fumarate dihydrate - BUDESONIDE/FORMOTEROL TEVA PHARMA B.V. (CAP) - EMEA/H/C/004882/II/0012/G

Applicant: Teva Pharma B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Grouped variations consisting of: 1) To replace the multidose dry powder inhaler to be used for the delivery of a combination of Budesonide/Formoterol fumarate dihydrate inhalation powder, as well as detect, record, store and transfer inhaler usage information to a mobile application (App); the inhaler is an integrated part of the primary packaging of the medicinal product; 2) To change the name of the medicinal product 3) To update sections 4.2 and 4.4 of the SmPC to reorganise the flow of information within these sections (as approved for DuoResp Spiromax EMEA/H/C/002348), following assessment of the same change for the reference product Symbicort Turbohaler; 4) other quality variations

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

5.3.10. Carglumic acid - CARBAGLU (CAP) - EMEA/H/C/000461/II/0045

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to include a proposed dose adjustment for patients with impaired renal function based on final results from study RCD-P0-027; this is a Phase I, multicenter, open-label, parallel-group adaptive pharmacokinetic single dose study of oral Carbaglu in subjects with normal and varying degrees of impaired renal function. The package leaflet is updated accordingly. The RMP version 2.2 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in Annex II and Labelling, and to bring the product information in line with the latest QRD template version 10.3

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

5.3.11. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - EMEA/H/C/002246/II/0057

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Submission of the 24-months' clinical study report (CSR) addendum of the MW2010-03-02 (DETECT) category 1 study; a multicentre, multinational, randomised, controlled, assessor blinded study, performed in subjects with thermal burns, to evaluate the efficacy and safety of NexoBrid compared to gel vehicle and compared to standard of care. The provision of the CSR addresses the post-authorisation measure ANX 001.7. An updated RMP version 8.0 was provided as part of the application

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

5.3.12. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0057

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include treatment of adults with unresectable hepatocellular carcinoma (uHCC), based on final results from study D419CC00002 (HIMALAYA); this was a randomised, open-label, multi-center phase III study of durvalumab and tremelimumab as first-line treatment in patients with unresectable hepatocellular carcinoma (HIMALAYA). As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 9, Succession 1 of the RMP has also been submitted. In addition, the product information is brought in line with the latest QRD template version 10.3

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

5.3.13. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS2409/0042; ROTEAS (CAP) - EMEA/H/C/004339/WS2409/0029

Applicant(s): Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Nathalie Gault

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC with available paediatric data based on final results from study DU176b-D-U312; this is a phase 3, open-label, randomised, multicentre, controlled trial to evaluate the pharmacokinetics and pharmacodynamics of edoxaban and to compare the efficacy and safety of edoxaban with standard-of-care anticoagulant therapy in paediatric subjects from birth to less than 18 years of age with confirmed venous thromboembolism (VTE). The package leaflet and Labelling are updated accordingly. The RMP version 15.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and to bring the product information in line with the latest QRD template version 10.3

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

5.3.14. Efgartigimod alfa - VYVGART (CAP) - EMEA/H/C/005849/X/0003, Orphan

Applicant: Argenx

PRAC Rapporteur: Rhea Fitzgerald

Scope: Extension application to introduce a new pharmaceutical form (solution for injection) associated with a new strength (1000 mg) and a new route of administration (subcutaneous use)

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

5.3.15. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/II/0074

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication to include treatment of chronic kidney disease (CKD) for JARDIANCE, based on final results from study EMPA-KIDNEY (1245-0137) listed as a category 3 study in the RMP; this is a Phase III, multicentre international randomised parallel group double-blind placebo controlled clinical trial of empagliflozin once daily to assess cardio-renal outcomes in patients with chronic kidney disease. 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 19.0 of the RMP has also been submitted. Furthermore, the product information is brought in line with the latest QRD template version 10.3

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

5.3.16. Enfortumab vedotin - PADCEV (CAP) - EMEA/H/C/005392/II/0007

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to introduce new posology recommendations in case of pneumonitis/interstitial lung disease (ILD), add a new warning on 'pneumonitis/ILD' and add it to the list of adverse drug reactions (ADRs) with frequency not known. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI

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

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

Applicant: Omrix Biopharmaceuticals N. V.

PRAC Rapporteur: Gabriele Maurer

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 product

information 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

5.3.18. Lanadelumab - TAKHZYRO (CAP) - EMEA/H/C/004806/X/0034/G, Orphan

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped application consisting of: 1) Extension application to add a new strength of 150 mg for lanadelumab solution for injection in pre-filled syringe and to extend the indication to include paediatric use (2 to <12 years). The new indication is only applicable to the new 150 mg strength presentations. The RMP (version 3.0) is updated in accordance; 2) A type IB variation (C.I.z) to update section 7 of the package leaflet (PL) for the 300 mg in 2 ml pre-filled syringe (EU/1/18/1340/004-006) in line with the proposed package leaflet for the 150 mg in 1 ml pre-filled syringe (new strength). In addition, the MAH has requested an extension of the Orphan Market Exclusivity from 10 to 12 years

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

5.3.19. Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/004731/II/0014

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP[3]

PRAC Rapporteur: Gabriele Maurer

Scope: Update of section 5.1 of the SmPC in order to update efficacy information based on final results from studies 017001 and JCAR-017-BCM-001 listed as obligations in the Annex II. These studies aimed to further characterise the long-term efficacy and safety of Breyanzi in patients treated with relapsed or refractory DLBCL, PMBCL, FL3B after two or more lines of systemic therapy. Study 017001 is a phase 1, open-label, single-arm, multicohort, multicenter, seamless design trial, while study JCAR-017-BCM-001 is a phase 2, open-label, single-arm, multicohort, multicenter trial. The Annex II is updated accordingly. The RMP version 3.0 has also been submitted

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

5.3.20. Melphalan flufenamide - PEPAXTI (CAP) - EMEA/H/C/005681/II/0002

Applicant: Oncopeptides AB

PRAC Rapporteur: Martin Huber

Scope: Extension of indication to include treatment of patients with Multiple Myeloma who have received at least two prior lines of therapies for PEPAXTI, based on final results from study OP-103 OCEAN; this is a randomised, open-label phase III study in patients with relapsed or refractory multiple myeloma following two to four lines of prior therapies and who were refractory to lenalidomide and the last line of therapy. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance.

[3] Advanced therapy medicinal product

Version 1.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC

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

5.3.21. Midostaurin - RYDAPT (CAP) - EMEA/H/C/004095/II/0028, Orphan

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to update efficacy and safety information in elderly patients based on final results from study CPKC412A2408 - An open-label, multi-center, Phase IIIb study to assess the safety and efficacy of midostaurin (PKC412) in patients 18 years of age or older with newly diagnosed FLT3-mutated Acute Myeloid Leukemia who are eligible for "7+3" or "5+2" chemotherapy, listed as a PAES in the Annex II. The RMP version 8.0 has also been submitted

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

5.3.22. 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

5.3.23. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/II/0032

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Extension of indication to include treatment and prophylaxis of bleeding in children below 12 years of age with haemophilia B including previously untreated patients for REFIXIA, based on interim results from studies NN7999-3774 and NN7999-3895. NN7999-3774 is a multicentre, open-label, non-controlled study evaluating the safety, efficacy and pharmacokinetics of nonacog beta pegol in previously treated children with haemophilia B, while NN7999-3895 is a multicentre, open-label, single-arm, non-controlled trial evaluating the safety and efficacy of nonacog beta pegol in previously untreated patients with haemophilia B. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet is updated accordingly. Version 5.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.24. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0052, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension of indication to include the pre-treatment to reduce the risk of cytokine release syndrome (CRS) induced by glofitamab for Gazyvaro, based on results from study NP30179; this is a a multicenter, open-label, Phase I/II study evaluating the safety, efficacy, tolerability and pharmacokinetics of escalating doses of glofitamab as a single agent and in combination with obinutuzumab administered after a fixed, single dose pre-treatment of Gazyvaro in patients with relapsed/refractory B-cell NHL. As a consequence, sections 4.1, 4.2, 4.4, 5.1, 5.3 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 10.0 of the RMP has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest QRD template version

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

5.3.25. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/II/0034/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Grouped variations consisting of: 1) submission of the final report from study BN29739 (VELOCE) listed as a category 3 study in the RMP. This is a phase 3b, multicentre, randomised, parallel-group, open-label study to evaluate the effectiveness of vaccinations in patients with relapsing forms of multiple sclerosis (RMS) undergoing treatment with ocrelizumab; 2) submission of the final report from studies MA30005 (CASTING) and MN30035 (CHORDS). These are prospective, multicentre, international, interventional, open-label phase 3b studies to assess the efficacy and safety of ocrelizumab in patients with relapsing multiple sclerosis who have a suboptimal response to an adequate course of disease-modifying treatment. The RMP version 8.0 has also been submitted

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

5.3.26. Odevixibat - BYLVAY (CAP) - EMEA/H/C/004691/II/0011, Orphan

Applicant: Albireo

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of cholestasis and pruritus in Alagille syndrome (ALGS) in patients from birth and older for BYLVAY, based on final results from Study A4250-012 and interim results from Study A4250-015. Study A4250-012 is a 24-week, randomised, double-blind, placebo-controlled Phase III study conducted in 52 patients with a genetically confirmed diagnosis of ALGS and presence of pruritus and high serum bile acid levels at baseline. Study A4250-015 is an ongoing 72-week open-label extension trial for patients who completed Study A4250-012 and evaluates the long-term safety and efficacy of

Bylvay in patients with ALGS. As a consequence, sections 4.1, 4.2, 4.8, 5.1, and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted

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

5.3.27. Olipudase alfa - XENPOZYME (CAP) - EMEA/H/C/004850/II/0001/G, Orphan

Applicant: Genzyme Europe BV

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update sections 4.6 of the SmPC in order to include a recommendation to conduct a pregnancy test for women of childbearing potential (WOCP) prior to treatment initiation based on embryo-foetal study in mice (study TER0694). In addition, the MAH proposes an update of section 5.3 of the SmPC based on a re-calculation of exposure margins for the embryo-foetal study. MAH also proposes to align the SmPC with the updated Company Core Data Sheet (CCDS); 2) update sections 4.6 and 5.3 of the SmPC in order to include data in lactating mice based on final results from study MSSM-1120 - Evaluation of Olipudase alfa Transfer Into Milk of Lactating Mice. The package leaflet is updated accordingly. The RMP version 2.0 has also been submitted

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

5.3.28. Oritavancin - TENKASI (CAP) - EMEA/H/C/003785/II/0037

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of paediatric population, aged between 3 months and less than 18 years for Tenkasi (oritavancin) 400 mg based on interim results from study TMC-ORI-11-01; this is a multicenter, open-label, dose-finding study of oritavancin single dose infusion in paediatric subjects less than 18 years of age with suspected or confirmed bacterial infections. The purpose of this Phase 1 study is to evaluate the safety, tolerability and PK of oritavancin in paediatric subjects and determine the optimal dose for a Phase 2 trial in paediatric subjects with acute bacterial skin structure infections (ABSSSI). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet is updated in accordance. Version 5.0 of the RMP has also been submitted. In addition, MAH is also taking this opportunity to update the contact details of the local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest QRD template version 10.2 rev 1

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

5.3.29. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - FOCLIVIA (CAP) - EMEA/H/C/001208/II/0081

Applicant: Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include children from 6 months to less than 18 years of age for Foclivia, based on final results from study V87_30; this is a phase 2, randomised,

observer-blind, multicenter study to evaluate the immunogenicity and safety of several doses of antigen and MF59 adjuvant content in a monovalent H5N1 pandemic influenza vaccine in healthy pediatric subjects 6 months to less than 9 years of age. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated accordingly. Version 4.9 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and to bring it in line with the latest QRD template

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

5.3.30. Parathyroid hormone - NATPAR (CAP) - EMEA/H/C/003861/II/0042, Orphan

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the updated protocol from study SHP634-403 listed as a specific obligation in the Annex II of the product information with twice-daily (BID) as the proposed alternative dosing regimen to be evaluated. This is a randomised, 2-Arm, double-blind, phase 4 study to evaluate once daily (QD) versus twice daily (BID) administration of recombinant human parathyroid hormone (rhPTH[1-84]; NATPARA) for the treatment of adults with hypoparathyroidism (HPT). The Annex II and the RMP (submitted version 3.4) are updated accordingly

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

5.3.31. Patiromer - VELTASSA (CAP) - EMEA/H/C/004180/X/0031/G

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kirsti Villikka

Scope: Extension application to introduce a new strength (1 g powder for oral suspension), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of population from 6 to 18 years old for Veltassa based on final results from paediatric study RLY5016-206P (EMERALD); this is a phase 2, open-label, multiple dose study to evaluate the pharmacodynamic effects, safety, and tolerability of patiromer for oral suspension in children and adolescents 2 to less than 18 years of age with chronic kidney disease and hyperkalaemia. As a consequence, sections 1, 2, 4.1, 4.2, 4.8, 4.9, 5.1 and 6.5 of the SmPC are updated. The package leaflet and Labelling are updated in accordance. Version 2 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce editorial changes

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

5.3.32. Pneumococcal polysaccharide conjugate vaccine (20-valent, adsorbed) - APEXXNAR (CAP) - EMEA/H/C/005451/II/0012

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication to include infants, children and adolescents from 6 weeks to less than 18 years of age for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae, based on final results from studies B7471003,

B7471011, B7471012, B7471013 and B7471014. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 3.0 of the RMP has also been submitted

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

5.3.33. Polatuzumab vedotin - POLIVY (CAP) - EMEA/H/C/004870/II/0020, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the updated final overall survival (OS) CSR for study GO39942 - A Phase III, multicenter, randomised, double-blind, placebo-controlled trial comparing the efficacy and safety of polatuzumab vedotin in combination with R-CHP versus R-CHOPin previously untreated patients with DLBCL (POLARIX) listed as a Category 3 study in the RMP. This submission will address the missing information of "long-term safety" in patients treated with polatuzumab vedotin. An updated RMP version 4.0 has also been submitted to remove the commitment for this study along with the missing information of "long-term safety"

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

5.3.34. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/II/0012

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4 and 4.5 of the SmPC in order to amend posology recommendations, warnings and drug-drug interaction information regarding the co-administration with CYP3A4 inhibitors, P-gp inhibitors and CYP3A4 inducers based on final results from the DDI study GP43162, listed as a category 3 study in the RMP, as well as results from the physiologically based pharmacokinetic (PBPK) analyses summarised in the PBPK Report 1120689. Study GP43162 is a phase 1, open-label, fixed-sequence study to evaluate the effect of a single dose of cyclosporine on the single dose pharmacokinetics of pralsetinib in healthy subjects. The RMP version 1.6 has also been submitted

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

5.3.35. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0046

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Update of sections 4.6 and 5.1 of the SmPC in order to update information on pregnancy and breast-feeding based on final results from study IMPAACT 2032 listed as a category 3 study in the RMP; this is a phase 4, prospective, open-label, non-randomised study to address PK and safety of remdesivir in pregnant women. The package leaflet is updated accordingly. The RMP version 5.2 has also been submitted

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

5.3.36. Sacituzumab govitecan - TRODELVY (CAP) - EMEA/H/C/005182/II/0020

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting, based on final results from study IMMU-132-09 (TROPiCS-02); this is an open-label, randomised, multicenter phase 3 study of sacituzumab govitecan (IMMU-132) versus treatment of physician's choice (TPC) in subjects with hormonal receptor-positive (HR+) human epidermal growth factor receptor 2 (HER2) negative metastatic breast cancer (mBC) who have failed at least two prior chemotherapy regimens. 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 2.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information 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

5.3.37. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/X/0044/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension application to introduce a new pharmaceutical form associated with two new strengths (6 mg/6 mg granules in capsule for opening and 15 mg/16 mg granules in capsule for opening), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of children and adolescents aged one year or older with chronic heart failure with left ventricular systolic dysfunction, based on the results of Study PANORAMA-HF (CLCZ696B2319): a multicentre, open-label, study to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of sacubitril/valsartan followed by a 52-week randomised, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of sacubitril/valsartan compared with enalapril in paediatric patients from 1 month to < 18 years of age with heart failure due to systemic left ventricle systolic dysfunction. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.2 of the SmPC are being updated and the package leaflet is updated accordingly. In addition, an updated RMP version 4.0 was provided as part of the application. Further, the MAH requested a one year extension of the market protection

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

5.3.38. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/X/0042/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension application to introduce a new pharmaceutical form associated with two new strengths (6 mg/6 mg granules in capsule for opening and 15 mg/16 mg granules in capsule for opening), grouped with a type II variation (C.I.6.a) in order to extend the indication to include treatment of children and adolescents aged one year or older with chronic heart failure

with left ventricular systolic dysfunction, based on the results of Study PANORAMA-HF (CLCZ696B2319); a multicentre, open-label, study to evaluate safety, tolerability, pharmacokinetics and pharmacodynamics of sacubitril/valsartan followed by a 52-week randomised, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of sacubitril/valsartan compared with enalapril in paediatric patients from 1 month to < 18 years of age with heart failure due to systemic left ventricle systolic dysfunction. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.2 of the SmPC are being updated and the package leaflet is updated accordingly. In addition, an updated RMP version 4.0 was provided as part of the application. Further, the MAH requested a one year extension of the market protection

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

5.3.39. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/II/0021

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the treatment of adults and adolescents 12 years and older with advanced RET fusion-positive thyroid cancer in the first-line setting for RETSEVMO based on interim data from studies LIBRETTO-001 (LOXO-RET-17001) and LIBRETTO-121; LIBRETTO-001 is an open-label, multicentre, global Phase 1/2 study of selpercatinib in patients with RET-altered advanced solid tumors. LIBRETTO-121 is a Phase 1/2 study of selpercatinib in paediatric patients with advanced RET-altered solid or primary central nervous system tumours. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 3.2 of the RMP has also been submitted

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

5.3.40. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/II/0022

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the treatment of adults with advanced or metastatic RET fusion-positive solid tumours with disease progression on or after prior systemic therapies or who have no satisfactory therapeutic options, based on interim data from study LIBRETTO-001 (LOXO-RET-17001); LIBRETTO-001 is an open-label, multicentre, global Phase 1/2 study of selpercatinib in in adult and adolescent patients with advanced RET-altered tumours. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. Version 3.1 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC

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

5.3.41. Somapacitan - SOGROYA (CAP) - EMEA/H/C/005030/X/0006/G, Orphan

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Extension application to add a new strength of 15 mg/1.5 mL solution for injection in

pre-filled pen grouped with a type II variation C.I.6 to add a new indication 'Replacement of endogenous growth hormone (GH) in children and adolescents with growth failure due to growth hormone deficiency (GHD)', based on results from the completed main 52-week period of the confirmatory phase 3 trial (4263), supported with long-term data from the phase 2 trial (4172), up to week 208 completed. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the package leaflet has been updated accordingly. A revised RMP version 3.0 was provided as part of the application

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

5.3.42. Sotorasib - LUMYKRAS (CAP) - EMEA/H/C/005522/II/0007

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.2 and 5.2 of the SmPC in order to update recommendations for patients with moderate to severe hepatic impairment following final results from study 20200362 listed as a category 3 PASS study in the EU RMP; this is a Phase I clinical study to evaluate the pharmacokinetics (PK) of a single oral dose of sotorasib administered in subjects with moderate or severe hepatic impairment compared with subjects who have normal hepatic function. The EU RMP version 1.0 has also been submitted. In addition, the MAH took the opportunity to bring the product information in line with the latest QRD template version 10.3

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

5.3.43. Tafasitamab - MINJUVI (CAP) - EMEA/H/C/005436/II/0008, Orphan

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.4 of the SmPC in order to add a new warning on Progressive Multifocal Leukoencephalopathy (PML) based on post-marketing data; the package leaflet is updated accordingly. The RMP version 2.0 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the SmPC and to bring the product information in line with the latest QRD template version 10.3

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

5.3.44. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/II/0042

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study EFC11759 listed as a category 3 study in the RMP. This is a two-year, multicentre, randomised, double-blind, placebo-controlled, parallel group trial to evaluate efficacy, safety, tolerability and pharmacokinetics of teriflunomide administered orally once daily in paediatric patients with relapsing forms of multiple sclerosis (MS) followed by an open-label extension. The RMP version 8.0 has also been submitted

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

5.3.45. Tralokinumab - ADTRALZA (CAP) - EMEA/H/C/005255/X/0007

Applicant: LEO Pharma A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension application to add a new strength of 300 mg (150 mg/ml) tralokinumab solution for injection in pre-filled pen for subcutaneous administration. The RMP (version 1.1) is updated accordingly

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

5.3.46. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/II/0027

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Extension of indication to include the indication treatment of non-small cell lung cancer for Enhertu (trastuzumab deruxtecan), based on results from study DS8201-A-U204 (DESTINY-Lung01) and study DS8201-A-U206 (DESTINY-Lung02). Study DESTINY-Lung01 is a phase 2, multicentre, open-label, 2-cohort study of trastuzumab deruxtecan (DS-8201a), an anti-HER2 antibody drug conjugate (ADC), for HER2-over-expressing or -mutated, unresectable and/or metastatic non-small cell lung cancer (NSCLC) conducted at sites in Japan, the United States and Europe. Study DESTINY-Lung02 is an ongoing phase 2, multicentre, randomised study to evaluate the safety and efficacy of trastuzumab deruxtecan in subjects with HER2-mutated metastatic non-small cell lung cancer, conducted in North America, Europe and Asia-Pacific. As a consequence, sections 4.1, 4.2, 4.8, 5.1, and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. Version 2.2 of the RMP has also been submitted

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

5.3.47. Tucatinib - TUKYSA (CAP) - EMEA/H/C/005263/II/0010

Applicant: Seagen B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study SGNTUC-017 (MOUNTAINEER) listed as a category 3 study in the RMP. This is a Phase 2, Open Label Study of Tucatinib Combined with Trastuzumab in Patients with HER2+ Metastatic Colorectal Cancer. Primary objective is to determine the antitumor activity of tucatinib given in combination with trastuzumab. The RMP version 1.1 has also been submitted

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

5.3.48. Vosoritide - VOXZOGO (CAP) - EMEA/H/C/005475/II/0006, Orphan

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: Extension of indication to include treatment of children less than 2 years of age for Voxzogo, based on final results from the category 1 study BMN 111-206 and interim results

from its open-label extension study 111-208. 111-206 is a phase 2 randomised, double-blind, placebo-controlled, multicentre study to assess the safety and efficacy of BMN 111 in infants and young children with achondroplasia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The Annex II and package leaflet are updated in accordance. Version 3.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes 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. Agalsidase beta - FABRAZYME (CAP) - PSUSA/00000070/202207

Applicant: Genzyme Europe BV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Anifrolumab - SAPHNELO (CAP) - PSUSA/00010980/202207

Applicant: AstraZeneca AB

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Asenapine - SYCREST (CAP) - PSUSA/00000256/202208

Applicant: N.V. Organon

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Ataluren - TRANSLARNA (CAP) - PSUSA/00010274/202207

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Avalglucosidase alfa - NEXVIADYME (CAP) - PSUSA/00011002/202208

Applicant: Genzyme Europe BV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Baricitinib - OLUMIANT (CAP) - PSUSA/00010578/202208

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Belantamab mafodotin - BLENREP (CAP) - PSUSA/00010869/202208

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Bempedoic acid - NILEMDO (CAP); bempedoic acid, ezetimibe - NUSTENDI (CAP) - PSUSA/00010841/202208

Applicant(s): Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Bimekizumab - BIMZELX (CAP) - PSUSA/00010953/202208

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Brentuximab vedotin - ADCETRIS (CAP) - PSUSA/00010039/202208 (with RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Bulevirtide - HEPCLUDEX (CAP) - PSUSA/00010873/202207

Applicant: Gilead Sciences Ireland Unlimited Company

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Burosumab - CRYSVITA (CAP) - PSUSA/00010669/202208

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Caplacizumab - CABLIVI (CAP) - PSUSA/00010713/202208

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Ciltacabtagene autoleucel - CARVYKTI (CAP) - PSUSA/00011000/202208

Applicant: Janssen-Cilag International NV, ATMP[4]

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.15. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - PSUSA/00010916/202208

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[4] Advanced therapy medicinal product

6.1.16. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - PSUSA/00011001/202208

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Darolutamide - NUBEQA (CAP) - PSUSA/00010843/202207

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - PSUSA/00010701/202208

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Defatted powder of Arachis hypogaea L., semen (peanuts) - PALFORZIA (CAP) - PSUSA/00010902/202207

Applicant: Aimmune Therapeutics Ireland Limited

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Difelikefalin - KAPRUVIA (CAP) - PSUSA/00010995/202208

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Doravirine - PIFELTRO (CAP) - PSUSA/00010729/202208 (with RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Doravirine, lamivudine, tenofovir disoproxil - DELSTRIGO (CAP) - PSUSA/00010731/202208 (with RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Dronedarone - MULTAQ (CAP) - PSUSA/00001180/202207

Applicant: Sanofi Winthrop Industrie

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Eptinezumab - VYEPTI (CAP) - PSUSA/00010966/202208

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Eravacycline - XERAVA (CAP) - PSUSA/00010718/202208

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Evinacumab - EVKEEZA (CAP) - PSUSA/00010945/202208

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/202208

Applicant: Holostem Terapie Avanzate s.r.l., ATMP[5]

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.28. Fedratinib - INREBIC (CAP) - PSUSA/00010909/202208

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Fostemsavir - RUKOBIA (CAP) - PSUSA/00010911/202208

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Hydrocortisone[6] [7] - ALKINDI (CAP) - PSUSA/00010674/202208

Applicant: Diurnal Europe BV

PRAC Rapporteur: Mari Thorn

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Imlifidase - IDEFIRIX (CAP) - PSUSA/00010870/202208

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[5] Advanced therapy medicinal product
[6] Centrally authorised product(s)
[7] Indication for adrenal insufficiency in paediatric patients only

6.1.32. Influenza vaccine (intranasal, live attenuated) - FLUENZ TETRA (CAP) - PSUSA/00001742/202208

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Ioflupane (^{123}I) - DATSCAN (CAP) - PSUSA/00001767/202207

Applicant: GE Healthcare B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Lanadelumab - TAKHZYRO (CAP) - PSUSA/00010743/202208

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Lefamulin - XENLETA (CAP) - PSUSA/00010872/202208

Applicant: Nabriva Therapeutics Ireland DAC

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Linaclotide - CONSTELLA (CAP) - PSUSA/00010025/202208

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Lisocabtagene maraleucel - BREYANZI (CAP) - PSUSA/00010990/202208

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP[8]

PRAC Rapporteur: Gabriele Maurer

[8] Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.38. Lomitapide - LOJUXTA (CAP) - PSUSA/00010112/202207

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Lonapegsomatropin - SKYTROFA (CAP) - PSUSA/00010969/202208

Applicant: Ascendis Pharma Endocrinology Division A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Mecasermin - INCRELEX (CAP) - PSUSA/00001942/202208

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Meropenem, vaborbactam - VABOREM (CAP) - PSUSA/00010727/202208

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Palbociclib - IBRANCE (CAP) - PSUSA/00010544/202208

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Panobinostat - FARYDAK (CAP) - PSUSA/00010409/202208

Applicant: Secura Bio Limited

PRAC Rapporteur: Sofia Trantza

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Patisiran - ONPATTRO (CAP) - PSUSA/00010715/202208

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.45. Pegaspargase[9] - ONCASPAR (CAP) - PSUSA/00010457/202207

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Pretomanid - DOVPRELA (CAP) - PSUSA/00010863/202208

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Regdanvimab - REGKIRONA (CAP) - PSUSA/00010964/202208 (with RMP)

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Valentina Di Giovanni

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Rimegepant - VYDURA (CAP) - PSUSA/00010997/202208

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Centrally authorised product(s) only

6.1.49. Risdiplam - EVRYSDI (CAP) - PSUSA/00010925/202208

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Risperidone[10] - OKEDI (CAP) - PSUSA/00010985/202208

Applicant: Laboratorios Farmaceuticos Rovi S.A.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Romiplostim - NPLATE (CAP) - PSUSA/00002660/202207

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Monica Martinez Redondo

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Rotavirus vaccine monovalent (live, oral) - ROTARIX (CAP) - PSUSA/00002665/202207

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Sacubitril, valsartan - ENTRESTO (CAP); NEPARVIS (CAP) - PSUSA/00010438/202207

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Smallpox and monkeypox vaccine (live, modified vaccinia virus Ankara) - IMVANEX (CAP) - PSUSA/00010119/202207

Applicant: Bavarian Nordic A/S

[10] Centrally authorised product(s) only

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Somapacitan - SOGROYA (CAP) - PSUSA/00010920/202208

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Sotrovimab - XEVUDY (CAP) - PSUSA/00010973/202208

Applicant: Glaxosmithkline Trading Services Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.57. Tafasitamab - MINJUVI (CAP) - PSUSA/00010951/202207

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Teduglutide - REVESTIVE (CAP) - PSUSA/00009305/202208

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. Tisagenlecleucel - KYMRIAH (CAP) - PSUSA/00010702/202208

Applicant: Novartis Europharm Limited, ATMP[11]

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

[11] Advanced therapy medicinal product

6.1.60. Tocofersolan - VEDROP (CAP) - PSUSA/00002981/202207

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Melinda Palfi

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.61. Upadacitinib - RINVOQ (CAP) - PSUSA/00010823/202208

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.62. Vosoritide - VOXZOGO (CAP) - PSUSA/00010952/202208

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.63. Voxelotor - OXBRYTA (CAP) - PSUSA/00010983/202208

Applicant: Global Blood Therapeutics Netherlands B.V.

PRAC Rapporteur: Jo Robays

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. Human protein C - CEPROTIN (CAP); NAP - PSUSA/00002563/202207

Applicant(s): Takeda Manufacturing Austria AG (Ceprotin), various

PRAC Rapporteur: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Oxybutynin - KENTERA (CAP); NAP - PSUSA/00002253/202207

Applicant(s): Teva B.V. (Kentera), various

PRAC Rapporteur: Jo Robays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Palonosetron - ALOXI (CAP); NAP - PSUSA/00002268/202207

Applicant(s): Helsinn Birex Pharmaceuticals Limited (Aloxi), various

PRAC Rapporteur: Rhea Fitzgerald

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. Alprostadil[12] (NAP) - PSUSA/00000111/202207

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Anastrozole (NAP) - PSUSA/00000210/202208

Applicant(s): various

PRAC Lead: Zane Neikena

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Beclometasone, formoterol[13] (NAP) - PSUSA/00010068/202207

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[12] Indicated in peripheral arterial occlusive diseases only
[13] For inhalation use only

6.3.4. Cefadroxil (NAP) - PSUSA/00000584/202207

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Clindamycin phosphate, tretinoin (NAP) - PSUSA/00010080/202207

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Diclofenac, misoprostol (NAP) - PSUSA/00001040/202207

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Diphtheria, tetanus, poliomyelitis (inactivated) vaccine (adsorbed, reduced antigens(s) content) (NAP) - PSUSA/00001127/202208

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Enalapril, hydrochlorothiazide (NAP) - PSUSA/00001212/202207

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Ethinylestradiol, norethisterone (NAP) - PSUSA/00001312/202208

Applicant(s): various

PRAC Lead: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Fludarabine (NAP) - PSUSA/00001406/202208

Applicant(s): various

PRAC Lead: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Fluvoxamine (NAP) - PSUSA/00001458/202207

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Fosfomycin[14] (NAP) - PSUSA/00010326/202207

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Fosfomycin[15] (NAP) - PSUSA/00010336/202207

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Human coagulation factor IX (NAP) - PSUSA/00001617/202207

Applicant(s): various

PRAC Lead: Gabriele Maurer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[14] Oral formulation
[15] Intravenous (IV) formulation

6.3.15. Ketorolac[16] (NAP) - PSUSA/00001810/202207

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Ketorolac[17] (NAP) - PSUSA/00001811/202207

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Meloxicam (NAP) - PSUSA/00010474/202207

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Norethisterone (NAP) - PSUSA/00002188/202208

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Pilocarpine[18] (NAP) - PSUSA/00002409/202207

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Pitavastatin (NAP) - PSUSA/00010502/202207

Applicant(s): various

PRAC Lead: Menno van der Elst

[16] Ophtalmic formulation(s) only
[17] Systemic formulation(s) only
[18] All formulations except ophthalmic

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. Poliovirus type 1, poliovirus type 2, poliovirus type 3 vaccine (oral, live, attenuated) (NAP) - PSUSA/00010801/202207

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. Triamcinolone[19] (NAP) - PSUSA/00003017/202207

Applicant(s): various

PRAC Lead: Inês Ribeiro-Vaz

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. Triazolam (NAP) - PSUSA/00003023/202207

Applicant(s): various

PRAC Lead: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/LEG 016.5

Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: From EMEA/H/C/002268/II/0035:
Proposal for additional pharmacovigilance activities to address the important potential risk of 'Increased mortality in younger ICU patients.'

Action: For adoption of advice to CHMP

[19] Topical and nasal formulation(s) only

6.5. Variation procedure(s) resulting from PSUSA evaluation

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

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marie Louise Schougaard Christiansen

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

6.5.2. 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

6.6. Expedited summary safety reviews[20]

6.6.1. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 014.8

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Gabriele Maurer

Scope: Ninth 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

[20] Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[21]

7.1.1. Lenalidomide - REVLIMID (CAP) - EMEA/H/C/PSA/S/0093.1

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Substantial amendment to a protocol for a post-authorisation, non-interventional, retrospective, drug-utilisation study to describe the pattern of use of lenalidomide in patients with myelodysplastic syndromes (MDS) [MAH's response to PSA/S/0093]

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

7.1.2. Rurioctocog alfa pegol - ADYNOVI (CAP) - EMEA/H/C/PSA/S/0095.1

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Substantial amendment to a protocol for study: evaluation of long-term safety of ADYNOVI/ADYNOVATE (Antihaemophilic Factor [Recombinant] PEGylated, rurioctocog alfa pegol) in adults and adolescents ⩾12 years of age with haemophilia A [MAH's response to PSA/S/0095]

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

7.1.3. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/PSA/S/0094.1

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Substantial amendment to a protocol for study: THE ALPHA-MANNOSIDOSIS REGISTRY: A multi-centre, multi-country, non-interventional, prospective cohort, in alpha-mannosidosis patients to evaluate the long-term effectiveness and safety profile of treatment with Lamzede under conditions of routine clinical care and to characterize the entire alpha-mannosidosis population, including variability of clinical manifestation, progression and natural history [MAH's response to PSA/S/0094]

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

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[22]

7.2.1. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.13

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Revised PASS protocol for study OBS13434: a prospective, multicentre, observational, PASS to evaluate the long term safety profile of alemtuzumab treatment in patients with relapsing forms of multiple sclerosis (RMS)

Action: For adoption of advice to CHMP

7.2.2. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 002.2

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 002.1 [Submission of a revised protocol for study PS0038: a non-interventional cohort study on the safety of bimekizumab in patients with plaque psoriasis comparing the risk of safety outcomes of interest in bimekizumab exposed patients compared to patients exposed to other biologics] as per the request for supplementary information (RSI) adopted in November 2022

Action: For adoption of advice to CHMP

7.2.3. Bimekizumab - BIMZELX (CAP) - EMEA/H/C/005316/MEA 003.2

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 003.1 [Submission of a revised protocol for study PS0036: bimekizumab pregnancy exposure and outcome registry - an OTIS autoimmune diseases in pregnancy study] as per the request for supplementary information (RSI) adopted in November 2022. PASS Study no PS0036: Bimekizumab Pregnancy Exposure and Outcome Registry: An OTIS Autoimmune Diseases in Pregnancy Study (NINI PASS protocol)

Action: For adoption of advice to CHMP

7.2.4. Birch bark extract - FILSUVEZ (CAP) - EMEA/H/C/005035/MEA 001

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Zane Neikena

Scope: Submission of a protocol for Filsuvez Observational Safety and Effectiveness Evaluation Registry-based study in epidermolysis bullosa (EB) (FOStER-EB) [(AEB-21)] (listed as category 3 study in the RMP) to evaluate the long-term safety of Filsuvez amongst patients treated for EB in relation to the incidence, severity and relatedness of skin malignancies

[22] 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

(including squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and malignant melanoma (MM)), and use in patients with different skin types regarding ethnic origin

Action: For adoption of advice to CHMP

7.2.5. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - EMEA/H/C/005737/MEA 008.3

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a protocol amendment for study VAC31518COV4003 (listed as category 3 study in the RMP): post-authorisation, observational study to assess the safety of Ad26.COV2.S using electronic health record (EHR) database(s) in Europe

Action: For adoption of advice to CHMP

7.2.6. Enfortumab vedotin - PADCEV (CAP) - EMEA/H/C/005392/MEA 003

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Protocol for study 7465-PV-0002: PASS to evaluate patients understanding and awareness of the content of the patient card related to risks of skin reactions and patients behaviours to minimise the risks

Action: For adoption of advice to CHMP

7.2.7. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/MEA 029.3

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Updated protocol for study study Instanyl-5002 (listed as a category 3 study in the RMP): a non-interventional study to assess the effectiveness of updated educational materials on prescribers' knowledge and behaviour with respect to risks associated with Instanyl (fentanyl) off-label use together with an interim report and the statistical analysis plan (SAP)

Action: For adoption of advice to CHMP

7.2.8. Filgotinib - JYSELECA (CAP) - EMEA/H/C/005113/MEA 016.2

Applicant: Galapagos N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 016.1 [revised protocol for study GLPG0634-CL-413: a non-interventional, PASS of filgotinib in patients with moderately to severely active ulcerative colitis (a European multi registry-based study)] as per the request for supplementary information (RSI) adopted in October 2022

Action: For adoption of advice to CHMP

7.2.9. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 002.3

Applicant: TEVA GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Revised protocol for observational cohort study TV48125-MH-50037: a pregnancy registry assessing pregnancy outcomes in patients treated with Ajovy (fremanezumab)

Action: For adoption of advice to CHMP

7.2.10. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/MEA 005.1

Applicant: Amgen Europe B.V., ATMP[23]

PRAC Rapporteur: Gabriele Maurer

Scope: MAH's response to MEA 001 [Substantial amendment to a protocol previously agreed within the initial application/marketing authorisation in 2015 for study 20130193 (listed as category 3 study in the RMP): a post-marketing, prospective cohort study of patients treated with talimogene laherparepvec in clinical practice to characterize the risk of herpetic illness among patients, close contacts, and healthcare providers; and long term safety in treated patients] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CAT and CHMP

7.2.11. Tebentafusp - KIMMTRAK (CAP) - EMEA/H/C/004929/MEA 002.1

Applicant: Immunocore Ireland Limited

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002 [Protocol for a physician's survey to evaluate the effectiveness of additional risk minimisation measure for (educational materials) cytokine release syndrome (CRS) associated with Kimmtrak administration] as per the request for supplementary information (RSI) adopted in September 2022

Action: For adoption of advice to CHMP

7.2.12. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 018.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Revised protocol for study A3921407: a Post-Authorisation Active Safety Surveillance Program Among Patients Treated with Tofacitinib for Polyarticular Course Juvenile Idiopathic Arthritis and Juvenile PsA within the German Biologics in Pediatric Rheumatology Registry (BIKER) and within the Juvenile Arthritis Methotrexate/Biologics long-term Observation (JuMBO) Registry

Action: For adoption of advice to CHMP

[23] Advanced therapy medicinal product

7.2.13. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 019.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Revised protocol for study A3921408: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the Swedish juvenile idiopatic arthritis (JIA) clinical registry

Action: For adoption of advice to CHMP

7.2.14. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 020.2

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Revised protocol for study A3921409: a PASS surveillance programme among patients treated with tofacitinib for polyarticular course juvenile idiopathic arthritis and juvenile psoriatic arthritis (PsA) within the UK juvenile idiopathic arthritis (JIA) biologics register

Action: For adoption of advice to CHMP

7.2.15. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 025

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study No921403 (listed as category 3 study in the RMP): a PASS of the Utilisation and Prescribing Patterns of Xeljanz (tofacitinib) Using an Administrative Healthcare Database in France: a descriptive drug utilisation study using real-world data collected from routine clinical care in France. The overall goal is to determine if there is evidence that prescribers in France are compliant with the recommendations and limitations for use described in the tofacitinib additional risk minimisation measures (aRMM) materials

Action: For adoption of advice to CHMP

7.2.16. Vutrisiran - AMVUTTRA (CAP) - EMEA/H/C/005852/MEA 002

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Third protocol amendment for study ALN-TTR02-013, ConTTRibute Study: Global, Prospective, Observational, Multicenter Long-Term Study.
Purpose of the study: This is a prospective, observational study that will provide a robust assessment of the long-term safety of Amvuttra in real-world clinical practice along with a comparator group being enrolled in ConTTRibute who follow local standard of care. ConTTRibute aims to document the natural history, clinical characteristics, and management of ATTR amyloidosis as part of routine clinical care. The study cohort will include patients with hATTR amyloidosis under care at the participating study site, as no exclusion criteria are intended with this observational cohort. Patients with hepatic impairment will be observed as part of the cohort. The study will also include data collection on the clinical consequences of

vitamin A deficiency, including delayed symptoms, and pregnancy exposure and pregnancy and infant outcomes

Action: For adoption of advice to CHMP

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

7.3.1. Chlormadinone acetate, ethinyl estradiol (NAP) - EMEA/H/N/PSR/J/0042

Applicant: GEDEON RICHTER Plc

PRAC Rapporteur: Martin Huber

Scope: Final study report for: risk of venous thromboembolism – The role of oral contraceptives – a case control study comparing levonorgestrel and chlormadinone acetate (CMA) to compare the VTE risk of combined oral contraceptives (COCs) containing CMA 2mg / ethinylestradiol (EE) 30 µg, compared to COCs containing levonorgestrel (LNG) 0.15mg, both combined with 30 µg ethinylestradiol (EE)

Action: For adoption of recommendation to CMDh (or request for supplementary information (RSI)

7.3.2. Retinoids[25]: acitretin (NAP), alitretinoin (NAP), isotretinoin (NAP) - EMEA/H/N/PSR/J/0040

Applicant: F.Hoffmann-La Roche Ltd.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Final study report for a Drug Utilisation Study to describe the prescribing practices before and after the update of the pregnancy prevention programme (PPP) for the oral retinoids acitretin, alitretinoin and isotretinoin in order to assess the effectiveness of these updated risk minimisation measures (RMMs) in women of childbearing potential, following an Article 31 referral on retinoid-containing medicinal products (EMEA/H/A-31/1446)

Action: For adoption of recommendation to CMDh (or request for supplementary information (RSI)

7.3.3. Roflumilast – DAXAS (CAP) - EMEA/H/C/PSR/S/0041

Applicant: AstraZeneca AB

PRAC Rapporteur: Monica Martinez Redondo

Scope: Final study report for a long-term post-marketing observational study of the safety of roflumilast

Action: For adoption of recommendation to CHMP (or request for supplementary information (RSI)

[24] In accordance with Article 107p-q of Directive 2001/83/EC
[25] Oral presentations

7.3.4. Valproate[26] (NAP) - EMEA/H/N/PSR/J/0036

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Survey among HCP to assess knowledge of healthcare professionals (HCP) and behaviour with regards to pregnancy prevention proramme (PPP) as well as receipt/use of DHPC and educational materials and Survey among patients to assess knowledge of the patients with regards to PPP as well as receipt/use of educational materials

Action: For adoption of recommendation to CMDh (or request for supplementary information (RSI)

7.4. Results of PASS non-imposed in the marketing authorisation(s)[27]

7.4.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0093

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Submission of the final non-interventional Pompe Registry Report 2022 (MEA 024 and MEA 025)

Action: For adoption of PRAC Assessment Report

7.4.2. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/II/0061, Orphan

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Jo Robays

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to update treatment duration based on final results from EU PASS (protocol no. 242-12-402), listed as a category 3 study in the RMP. This is a "A Multicentre, EU-wide, Non-Interventional Post-Authorisation Study to Assess the Safety and Usage of Delamanid in Routine Medical Practice in Multidrug-Resistant Tuberculosis (MDR-TB) Patients". This treatment registry was for monitoring and documenting Deltyba use in routine medical practice and aimed to assess compliance with the recommendations in the authorised product information when prescribed as part of an appropriate combination regimen (ACR) for the treatment of MDR-TB. The package leaflet is updated accordingly. The RMP version 4.2 has also been submitted. In addition, the MAH took the opportunity to update Annex II section D of the SmPC

Action: For adoption of PRAC Assessment Report

7.4.3. Etelcalcetide - PARSABIV (CAP) - EMEA/H/C/003995/II/0021

Applicant: Amgen Europe B.V.

[26] Valproic acid, sodium valproate, valproate pivoxil, valproate semisodium, valpriomide, valproate bismuth, calcium valproate, valproate magnesium
[27] 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

PRAC Rapporteur: Valentina Di Giovanni

Scope: Submission of the final report from study 20170561 listed as a category 3 study in the RMP. This is an observational PASS to evaluate the potential association between Parsabiv and gastrointestinal bleeding

Action: For adoption of PRAC Assessment Report

7.4.4. Gilteritinib - XOSPATA (CAP) - EMEA/H/C/004752/II/0012, Orphan

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study 2215-PV-0001 - Evaluation of the effectiveness of the Xospata Routine Risk Minimization Measures (RMMs) and an additional Risk Minimisation Measure (aRMM): A Cross sectional study among Healthcare Professionals to assess awareness and knowledge, listed as a category 3 study in the RMP. The RMP version 3.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.5. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0111

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.6 of the SmPC in order to update information on pregnancy based on final results from PASS study CNTO148ART4001 listed as a category 3 study in the RMP; this is an observational prospective cohort study to collect and analyse information pertaining to pregnancy outcomes of women exposed to golimumab during pregnancy. The RMP version 23.2 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.6. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/II/0112

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study P04480 (RABBIT) listed as a category 3 study in the RMP. This is an observational prospective cohort study to evaluate the long-term safety of treatment with biologics in rheumatoid arthritis. The RMP version 23.3 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.7. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0127

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from the PASS CA209835: A registry study in patients

who underwent post-nivolumab allogeneic haematopoetic stem-cell transplantation (HSCT). This study is listed as a Category 3 study in the RMP. An updated RMP version 31.0 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.8. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/WS2435/0048; NEPARVIS (CAP) - EMEA/H/C/004343/WS2435/0046

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from study CLCZ696B2013 listed as a category 3 study in the RMP. Study CLCZ696B2013 is a non-interventional, post-authorisation, database cohort study to assess the risk of serious angioedema in association with LCZ696 (sacubitril/valsartan; Entresto) use in Black patients with heart failure in the United States

Action: For adoption of PRAC Assessment Report

7.4.9. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/II/0039, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final report from PASS study VX17-661-117 listed as a category 3 study in the RMP. This is an Observational Study to Evaluate the Utilization Patterns and Real-World Effects of Tezacaftor and Ivacaftor Combination Therapy (TEZ/IVA) in Patients With Cystic Fibrosis (CF). The RMP version 3.4 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.10. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0095

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final report from study PSOLAR (C0168Z03) (listed as a category 3 study in the RMP): a multicenter, open registry of patients with psoriasis who are candidates for systemic therapy including biologics: PSOLAR. The RMP (version 22.2) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.11. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/II/0073

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Submission of the final report from study MLN0002_401 (listed as a category 3 study in the RMP in order to fulfil MEA/001.2): an international observational prospective cohort

study comparing vedolizumab to other biologic agents in patients with ulcerative colitis or Crohn's disease. The RMP version 8.0 has also been submitted

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. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/MEA 005.3

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Interim report for study 215163 (listed as category 3 study in the RMP): a study on pregnancy and neonatal outcomes following prenatal exposure to cabotegravir long acting (CAB LA) – data from the European Pregnancy and Paediatric human immunodeficiency virus (HIV) Cohort Collaboration (EPPICC)

Action: For adoption of advice to CHMP

7.5.2. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/MEA 006.3

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Interim report for study 215325 (listed as category 3 study in the RMP): a study on pregnancy and neonatal outcomes following prenatal exposure to cabotegravir – data from the Antiretroviral Pregnancy Registry (APR)

Action: For adoption of advice to CHMP

7.5.3. Cinacalcet - MIMPARA (CAP) - EMEA/H/C/000570/MEA 035.6

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: Third interim report for study 20180204: a registry study to evaluate the incidence and risk of hypocalcaemia in paediatric patients treated with cinacalcet with secondary hyperparathyroidism receiving maintenance dialysis within the International Pediatric Dialysis Network (IPDN) registry

Action: For adoption of advice to CHMP

7.5.4. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - EMEA/H/C/005737/MEA 008.2

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: From Initial MAA: Post-authorisation, observational study (VAC31518COV4003) to assess the safety of Ad26.COV2.S using electronic health record (EHR) database(s) in Europe

Action: For adoption of advice to CHMP

7.5.5. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/ANX 038.14

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Ninth annual interim report for study CICL670E2422: an observational, multicentre cohort study to evaluate the long-term exposure and safety of deferasirox in the treatment of paediatric non-transfusion dependent thalassaemia patients over 10 years old for whom deferoxamine is contraindicated or inadequate]

Action: For adoption of advice to CHMP

7.5.6. Eculizumab - SOLIRIS (CAP) - EMEA/H/C/000791/MEA 053.5

Applicant: Alexion Europe SAS

PRAC Rapporteur: Monica Martinez Redondo

Scope: Biennial interim report for study M07-001: a prospective registry for an observational, multicentre, multinational study of patients with paroxysmal nocturnal haemoglobinuria (PNH)

Action: For adoption of advice to CHMP

7.5.7. Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/MEA 002.5

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Second interim report for study MK8835-062: a PASS to assess the risk of diabetic ketoacidosis among type 2 diabetes mellitus patients (T2DM) treated with ertugliflozin compared to patients treated with other antihyperglycemic agents

Action: For adoption of advice to CHMP

7.5.8. Ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/MEA 002.5

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Second interim report for study MK-8835-062: a PASS to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus (T2DM) patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents

Action: For adoption of advice to CHMP

7.5.9. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/MEA 002.5

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Second interim report for study MK-8835-062: a PASS to assess the risk of diabetic ketoacidosis (DKA) among type 2 diabetes mellitus (T2DM) patients treated with ertugliflozin compared to patients treated with other antihyperglycemic

Action: For adoption of advice to CHMP

7.5.10. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038.5

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Third interim report for study CFTY720D2311: a two-year, double-blind, randomised, multicentre, active-controlled core phase study to evaluate the safety and efficacy of fingolimod administered orally once daily versus interferon β-1a intramuscular (IM) once weekly in paediatric patients with multiple sclerosis with five-year fingolimod extension phase

Action: For adoption of advice to CHMP

7.5.11. Galcanezumab - EMGALITY (CAP) - EMEA/H/C/004648/MEA 002.1

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Interim report for study I5Q-MC-B003: Observational Cohort Study of Exposure to Galcanezumab during Pregnancy among Women with Migraine

Action: For adoption of advice to CHMP

7.5.12. Golimumab - SIMPONI (CAP) - EMEA/H/C/000992/MEA 033.6

Applicant: Janssen Biologics B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Fourth anual progress report for study MK-8259-050: an observational PASS for golimumab in the treatment of poly-articular juvenile idiopathic arthritis (pJIA) using the German Biologics JIA registry (BiKeR)

Action: For adoption of advice to CHMP

7.5.13. Human papillomavirus vaccine [types 16, 18] (recombinant, adjuvanted, adsorbed) - CERVARIX (CAP) - EMEA/H/C/000721/II/0117

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the interim report for study EPI-HPV-099 (217743): an observational, retrospective database post-authorisation safety study (PASS) assessing trends and changes over time in incidence of anal cancer and feasibility for a case-control study in European countries that introduced Cervarix in their National Immunisation Programme. The study was set up to address the missing information on the impact and effectiveness of Cervarix against anal lesions and cancer in the Cervarix RMP. The RMP version 26 has also been submitted

Action: For adoption of advice to CHMP

7.5.14. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/MEA 002.5

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Second annual interim report for study VX20-445-120: Real-World Effects and Utilisation Patterns of Elexacaftor, Tezacaftor, and Ivacaftor Combination Therapy (ELX/TEZ/IVA) in Patients with Cystic Fibrosis (CF)

Action: For adoption of advice to CHMP

7.5.15. Naldemedine - RIZMOIC (CAP) - EMEA/H/C/004256/MEA 001.4

Applicant: Shionogi B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: First progress report for an observational PASS of patients with chronic opioid use for non-cancer and cancer pain who have opioid-induced constipation (OIC)

Action: For adoption of advice to CHMP

7.5.16. Nonacog beta pegol - REFIXIA (CAP) - EMEA/H/C/004178/LEG 006.3

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Gabriele Maurer

Scope: Fourth yearly progress report for PASS NN7999-4031 (Paradigm 8): a non-interventional study in male haemophilia B patients receiving nonacog beta pegol (N9-GP) prophylaxis treatment to investigate the potential effects of polyethylene glycol (PEG) accumulation in the choroid plexus of the brain and other tissues/organs

Action: For adoption of advice to CHMP

7.5.17. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 002.3

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: First annual interim report for study COMB157G2407] category 3 study listed in the RMP version 2.0: evaluation of pregnancy and infant outcomes in Kesimpta patients using Pregnancy outcomes Intensive Monitoring (PRIM) data – The Kesimpta-PRIM study

Action: For adoption of advice to CHMP

7.5.18. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[28]) - EMEA/H/W/002300/MEA 003.8

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Seventh progress report for study EPI-MAL-003: Estimate the incidence of protocol-defined potential adverse events of special interest (AESI) and other adverse events leading to hospitalisation or death, in children vaccinated with RTS,S/AS01E enrolled during the EPI-MAL-003 study

Action: For adoption of advice to CHMP

7.5.19. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/ANX 003.9

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Fourth interim report for study TED-R-13-002: an international short bowel syndrome registry - a prospective, long-term observational cohort study of patients with short bowel syndrome

Action: For adoption of advice to CHMP

7.5.20. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.6

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Third annual progress report for study M14745-40 (Tildrakizumab PASS in European Psoriasis Registry): To collect long-term safety data in particular relating to event of special interest (important potential risks and pregnancy related outcomes) for tildrakizumab. (Malignancies, MACEs, Serious infections, SIBH, Hypersensitivity, IBD, Safety in pregnant and lactating women). To further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine clinical care

Action: For adoption of advice to CHMP

7.5.21. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/ANX 003.10

Applicant: Novartis Europharm Limited, ATMP[29]

PRAC Rapporteur: Gabriele Maurer

Scope: Sixth semi-annual report for study CCTL019B2401: a non-interventional PASS to further characterise the safety, including long-term safety, of Kymriah (tisagenlecleucel) based on data from a disease registry in acute lymphoblastic leukaemia (ALL) and diffuse large

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

[29] Advanced therapy medicinal product

B-cell lymphoma (DLBCL) patients (European Society for Blood and Marrow Transplant Society Registry (EBMT) data only)

Action: For adoption of advice to CAT and CHMP

7.5.22. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 041.2

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Justification for not submitting an interim study report for study C4591036 (former paediatric heart network study): a safety surveillance study of myocarditis and myopericarditis associated with Comirnaty (tozinameran) in persons less than 21 years of age to characterize the clinical course, risk factors, long-term sequelae, and quality of life in children and young adults under 21 years with acute post-vaccine myocarditis, including a protocol amendment

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 001.1

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Position paper on the design and conduct of a pregnancy Exposure registry (C-VIPER) to estimate the risk of the most common obstetric outcomes, i.e. pregnancy losses, placentation disorders, gestational diabetes, premature delivery, and COVID-19, neonatal outcomes, i.e. congenital anomalies, low birth weight for gestational age, neonatal intensive care unit admission, and COVID-19, among pregnant women exposed to COVID-19 Vaccine (inactivated, adjuvanted) Valneva from 30 days prior to the first day of the last menstrual period (LMP) to end of pregnancy and their offspring relative to a matched unexposed reference group

Action: For adoption of advice to CHMP

7.6.2. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 002.1

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Position paper on the design and conduct of a PASS protocol to estimate the incidence of adverse events of special interest (AESIs), including the potential risk of vaccine associated enhanced disease (VAED) and vaccine associated respiratory disease (VAERD), that are medically attended following the administration of COVID-19 Vaccine (inactivated, adjuvanted) Valneva in the real-world immunisation setting. A retrospective study using health care

databases

Action: For adoption of advice to CHMP

7.6.3. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - COVID-19 VACCINE (INACTIVATED, ADJUVANTED) VALNEVA (CAP) - EMEA/H/C/006019/MEA 006.2

Applicant: Valneva Austria GmbH

PRAC Rapporteur: Gabriele Maurer

Scope: Position paper on the design and conduct of a post-authorisation effectiveness study (PAES) to estimate effectiveness against hospitalization due to laboratory-confirmed SARS-CoV-2 in severe acute respiratory infection (SARI) patients who have been vaccinated with COVID-19 Vaccine (inactivated, adjuvanted) Valneva

Action: For adoption of advice to CHMP

7.6.4. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 032.3

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: MAH's response to MEA 032.2 [submission of a critical analysis of the feasibility of using alternative data sources to complement the Transplantation Pregnancy Registry International (TPRI) study outcomes on pregnancy and breastfeeding] as per the request for supplementary information (RSI) adopted in October 2022

Action: For adoption of advice to CHMP

7.6.5. Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 024.3

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Mari Thorn

Scope: MAH's response to MEA 032.2 [submission of a critical analysis of the feasibility of using alternative data sources to complement the Transplantation Pregnancy Registry International (TPRI) study outcomes on pregnancy and breastfeeding] as per the request for supplementary information (RSI) adopted in October 2022

Action: For adoption of advice to CHMP

7.6.6. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 047.2

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Initial statistical analysis plan (SAP) for study C4591038 (listed as a category 3 study in the RMP): a post conditional approval active surveillance study among individuals in Europe receiving the Pfizer BioNTech coronavirus disease 2019 (COVID-19) vaccine to investigate

natural history of post-vaccination myocarditis and pericarditis

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/S/0060 (without RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Mari Thorn

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Susoctocog alfa - OBIZUR (CAP) - EMEA/H/C/002792/S/0050 (without RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Gabriele Maurer

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. Budesonide - KINPEYGO (CAP) - EMEA/H/C/005653/R/0003 (without RMP)

Applicant: STADA Arzneimittel AG

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Entrectinib - ROZLYTREK (CAP) - EMEA/H/C/004936/R/0015 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. 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. Abemaciclib - VERZENIOS (CAP) - EMEA/H/C/004302/R/0025 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Adalimumab - HULIO (CAP) - EMEA/H/C/004429/R/0041 (without RMP)

Applicant: Viatris Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. 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

8.3.4. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - EMEA/H/C/004282/R/0037 (without RMP)

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Inês Ribeiro-Vaz

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/R/0061 (with RMP)

Applicant: Gentium S.r.l.

PRAC Rapporteur: Mari Thorn

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. 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

8.3.7. Melatonin - SLENYTO (CAP) - EMEA/H/C/004425/R/0021 (with RMP)

Applicant: RAD Neurim Pharmaceuticals EEC SARL

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. 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

8.3.9. Pegfilgrastim - PELGRAZ (CAP) - EMEA/H/C/003961/R/0040 (with RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Selumetinib - KOSELUGO (CAP) - EMEA/H/C/005244/R/0010 (with RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/R/0038 (with RMP)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/R/0042 (with RMP)

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Vestronidase alfa - MEPSEVII (CAP) - EMEA/H/C/004438/R/0033 (without RMP)

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.14. Vigabatrin - KIGABEQ (CAP) - EMEA/H/C/004534/R/0012 (with RMP)

Applicant: ORPHELIA Pharma SAS

PRAC Rapporteur: Kirsti Villikka

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. Testosterone (NAP) - EE/H/PSUFU/00010631/202112; EE/H/PSUFU/00002908/202112

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: PRAC consultation on the labelling updates concerning the risk of central serous chorioretinopathy for all formulations of products containing testosterone, as per the conclusions of the PSUSA procedure follow-up measures (PSUFUs) referring to all formulations of testosterone (apart from topical use) (EE/H/PSUFU/00010631/202112) and to testosterone products of topical use (EE/H/PSUFU/00002908/202112) concluded in September 2022, on request of Estonia

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

None

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

None

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uuskü**Action:** For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.10.5. Coronavirus (COVID-19) pandemic - Consideration on core requirements for PSURs of COVID-19 vaccines - corePSUR19 guidance

Action: For adoption

12.10.6. Periodic safety update reports single assessment (PSUSA) – review of 'other considerations' section in the assessment report

PRAC lead: Sabine Straus
Action: For discussion

12.10.7. Periodic safety update reports single assessment (PSUSA) – review of PSUSA assessment report templates for nationally authorised products (NAPs) only

Action: For discussion

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

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.13.2. EudraVigilance – annual report 2022

Action: For discussion

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. Study report on the impact of EU label changes for medicinal products containing methotrexate for weekly administration: risk awareness and adherence

PRAC lead: Martin Huber, Nikica Mirošević Skvrce

Action: For discussion

12.21. Others

12.21.1. IRIS platform – update on SharePoint functionality

Action: For discussion

12.21.2. Pharmacovigilance business team - activities and work plan for 2023

Action: For discussion

13. Any other business

Next meeting on: 11-14 April 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/