04 July 2022
EMA/PRAC/573334/2022
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 04-07 July 2022

Chair: Sabine Straus – Vice-Chair: Martin Huber

04 July 2022, 13:00 – 19:30, room 1C / via teleconference

05 July 2022, 08:30 – 19:30, room 1C / via teleconference

06 July 2022, 08:30 – 19:30, room 1C / via teleconference

07 July 2022, 08:30 – 16:00, room 1C / via teleconference

Organisational, regulatory and methodological matters (ORGAM)

20 July 2022, 09:00 – 12:00, via teleconference

Health and safety information

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

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).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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 04-07 July 2022. See July 2022 PRAC minutes (to be published post September 2022 PRAC meeting).

1.2. Agenda of the meeting on 04-07 July 2022

Action: For adoption

1.3. Minutes of the previous meeting on 07-10 June 2022

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Terlipressin (NAP) - EMEA/H/A-31/1514

Applicant(s): various

PRAC Rapporteur: Krõõt Aab; PRAC Co-rapporteur: Anette Kirstine Stark

Scope: Review of the benefit-risk balance following notification by Denmark 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

3.3.1. Chlormadinone (NAP); chlormadinone, ethinylestradiol (NAP); nomegestrol (NAP); nomegestrol, estradiol – ZOELY (CAP); NAP - EMEA/H/A-31/1510

Applicant(s): Theramex Ireland Limited (Zoely), various

PRAC Rapporteur: Martin Huber; PRAC Co-rapporteur: Željana Margan Koletić

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 PRAC recommendation to CHMP

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. Diphtheria, tetanus, pertussis (acellular, component), poliomyelitis (inactivated) vaccine (adsorbed) (NAP); diphtheria, tetanus, pertussis (acellular, component), poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content) (NAP)

Applicant(s): various

[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

PRAC Rapporteur: To be appointed

Scope: Signal of immune thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT: 19831 – New signal

Lead Member State(s): DK

4.1.2. 3-hydroxy 3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins): atorvastatin (NAP); fluvastatin (NAP); lovastatin (NAP); pitavastatin (NAP); pravastatin (NAP); rosuvastatin (NAP); simvastatin (NAP) and other relevant fixed dose combinations; pravastatin, fenofibrate – PRAVAFENIX (CAP); simvastatin, fenofibrate – CHOLIB (CAP)

Applicant(s): Laboratoires SMB s.a. (Pravafenix), Mylan IRE Healthcare Limited (Cholib); various

PRAC Rapporteur: To be appointed

Scope: Signal of myasthenia gravis

Action: For adoption of PRAC recommendation

EPITT 19822 – New signal

Lead Member State(s): AT, CZ, DE, EE, FI, FR, HR, HU, IT, NL, SI

4.2. New signals detected from other sources

4.2.1. Cetuximab – ERBITUX (CAP)

Applicant: Merck Europe B.V.

PRAC Rapporteur: Annika Folin

Scope: Signal of nephrotic syndrome

Action: For adoption of PRAC recommendation

EPITT 19819 – New signal

Lead Member State(s): SE

4.2.2. Topiramate (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of neurodevelopmental disorders due to in utero exposure

Action: For adoption of PRAC recommendation

EPITT 19825 – New signal

Lead Member State(s): SE

4.3. Signals follow-up and prioritisation

4.3.1. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/SDA/061

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of drug reaction with eosinophilia and systemic symptoms (DRESS)

Action: For adoption of PRAC recommendation

EPITT 19360 – Follow-up to February 2022

4.3.2. Tocilizumab – ROACTEMRA (CAP) - EMEA/H/C/000955/SDA/060.1

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of encephalopathy including posterior reversible encephalopathy syndrome (PRES)

Action: For adoption of PRAC recommendation

EPITT 19731 – Follow-up to April 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. Coronavirus (COVID-19) vaccine (recombinant protein receptor binding domain fusion heterodimer) - EMEA/H/C/006058

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

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

5.1.2. Deucravacitinib - EMEA/H/C/005755

Scope: Treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy

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

5.1.3. Efbemalenograstim alfa - EMEA/H/C/005828

Scope: Treatment to reduce the duration of neutropenia and the incidence of febrile neutropenia

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

5.1.4. Etranacogene dezaparvovec - EMEA/H/C/004827, PRIME, Orphan

Applicant: CSL Behring GmbH, ATMP[3]

Scope (accelerated assessment): Treatment of adults with Haemophilia B

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

5.1.5. Gozetotide - EMEA/H/C/005488

Scope: Indicated for the identification of prostate-specific membrane antigen (PSMA)-positive lesions after radiolabelling with gallium-68

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

5.1.6. Loncastuximab tesirine - EMEA/H/C/005685, Orphan

Applicant: FGK Representative Service GmbH

Scope: Treatment of adult patients with relapsed or refractory large B-cell lymphoma

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

5.1.7. Lutetium (^{177}Lu) vipivotide tetraxetan - EMEA/H/C/005483

Scope: Treatment of prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC)

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

5.1.8. Mavacamten - EMEA/H/C/005457

Scope: Treatment of symptomatic obstructive hypertrophic cardiomyopathy

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

5.1.9. Plerixafor - EMEA/H/C/005943

Scope: Treatment of lymphoma and multiple myeloma

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

[3] Advanced therapy medicinal product

5.1.10. Spesolimab - EMEA/H/C/005874

Scope: Treatment of flares in adult patients with generalised pustular psoriasis

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

5.1.11. Teriflunomide - EMEA/H/C/005960

Scope: Treatment of multiple sclerosis (MS)

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. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/II/0041

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 10.0) in order to include the new important identified risk of 'autoimmune encephalitis' and to introduce changes in accordance to the Rapporteurs' requests made in the conclusions of variation II/0038 finalised in January 2022

Action: For adoption of PRAC Assessment Report

5.2.2. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/II/0032

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP version 3.2 in order to reflect the updated study milestones and completion of the post authorisation safety study of CE/BZA in the United States (US PASS, Study B2311060) previously assessed as part of II/0030 (MEA002.15), as well as to update the post marketing data with the data lock point of 31 October 2021

Action: For adoption of PRAC Assessment Report

5.2.3. Fentanyl - EFFENTORA (CAP); NAP - EMEA/H/C/000833/WS2212/0060

Applicant: Teva B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 5.1) in order to bring it in line with revision 2 of GVP module V on 'Risk management systems' and to implement PRAC requests arising from previous assessments as follows: 1) revision of the list of safety concerns; 2) update of the key messages of the educational materials in line with another centrally authorised product containing fentanyl (Instanyl (fentanyl)). As a result, Annex II on additional risk minimisation measures is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.4. Fentanyl - PECFENT (CAP) - EMEA/H/C/001164/II/0054

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 7.1) in line with the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA 00001369/202004) finalised in January 2021 in order to update the key messages of the educational materials in line with another centrally authorised product containing fentanyl (Instanyl (fentanyl)). As a result, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated accordingly. Finally, the MAH took the opportunity to bring the RMP in line with revision 2 of GVP module V on 'Risk management systems' and the product information in line with the latest quality review of documents (QRD) template (version 10.2)

Action: For adoption of PRAC Assessment Report

5.2.5. Mepolizumab - NUCALA (CAP) - EMEA/H/C/003860/II/0048

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated RMP (version 9) to reflect the proposal to stop the enrolment and to close the pregnancy registry known as mepolizumab pregnancy exposure study 200870 (listed as category 3 study in the RMP): a phase 4, prospective, observational, exposure cohort study of pregnancy outcomes in women. The application also includes details of the proposed enhanced data collection for all pregnancies reported as an alternative

Action: For adoption of PRAC Assessment Report

5.2.6. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/II/0038

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of an updated RMP (version 7.2) to remove study D3820R00009 (listed as a category 3 study in the RMP): an observational drug utilisation PASS of Moventig (naloxegol) in selected European populations, following the completion of procedure MEA 006.11 in November 2021

Action: For adoption of PRAC Assessment Report

5.2.7. Nintedanib - VARGATEF (CAP) - EMEA/H/C/002569/II/0044

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Georgia Gkegka

Scope: Submission of an updated RMP (version 10.0) in order to remove safety concerns that were classified as important identified risks, important potential risks and missing information, based on cumulative post-marketing experience. The MAH also proposed an

update of the anatomical therapeutic chemical (ATC) code, an update of post-marketing exposure, the removal of adverse event follow-up forms and an update of search strategies

Action: For adoption of PRAC Assessment Report

5.2.8. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/II/0035

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault

Scope: Submission of an updated RMP (version 9.3) in order to reflect amendments to the protocol of ongoing EXPOSURE PASS study: an international, observational, cohort study of pulmonary arterial hypertension (PAH) patients newly treated with either Uptravi (selexipag) or any other PAH-specific therapy, in clinical practice; to add the EXTRACT study (67896049PAH0002): a retrospective medical chart review of patients with PAH newly treated with either Uptravi (selexipag) or any other PAH-specific therapy as an additional pharmacovigilance activity; and to reflect amendments to the protocol of study EDUCATE (listed as category 3 study in the RMP): a PASS to evaluate risk minimisation measures for medication errors with Uptravi (selexipag) during the titration phase in patients with PAH in clinical practice (assessed and approved in MEA 003.4)

Action: For adoption of PRAC Assessment Report

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

5.3.1. Abrocitinib - CIBINQO (CAP) - EMEA/H/C/005452/II/0001

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of sections 4.4 and 4.8 of the SmPC based on updated safety data from the full cumulative pool from ongoing long-term extension study B7451015: a phase 3 multicentre, long-term extension study investigating the efficacy and safety of abrocitinib, with or without topical medications, administered to subjects aged 12 years and older with moderate to severe atopic dermatitis. The RMP (version 1.0) is updated accordingly. In addition, MAH took the opportunity to implement editorial changes in the SmPC and to update the contact details of the local representatives in the package leaflet

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

5.3.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/004480/II/0046, Orphan

Applicant: Kite Pharma EU B.V., ATMP[4]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 5.3) are updated in accordance. In addition, the

[4] Advanced therapy medicinal product

MAH took the opportunity to update the product information with minor editorial changes

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

5.3.3. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/II/0028

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of coronavirus disease 2019 (COVID-19) in hospitalised adult and paediatric patients aged 10 years and older who require low-flow oxygen or non-invasive ventilation/high flow oxygen. As a consequence, sections 4.1, 4.2, 4.4, 4.6, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. Annex II, the package leaflet and the RMP (version 11.1) are updated in accordance

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

5.3.4. Bictegravi, emtricitabine, tenofovir alafenamide - BIKTARVY (CAP) - EMEA/H/C/004449/X/0040/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped application consisting of: 1) extension application to introduce a new strength 30/120/15 mg; 2) extension of indication to include a paediatric indication by adding the use in patients of 2 years of age and older and weighing at least 14 kg. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet are updated to support the extension of indication. The RMP (version 3.1) is updated in accordance

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

5.3.5. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/II/0008/G, Orphan

Applicant: Kite Pharma EU B.V., ATMP[5]

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) extension of indication to include treatment of adult patients with relapsed or refractory (r/r) B-cell acute lymphoblastic leukaemia (B-ALL); 2) change the drug product dose specification for the new indication. As a consequence, sections 2.2, 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet, labelling and the RMP (version 1.1) are updated in accordance. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2)

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

[5] Advanced therapy medicinal product

5.3.6. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/II/0028, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the frequency of adverse drug reactions, to split immunogenicity data into paediatric and adult populations and to update clinical efficacy in paediatric patients upon request by the CHMP, following procedures P46/006, P46/007 and variations II/04 and II/10/G finalised in October 2019 and July 2020 respectively, based on the final results from: 1) study UX023-CL201: a randomised, open-label, dose finding, phase 2 study to assess the pharmacodynamics and safety of KRN23 (burosumab) in paediatric patients with X-linked hypophosphatemia (XLH); 2) study UX023-CL205: an open-label, phase 2 study to assess the safety, pharmacodynamics, and efficacy of KRN23 in children from 1 to 4 years old with XLH; 3) study UX023-CL301: randomized, open-label, phase 3 study to assess the efficacy and safety of krn23 versus oral phosphate and active vitamin D treatment in paediatric patients with XLH. In addition, the MAH proposed to delete the remaining specific obligation (SO) for study UX023-CL205 from Annex II, and to request a switch from a conditional marketing authorisation (MA) to standard MA. The package leaflet and the RMP (version 5.0) are updated accordingly

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

5.3.7. Cenobamate - ONTOZRY (CAP) - EMEA/H/C/005377/II/0009

Applicant: Angelini S.p.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 5.3 of the SmPC in order to update information on toxicity to reproduction and development based on final results from nonclinical study "Effects of Cenobamate (YKP3089) on Embryo-Fetal Development in Rats after Twice Daily Oral Administration". The RMP version 3.0 has also been submitted

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

5.3.8. Clopidogrel - ISCOVER (CAP) - EMEA/H/C/000175/WS2150/0146; PLAVIX (CAP) - EMEA/H/C/000174/WS2150/0145; clopidogrel, acetylsalicylic acid - DUOPLAVIN (CAP) - EMEA/H/C/001143/WS2150/0060

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infraction (STEMI) patients undergoing percutaneous coronary intervention (PCI). As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The RMP (version 1.5) for Iscover/Plavix (clopidogrel) is updated accordingly. In addition, the MAH took the opportunity to introduce an editorial update in the labelling

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

5.3.9. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) (NVX-CoV2373) - NUVAXOVID (CAP) - EMEA/H/C/005808/II/0014

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to include a 0.5 mL third dose for Nuvaxovid, to boost subjects that have previously completed a primary vaccination series with Nuvaxovid (homologous booster dose) or with an authorised mRNA or adenoviral vector vaccine (heterologous booster dose), based on interim data from study 2019nCoV-101 (Part 2), a Phase 1/2, Randomized, Observer-Blinded Study to Evaluate the Safety and Immunogenicity of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) With or Without Matrix-M Adjuvant in Healthy Subjects (NCT04368988), final data from study 2019nCoV-501, a Phase 2a/b, Randomized, Observer-Blinded, Placebo-Controlled Study to Evaluate the Efficacy, Immunogenicity, and Safety of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) With Matrix-M Adjuvant in South African Adult Subjects Living Without HIV; and Safety and Immunogenicity in Adults Living With HIV (NCT04533399) and data from the COV-BOOST study (Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial); the Package Leaflet is updated accordingly. The RMP version 1.2 has also been submitted. In addition, the Marketing Authorisation Holder (MAH) took the opportunity to make minor editorial corrections throughout the product information

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

5.3.10. Deferasirox - EXJADE (CAP) - EMEA/H/C/000670/II/0082/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped variations consisting of: 1) submission of the final report from study CICL670F2202 (Calypso study) (listed as a category 3 study in the RMP): a randomized, open-label, multicentre, two arm, phase 2 study to evaluate treatment compliance, efficacy and safety of deferasirox (granules) in paediatric patients with iron overload; 2) removal of the risk of 'medication error' from the RMP and of the information related to the discontinuation of the dispersible tablets in the EU. The RMP (version 20.0) is updated accordingly

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

5.3.11. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0062

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of eosinophilic esophagitis (EoE) in adults and adolescents 12 years and older who are inadequately controlled by, are intolerant to, or who are not candidates for conventional medicinal therapy, based on the pivotal Study R668-EE-1774. This is an ongoing phase 3, randomized, double-blind, placebo-controlled, 3-part (A, B, C) safety and efficacy study with an initial 24-week

treatment period in adults (≥18 years of age) and adolescents (≥12 to <18 years of age) with EoE, and which includes an extended treatment period to a total of 52 weeks. 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 8.0 of the RMP has also been submitted

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

5.3.12. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0063

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of adults with moderate to severe prurigo nodularis (PN) who are candidates for systemic therapy, based on results from studies EFC16459 and EFC16460 (PRIME and PRIME2); these are two phase 3, 24-week, randomized, double-blind, placebo-controlled, multi-centre, parallel group studies undertaken to evaluate the efficacy and safety of dupilumab in patients 18 years of age and older with moderate to severe PN, who are inadequately controlled on topical prescription therapies or when those therapies are not advisable. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.0 of the RMP has also been submitted. As part of this application, the MAH is also requesting a 1-year extension of the market protection

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

5.3.13. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0045

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include IMFINZI in combination with tremelimumab for the treatment of adults with unresectable hepatocellular carcinoma (uHCC), based on final results from Study D419CC00002 (HIMALAYA): a randomized, open-label, multi-center phase III study of durvalumab and tremelimumab as first-line treatment in patients with unresectable hepatocellular carcinoma. 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. In addition, the MAH took the opportunity to implement minor editorial changes in the SmPC and Package Leaflet. Version 6.1 of the RMP has also been submitted

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

5.3.14. Durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/II/0046

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Extension of indication to include IMFINZI in combination with chemotherapy for the treatment of adults with locally advanced or metastatic biliary tract cancer (BTC), based on the second interim analysis from the ongoing pivotal study D933AC00001 (TOPAZ-1): a phase III randomized, double-blind, placebo-controlled, multi-regional, international study conducted to assess the efficacy and safety of durvalumab in combination with the current

standard of care Gemcitabine/Cisplatin for the first-line treatment of patients with locally advanced or metastatic BTC. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC have been updated and the Package leaflet has been updated accordingly. Version 7.1 of the RMP has also been submitted

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

5.3.15. Emtricitabine, tenofovir alafenamide - DESCOVY (CAP) - EMEA/H/C/004094/II/0057

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the clinical study report and supporting modular summaries for study GS-US-311-1269: a phase 2/3, open label, multi-cohort switch study to evaluate emtricitabine/tenofovir alafenamide (F/TAF) in human immunodeficiency virus type 1 (HIV-1) infected children and adolescents virologically suppressed on a two nucleoside reverse transcriptase inhibitors (NRTI) containing regimen in fulfilment of the milestone for the category 3 additional pharmacovigilance activity to address long-term safety information in adolescents as missing information. The RMP (version 6.1) is updated accordingly

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

5.3.16. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0010/G, Orphan

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of an update of section 5.3 of the SmPC in order to update the non-clinical information based on data from: 1) study 20147822: a 6-month carcinogenicity study of fenfluramine hydrochloride in mice; 2) study 8001993: a 2-year oral gavage carcinogenicity study of fenfluramine hydrochloride in rats, together with the final reports for dose range finding studies 20147821 and 20166554 and the final report for study 2021006-Z001-01: in-vitro evaluation of potential melanin binding by fenfluramine and norfenfluramine. The RMP (version 3.1) is updated accordingly

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

5.3.17. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/II/0011/G, Orphan

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 4.2 and 5.2 of the SmPC to include the relevant information regarding patients with renal impairment following the study 1902: a pharmacokinetic study of fenfluramine hydrochloride in subjects with varying degrees of impaired and normal renal function; 2) update of section 4.4 and 4.5 of the SmPC in order to reflect the relevant information on cytochrome (CYP)1A2 or CYP2B6 or CYP2D6 inducers following study 1904: a pharmacokinetic drug-drug interaction study of fenfluramine hydrochloride with and without fluvoxamine (CYP1A2 inhibitor), paroxetine (CYP2D6 inhibitor) and rifampin (CYP2B6 inducer) in healthy subjects. The RMP (version 2.2) is updated accordingly

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

5.3.18. Fluticasone furoate, vilanterol - RELVAR ELLIPTA (CAP) - EMEA/H/C/002673/WS2274/0054; REVINTY ELLIPTA (CAP) - EMEA/H/C/002745/WS2274/0052

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study HZA114971 (listed as a category 3 study in the RMP): a multicentre randomised, double-blind, placebo-controlled, parallel-group study to evaluate the effects of a one-year regimen of orally inhaled fluticasone furoate 50 mcg once daily on growth velocity in prepubertal, paediatric subjects with asthma. The RMP version 11.1 has also been submitted

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

5.3.19. Human normal immunoglobulin - HYQVIA (CAP) - EMEA/H/C/002491/II/0078

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.8 and 5.1 of the SmPC in order to update safety data in paediatric population based on final results from study 161504 (listed as a category 3 study in the RMP) – Post-Authorization Safety, Tolerability and Immunogenicity Evaluation of HyQvia in Pediatric Subjects With Primary Immunodeficiency Diseases. This is a paediatric interventional Phase 4 study performed to acquire additional data on safety, tolerability and immunogenicity of HyQvia in pediatric (age two to <18 years) patients with Primary Immunodeficiency Diseases (PIDD). In addition, the MAH is taking this opportunity to update Annex II-D of the PI following procedure EMEA/H/C/002491/II/0070/G. The RMP version 13.1 has also been submitted

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

5.3.20. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0069

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of section 4.4 of the SmPC to include information on fatal and serious cardiac arrythmias and cardiac failure, relevant warnings and periodical monitoring of patients following a safety assessment for increased risk of sudden death/cardiac death with the use of ibrutinib. The MAH took the opportunity to correct typographical errors throughout the product information. The package leaflet and the RMP (version 11.0) are updated accordingly

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

5.3.21. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/II/0017/G, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 5.3 of the SmPC in order to update the non-clinical information based on final results from study VX-445-TX-015: a 2-year oral carcinogenicity study in rats evaluating the carcinogenic potential of up to 10 mg/kg/day of elexacaftor. The RMP (version 6.0) is updated accordingly; 2) submission of the final report for study VX-661-TX-038: a tezacaftor juvenile toxicity study

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

5.3.22. Lorlatinib - LORVIQUA (CAP) - EMEA/H/C/004646/II/0022

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Submission of an updated RMP version 5.0 to revise plans for conduct of hepatic impairment studies. The RMP is updated to reflect the termination of the hepatic impairment study B7461009: a Phase 1 Study to Evaluate the Effect of Hepatic Impairment on the Pharmacokinetics and Safety of Lorlatinib in Advanced Cancer Patients and to include new hepatic impairment study B7461040: a Phase 1, Open-label, Single-dose, Parallel-group Study to Evaluate The Plasma Pharmacokinetics and Safety of Lorlatinib in Participants with Moderate and Severe Hepatic Impairment Relative to Participants with Normal Hepatic Function

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

5.3.23. Metreleptin - MYALEPTA (CAP) - EMEA/H/C/004218/II/0025, Orphan

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Adam Przybylkowski

Scope: Proposal for an alternative study to the currently agreed protocol for study AEGR-734-002 (specific obligation SOB002): a 24-month, multicentre, open label phase 4 post-authorisation efficacy study (PAES) to evaluate the efficacy, safety and immunogenicity of daily subcutaneous metreleptin treatment in patients with partial lipodystrophy due to the challenges of implementing the existing protocol. Annex II and the RMP (version 2.1) are updated accordingly. The MAH took the opportunity to update the RMP in line with the outcome of previous procedures and to include editorial changes

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

5.3.24. Olaparib - LYNPARZA (CAP) - EMEA/H/C/003726/II/0053

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Extension of indication to include treatment of adults with metastatic castration

resistant prostate cancer (mCRPC) with olaparib in combination with abiraterone and prednisone or prednisolone, based on the results of the pivotal study D081SC00001 (PROpel study): a phase 3, randomised, double-blind, placebo-controlled, multicentre study evaluating olaparib vs placebo in combination with abiraterone as first line treatment for men with mCRPC, and supportive evidence from study D081DC00008 (study 8): a randomised, double-blind, placebo-controlled, multicentre phase 2 study to compare the efficacy, safety and tolerability of olaparib versus placebo when given in addition to abiraterone treatment in patients with mCRPC who have received prior chemotherapy containing docetaxel. Consequently, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC for Lynparza (olaparib) tablets are updated. In addition, sections 4.4 and 4.8 of the SmPC for Lynparza (olaparib) hard capsules are revised based on the updated safety data analysis. The package leaflet and the RMP (version 24) are updated accordingly

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

5.3.25. Oritavancin - TENKASI (CAP) - EMEA/H/C/003785/X/0036

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension application to add a new strength of 1200 mg for powder for concentrate for solution for infusion. The RMP (version 4) is updated accordingly

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

5.3.26. 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 Randomized, 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

5.3.27. Peginterferon alfa-2a - PEGASYS (CAP) - EMEA/H/C/000395/II/0112

Applicant: Zr Pharma& GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.8 of the SmPC in order to include information on post-treatment recovery in growth based on final results from study YV25718 listed as a category 3 study in the RMP; this is a Phase IIIb parallel group, open label study of pegylated interferon alfa-2a monotherapy (PEG-IFN, RO0258310) compared to untreated control in children with HBeAg-Positive Chronic Hepatitis B in the immune active phase. The RMP version 9.1 has also been submitted. In addition, the MAH took the opportunity to implement editorial changes in the

Package Leaflet

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

5.3.28. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0121

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include Keytruda as monotherapy for the adjuvant treatment of adults with Stage IB (T2a ≥ 4 cm), II or IIIA non-small cell lung carcinoma (NSCLC) who have undergone complete resection, based on study KEYNOTE-091: an ongoing Phase 3, randomized, triple-blinded, placebo-controlled, multicenter study of pembrolizumab versus placebo in patients with early-stage NSCLC after resection and completion of standard adjuvant therapy. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are being updated and the Package Leaflet is updated in accordance. An updated RMP version 39.1 was also submitted

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

5.3.29. Pneumococcal polysaccharide conjugate vaccine (adsorbed) - VAXNEUVANCE (CAP) - EMEA/H/C/005477/II/0001

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of infants, children and adolescents from 6 weeks to less than 18 years of age for active immunisation for the prevention of invasive disease, pneumonia and acute otitis media for Vaxneuvance, based on final results from: 1) study V114-008: a phase 2, double-blind, randomized, multicentre trial to evaluate the safety, tolerability, and immunogenicity of V114 (pneumococcal polysaccharide conjugate vaccine (adsorbed)) compared to Prevenar 13 (pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)) in healthy infants; 2) seven phase 3 studies (V114-023, V114-024, V114-025, V114-027, V114-029, V114-030, V114-031): interventional studies to evaluate the safety, tolerability and immunogenicity of V114 (pneumococcal polysaccharide conjugate vaccine (adsorbed)) in healthy and immunocompromised infants, children and adolescents. 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. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to include editorial changes in the product information. The RMP (version 1.1) is updated accordingly

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

5.3.30. Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/X/0027/G

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped application consisting of: 1) extension application to introduce a new pharmaceutical form (solution for injection) associated with new strength (245 mg) and route of administration (subcutaneous use); 2) update of the Summary of product

characteristics and Labelling for Ultomiris intravenous formulation (IV) in order to align with the proposed Ultomiris subcutaneous formulation (SC). The RMP (version 5.0) is updated in accordance

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

5.3.31. Remdesivir - VEKLURY (CAP) - EMEA/H/C/005622/II/0034/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Grouped variations consisting of: 1) update sections 5.1 and 5.2 of the SmPC as a consequence of the submission of the final component of specific obligation (SO) 012 agreed in the renewal procedure of the conditional marketing authorisation (CMA) (R/0015) finalised in April 2021 and listed in Annex II of the product information. This submission includes the adaptive COVID-19 treatment trial (ACTT-1) final sequencing and phenotyping analysis and the full virology report including activity against variants. The package leaflet and the RMP (version 3.1) are updated accordingly

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

5.3.32. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/X/0020/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Grouped variations consisting of: 1) extension of application to introduce a new pharmaceutical form (concentrate for solution for infusion), a new strength (600 mg) and a new route of administration (intravenous use); 2) extension of application to add a new strength of 360 mg (150 mg/mL) for risankizumab solution for injection (in cartridge) for subcutaneous use. The new presentations are indicated for the treatment of patients 16 years and older with moderately to severely active Crohn’s disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy, or if such therapies are not advisable. The RMP (version 4.0) is updated in accordance

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

5.3.33. Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/II/0005/G, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Grouped variations consisting of: 1) extension of indication to include treatment of patients below 2 months of age based on interim results from pivotal study BN40703 (RAINBOWFISH): an ongoing phase 2 multicentre, open-label, and single-arm study designed to evaluate the efficacy, safety, tolerability, and pharmacokinetic/pharmacodynamic (PK/PD) of risdiplam in pre-symptomatic infants below 2 months of age who were genetically diagnosed with spinal muscular atrophy (SMA). As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. In addition, the MAH took the opportunity to make some editorial improvements in the product information;

2) update of Evrysdi (risdiplam) pack configuration. As a consequence, section 6.5 of the SmPC and the labelling are updated; 3) removal of a device. As a consequence, section 6.5 of the SmPC and the labelling are updated. The package leaflet and the RMP (version 1.1) are updated in accordance

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

5.3.34. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/II/0014/G

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) extension of indication to include first-line treatment of advanced rearranged during transfection (RET)-mutant medullary thyroid cancer (MTC) in adults and adolescents 12 years and older based on interim results from Study LIBRETTO-001 (LOXO-RET-17001) on the clinical safety and efficacy of selpercatinib in patients with RET-mutant MTC who are cabozantinib and vandetanib treatment-naïve (MTC:-Cab/-Van). LIBRETTO-001 is a global, multicohort, open-label, Phase 1/2 study in adult and adolescent patients with advanced RET-altered tumours. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted; 2) submission of an updated Phase II Environmental Risk Assessment in order to reflect the patient population as per the approved indication. 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

5.3.35. Setmelanotide - IMCIVREE (CAP) - EMEA/H/C/005089/II/0002/G, Orphan

Applicant: Rhythm Pharmaceuticals Netherlands B.V.,

PRAC Rapporteur: Anna Mareková

Scope: Grouped variations consisting of: 1) addition of a new therapeutic indication for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.0) are updated accordingly; 2) addition of a new therapeutic indication for the treatment of obesity and the control of hunger associated with genetically confirmed Alström syndrome (AS). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated accordingly. The package leaflet and the RMP (version 1.0) are updated in accordance

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

5.3.36. Smallpox vaccine (live modified vaccinia virus Ankara) - IMVANEX (CAP) - EMEA/H/C/002596/II/0076

Applicant: Bavarian Nordic A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include active immunisation against monkeypox and related orthopoxvirus infection and disease in adults 18 years of age and older for

IMVANEX; as a consequence, sections 1, 4.1, 4.2, 4.4, 4.6 and 5.1 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 9.0 of the RMP has also been submitted

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

5.3.37. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/II/0060, Orphan

Applicant: Novartis Europharm Limited, ATMP[6]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.2 of the SmPC in order to update the paediatric statement for the B-cell ALL indication and section 4.4 to update the warning on 'prior treatment with anti-CD19 therapy' as well as sections 4.4 and 4.8 in order to update safety data to reflect the pool of the 3 studies B2202, B2205J and B2001X. The proposed changes are in line with the request of the CHMP following the assessment of P46/012. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to correct the Complete Response Rate (CRR) 95% Confidence Interval (CI) on Enrolled set for E2202 study presented in Table 8 in section 5.1 of the SmPC. The RMP version 5.0 has also been submitted

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

5.3.38. Trastuzumab emtansine - KADCYLA (CAP) - EMEA/H/C/002389/II/0064

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of the final report from study BO28407 (KAITLIN): A randomized, multicenter, open-label, Phase III trial comparing trastuzumab plus pertuzumab plus a taxane following anthracyclines versus trastuzumab emtansine plus pertuzumab following anthracyclines as adjuvant therapy in patients with operable HER2-positive primary breast cancer listed as a category 3 study in the RMP. The RMP version 15.0 has also been submitted

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

5.3.39. Treosulfan - TRECONDI (CAP) - EMEA/H/C/004751/II/0012, Orphan

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Julia Pallos

Scope: Update of sections 4.5 and 5.2 of the SmPC in order to add drug-drug interaction information with regards to CYP3A4, CYP2C19 and P-gp including physiologically based pharmacokinetic (PBPK) modelling. Version 1.0 of the RMP has also been submitted

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

[6] Advanced therapy medicinal product

5.3.40. Treosulfan - TRECONDI (CAP) - EMEA/H/C/004751/II/0013, Orphan

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Julia Pallos

Scope: Update of section 5.3 of the SmPC in order to update the description of non-clinical information regarding musculoskeletal and connective tissue disorders in form of lympho-histiocytic infiltration in the skeletal muscles and renal and urinary disorders which show up as haematuria. These new determinations are based on results from study LPT 37259. A revised RMP version 1.0 was also submitted

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

5.3.41. Treosulfan - TRECONDI (CAP) - EMEA/H/C/004751/II/0014, Orphan

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Julia Pallos

Scope: Extension of indication to include additional non-malignant transplant indications (non-malignant diseases in the paediatric population) for Trecondi 1 g/5 g powder for solution for infusion based on final 12-months follow-up results of study MC-FludT.16/NM; a randomised phase II interventional study aimed to compare Treosulfan-based conditioning therapy with Busulfan-based conditioning prior to allogeneic haematopoietic stem cell transplantation in paediatric patients with non-malignant diseases.
Further, the MAH proposes to amend an existing warning on skin toxicity based on new literature data. Moreover, the MAH proposes to introduce a slightly modified dosing regimen according to the patient's body surface based on long-term follow-up data of paediatric study MC-FludT.17/M, a Phase II trial to describe the safety and efficacy of Treosulfan based conditioning therapy prior to allogeneic haematopoietic stem cell transplantation in paediatric patients with haematological malignancies, as well as a final analysis of the population pharmacokinetics of treosulfan in paediatric patients. 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 1.0 of the RMP has also been submitted

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

5.3.42. Turoctocog alfa pegol - ESPEROCT (CAP) - EMEA/H/C/004883/II/0010, Orphan

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.4 and 4.8 of the SmPC to add a new warning and update the list of adverse drug reactions (ADRs) based on post-marketing data concerning a lack of factor VIII activity in patients switching from a similar factor VIII product to Esperoct (turoctocog alfa pegol). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and to bring the product information in line with the latest quality review of documents (QRD) (template 10.2). The RMP (version 2.0) is updated accordingly

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

5.3.43. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/003922/II/0027, Orphan

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of section 4.2 the SmPC in order to include the home infusion statement, following the assessment of PSUSA/00010677/202009, based on results from LAMAN-07, Sparkle and Italian Patient Support Program (PSP). The Package Leaflet and Annex II are updated accordingly. The RMP version 9.1 has also been submitted

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

5.3.44. Volanesorsen - WAYLIVRA (CAP) - EMEA/H/C/004538/II/0017/G, Orphan

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.8 and 5.1 of the SmPC based on the final results from study ISIS 304801 CS7: a multicentre open label extension study of volanesorsen administered subcutaneously to patients with familial chylomicronemia syndrome. The package leaflet and the RMP (version 2.1) are updated accordingly. The RMP is updated: 1) to reflect a change in the distribution methodology of the educational materials and to clarify what is meant by the prescriber kit; 2) to reflect the final results from study ISIS 304801 (CS17): a phase 2/3 double blind, randomized, placebo controlled study, with an open label extension of volanesorsen (ISIS 304801) administered subcutaneously to patients with familial partial lipodystrophy. In addition, the MAH took the opportunity to implement editorial changes to the product information in order to align with the latest quality review of documents (QRD) template and to introduce minor linguistic update to Annex III of the product information to support product launch

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. Angiotensin II - GIAPREZA (CAP) - PSUSA/00010785/202112

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Atidarsagene autotemcel - LIBMELDY (CAP) - PSUSA/00010899/202112

Applicant: Orchard Therapeutics (Netherlands) BV

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Berotralstat - ORLADEYO (CAP) - PSUSA/00010930/202112

Applicant: BioCryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Betibeglogene autotemcel - ZYNTEGLO[7] (CAP) - PSUSA/00010769/202111

Applicant: bluebird bio (Netherlands) B.V, ATMP[8]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.5. Blinatumomab - BLINCYTO (CAP) - PSUSA/00010460/202112

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Cabozantinib - CABOMETYX (CAP); COMETRIQ (CAP) - PSUSA/00010180/202111

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Cholera vaccine, oral, live - VAXCHORA (CAP) - PSUSA/00010862/202112

Applicant: Emergent Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[7] European Commission (EC) decision on the withdrawal of the marketing authorisation (MA) for Zynteglo dated 24 March 2022
[8] Advanced therapy medicinal product

6.1.8. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - PSUSA/00010912/202112

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Delafloxacin - QUOFENIX (CAP) - PSUSA/00010822/202112

Applicant: A. Menarini Industrie Farmaceutiche Riunite s.r.l.

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Dengue tetravalent vaccine (live, attenuated) - DENGVAXIA (CAP) - PSUSA/00010740/202112

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Elasomeran - SPIKEVAX (CAP) - PSUSA/00010897/202112

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Elotuzumab - EMPLICITI (CAP) - PSUSA/00010500/202111

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Entrectinib - ROZLYTREK (CAP) - PSUSA/00010874/202112

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Fenfluramine - FINTEPLA (CAP) - PSUSA/00010907/202112

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Fondaparinux - ARIXTRA (CAP) - PSUSA/00001467/202112

Applicant: Mylan Ire Healthcare Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Formoterol fumarate dihydrate, glycopyrronium bromide, budesonide - TRIXEO AEROSPHERE (CAP) - PSUSA/00010908/202112

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Inotuzumab ozogamicin - BESPONSA (CAP) - PSUSA/00010659/202112

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Lamivudine[9] - EPIVIR (CAP); lamivudine, zidovudine - COMBIVIR (CAP) - PSUSA/00009207/202111

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Treatment of human immunodeficiency virus (HIV) infections only

6.1.19. Latanoprost, netarsudil - ROCLANDA (CAP) - PSUSA/00010905/202112

Applicant: Santen Oy

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Levodopa - INBRIJA (CAP) - PSUSA/00107800/202112

Applicant: Acorda Therapeutics Ireland Limited

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Luspatercept - REBLOZYL (CAP) - PSUSA/00010860/202112

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/202112

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Metformin, saxagliptin - KOMBOGLYZE (CAP) - PSUSA/00002686/202111

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Mexiletine[10] - NAMUSCLA (CAP) - PSUSA/00010738/202112

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

[10] Centrally authorised product(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Olaparib - LYNPARZA (CAP) - PSUSA/00010322/202112

Applicant: AstraZeneca AB

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Osimertinib - TAGRISSO (CAP) - PSUSA/00010472/202111

Applicant: AstraZeneca AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Pertuzumab, trastuzumab - PHESGO (CAP) - PSUSA/00010906/202112

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Polatuzumab vedotin - POLIVY (CAP) - PSUSA/00010817/202112

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Roxadustat - EVRENZO (CAP) - PSUSA/00010955/202112

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Rucaparib - RUBRACA (CAP) - PSUSA/00010694/202112

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Sapropterin - KUVAN (CAP) - PSUSA/00002683/202112

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Saquinavir - INVIRASE (CAP) - PSUSA/00002684/202112

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Satralizumab - ENSPRYNG (CAP) - PSUSA/00010944/202111

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Semaglutide - OZEMPIC (CAP); RYBELSUS (CAP); WEGOVY (CAP) - PSUSA/00010671/202111

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Sofosbuvir - SOVALDI (CAP) - PSUSA/00010134/202112

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Sucroferric oxyhydroxide - VELPHORO (CAP) - PSUSA/00010296/202111

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Thyrotropin alfa - THYROGEN (CAP) - PSUSA/00002940/202111

Applicant: Genzyme Europe BV

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Tirbanibulin - KLISYRI (CAP) - PSUSA/00010943/202112

Applicant: Almirall, S.A.

PRAC Rapporteur: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Tozinameran - COMIRNATY (CAP) - PSUSA/00010898/202112

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.40. Tralokinumab - ADTRALZA (CAP) - PSUSA/00010937/202112

Applicant: LEO Pharma A/S

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Trastuzumab deruxtecan - ENHERTU (CAP) - PSUSA/00010894/202112

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Turoctocog alfa pegol - ESPEROCT (CAP) - PSUSA/00010782/202112

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Venetoclax - VENCLYXTO (CAP) - PSUSA/00010556/202112

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

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. Bimatoprost, timolol - GANFORT (CAP); NAP - PSUSA/00002961/202111

Applicant: AbbVie Deutschland GmbH & Co. KG (Ganfort), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Doxorubicin - CAELYX PEGYLATED LIPOSOMAL (CAP); MYOCET LIPOSOMAL (CAP); NAP - PSUSA/00001172/202111

Applicant: Baxter Holding B.V. (Caelyx pegylated liposomal), Teva B.V. (Myocet liposomal), various

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Edotreotide - SOMAKIT TOC (CAP); NAP - PSUSA/00010552/202112

Applicant: Advanced Accelerator Applications (SomaKit TOC), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Erlotinib - TARCEVA (CAP); NAP - PSUSA/00001255/202111

Applicant: Roche Registration GmbH (Tarceva), various

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Levetiracetam - KEPPRA (CAP); NAP - PSUSA/00001846/202111

Applicant: UCB Pharma S.A. (Keppra), various

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Sufentanil - DZUVEO (CAP); ZALVISO (CAP); NAP - PSUSA/00002798/202111

Applicant: FGK Representative Service GmbH (Zalviso), Laboratoire Aguettant (Dzuveo), various

PRAC Rapporteur: Adam Przybylkowski

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. Aprotinin, calcium chloride, human factor XIII, human fibrinogen, human thrombin (NAP); aprotinin, fibrinogen, fibronectin, human coagulation factor XIII, plasma protein fraction, plasminogen, thrombin (NAP); aprotinin, human fibrinogen, thrombin, calcium chloride (NAP); aprotinin, calcium chloride, factor XIII, human thrombin, human clottable protein containing mainly fibrinogen and fibronectin (NAP); bovine aprotinin, calcium chloride, human fibrinogen, factor XIII, fibronectin, plasminogen, human thrombin (NAP); bovine aprotinin, calcium chloride, human fibrinogen, factor XIII, fibronectin, human thrombin (NAP); bovine aprotinin, human fibrinogen, calcium chloride dihydrate, plasma fibronectin, thrombin, human coagulation factor XIII (NAP), bovine aprotinin, human fibrinogen, calcium chloride dihydrate, plasma protein fraction, fibronectin, thrombin, human coagulation factor XIII (NAP); bovine aprotinin, human fibrinogen, plasminogen, human thrombin, human coagulation factor XIII, human fibronectin (NAP) - PSUSA/00010346/202111

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Bisoprolol, hydrochlorothiazide (NAP) - PSUSA/00000420/202111

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Caffeine, ergotamine (NAP) - PSUSA/00000485/202111

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Cefazolin (NAP) - PSUSA/00000589/202111

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Ceftobiprole (NAP) - PSUSA/00010734/202111

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Chlormadinone acetate, ethinylestradiol (NAP) - PSUSA/00000679/202111

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Ciprofibrate (NAP) - PSUSA/00000771/202112

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Donepezil (NAP) - PSUSA/00001160/202111

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Hydromorphone (NAP) - PSUSA/00001686/202111

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Hydroxycarbamide[11] (NAP) - PSUSA/00009182/202112

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Indapamide, perindopril (NAP) - PSUSA/00010230/202111

Applicant(s): various

PRAC Lead: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Ketamine (NAP) - PSUSA/00001804/202112

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[11] Non-centrally authorised product(s) only

6.3.13. Metoclopramide (NAP) - PSUSA/00002036/202111

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Quinine (NAP) - PSUSA/00002598/202111

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Tapentadol (NAP) - PSUSA/00002849/202111

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/LEG 008

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Cumulative review of cases of colitis, diarrhoea, alopecia/alopecia aerate and appendicitis, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010662/202103) adopted in November 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

None

6.6. Expedited summary safety reviews[12]

6.6.1. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 014.3

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Fourth expedited summary safety report (SSR) for Nuvaxovid (COVID-19 vaccine (recombinant, adjuvanted)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[13]

7.1.1. Afamelanotide - SCENESSE (CAP) - EMEA/H/C/PSA/S/0076.2

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSA/0076.1 [substantial amendment to a protocol previously agreed in March 2016 (PSP/0022.1.A.1 (PSA/0002)) for study CUV-PA001: a post-authorisation disease registry safety study to generate data on the long-term safety and clinical effectiveness of Scenesse (afamelanotide) in patients with erythropoietic protoporphyria (EPP)] as per the request for supplementary information (RSI) adopted in February 2022

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

7.1.2. Axicabtagene ciloleucel - YESCARTA (CAP) - EMEA/H/C/PSA/S/0087

Applicant: Kite Pharma EU B.V., ATMP[14]

PRAC Rapporteur: Anette Kirstine Stark

Scope: Amendment to a previously agreed protocol [EMEA/H/C/PSP/S/0079] for study KT-EU-471-0117 (EU PAS Register no.: EUPAS32539): a long-term, imposed non-interventional study of recipients of Yescarta for treatment of relapsed or refractory Diffuse Large B-cell Lymphoma and Primary Mediastinal B-cell Lymphoma

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

[12] 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
[13] In accordance with Article 107n of Directive 2001/83/EC
[14] Advanced therapy medicinal product

7.1.3. Lisocabtagene maraleucel - BREYANZI (CAP) - EMEA/H/C/PSP/S/0098

Applicant: Bristol-Myers Squibb Pharma EEIG, ATMP[15]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of a non-interventional, post-authorization safety study (PASS) of patients treated with commercially available liso-cel (lisocabtagene maraleucel) for relapsed/refractory diffuse large B-cell lymphoma, primary mediastinal B-cell lymphoma, and follicular lymphoma Grade 3B after 2 or more lines of systemic therapy in the postmarketing setting to characterize the incidence and severity of selected adverse drug reactions (ADRs), as outlined in the SmPC, and to monitor for potential clinically important adverse events (AEs) that have not yet been identified as part of the liso-cel safety profile

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[16]

7.2.1. Avacopan - TAVNEOS (CAP) - EMEA/H/C/005523/MEA 002

Applicant: Vifor Fresenius Medical Care Renal Pharma France

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study CS-AVA-2022-0016 (listed as category 3 study in the RMP): avacopan real world evidence in anti-neutrophil cytoplasmic autoantibody (ANCA) associated vasculitis - characterisation of the safety concerns of avacopan (i.e. liver injury, serious infections, malignancies and cardiovascular events) beyond the known safety profile based on clinical trial data limited to 52 weeks of exposure

Action: For adoption of advice to CHMP

7.2.2. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/MEA 004.5

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: MAH's response to MEA 004.3 [substantial amendment to a protocol previously agreed in July 2019 for study D3250R00042: a descriptive study of the incidence of malignancy in patients with severe asthma overall and among those receiving benralizumab and other therapies in real-world settings] as per the request for supplementary information (RSI) adopted in December 2020

Action: For adoption of advice to CHMP

7.2.3. Brodalumab - KYNTHEUM (CAP) - EMEA/H/C/003959/MEA 002.6

Applicant: LEO Pharma A/S

PRAC Rapporteur: Eva Segovia

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

Scope: Amendment to a protocol previously agreed in 2019 for PASS KYNTHEUM-1345: The BRodalumab Assessment of Hazards: A Multinational Safety (BRAHMS) study in electronic healthcare databases – an observational post-authorisation safety study of suicidal behaviour, serious infections, major adverse cardiac events (MACE) and malignancy in psoriasis patients treated with brodalumab (Kyntheum)

Action: For adoption of advice to CHMP

7.2.4. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) (NVX-CoV2373) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 004

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Action: For adoption of advice to CHMP

7.2.5. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) (NVX-CoV2373) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 005

Applicant: Novavax CZ, a.s.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Protocol for study 2019nCoV-405: Global Safety Surveillance Study of Pregnancy and Infant Outcomes Study Using C-VIPER. A registry-based observational cohort safety surveillance study to characterise the population of pregnant women who are vaccinated with Nuvaxovid, estimate the frequency of selected adverse pregnancy outcomes in women and selected adverse foetal/neonatal/infant outcomes at birth and up to the first 12 months of life of infants from pregnancies in women who received Nuvaxovid during pregnancy

Action: For adoption of advice to CHMP

7.2.6. Drospirenone, estetrol - DROVELIS (CAP) - EMEA/H/C/005336/MEA 001.2

Applicant: Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.)

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 001.1 [protocol for an international active surveillance study (INAS-NEES): a prospective non-interventional comparative cohort observational study to characterize and compare the risks of estetrol/drospirenone with combined oral contraceptive-containing levonorgestrel (COC-LNG) in a study population that is representative of the actual users of these preparations. The main clinical outcome of interest is venous thromboembolism (VTE), specifically deep venous thrombosis (DVT) and pulmonary embolism (PE)] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.2.7. Drospirenone, estetrol - LYDISILKA (CAP) - EMEA/H/C/005382/MEA 001.2

Applicant: Estetra SRL

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 001.1 [protocol for an international active surveillance study (INAS-NEES): a prospective non-interventional comparative cohort observational study to characterize and compare the risks of estetrol/drospirenone with combined oral contraceptive-containing levonorgestrel (COC-LNG) in a study population that is representative of the actual users of these preparations. The main clinical outcome of interest is venous thromboembolism (VTE), specifically deep venous thrombosis (DVT) and pulmonary embolism (PE) [final study report expected in December 2029] (from initial opinion/marketing authorisation (MA))] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.2.8. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 065

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Protocol for study mRNA-1273-P910: clinical course, outcomes and risk factors of myocarditis following administration of mRNA-1273 (Spikevax)

Action: For adoption of advice to CHMP

7.2.9. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 066

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Protocol for study mRNA-1273-P911: long-term outcomes of myocarditis following administration of Spikevax (COVID-19 vaccine mRNA)

Action: For adoption of advice to CHMP

7.2.10. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 006.2

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 006.1 [protocol for study ZX008-2104: a European study of the effectiveness of risk minimisation measures for fenfluramine in Dravet syndrome] as per the request for supplementary information (RSI) adopted April 2022

Action: For adoption of advice to CHMP

7.2.11. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - EMEA/H/C/004123/MEA 001.10

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Amendment to a protocol previously agreed in 2018 for study A-LUT-T-E02-402 (SALUS study) (listed as a category 3 study in the RMP): an international post-authorisation safety registry to assess the long-term safety of Lutathera (lutetium (^{177}Lu)) for unresectable or metastatic, somatostatin receptor positive gastroenteropancreatic neuroendocrine tumours (GEP-NETs)

Action: For adoption of advice to CHMP

7.2.12. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/MEA 003.12

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 003.11 [protocol for study NB-451: an observational retrospective drug utilisation study (DUS) of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) in Europe and the United States to describe the demographic and baseline characteristics of users of Mysimba (naltrexone hydrochloride/bupropion hydrochloride), evaluate patterns of Mysimba (naltrexone hydrochloride/bupropion hydrochloride) initiation and use] as per the request for supplementary information (RSI) adopted in February 2022

Action: For adoption of advice to CHMP

7.2.13. Netarsudil - RHOKIINSA (CAP) - EMEA/H/C/004583/MEA 001.4

Applicant: Santen Oy

PRAC Rapporteur: Eva Segovia

Scope: MAH Response to MEA 001.3 [protocol for study AR-13324-OBS02: a non-interventional, observational cohort study of 2-year of treatment with Rhokiinsa (netarsudil) compared with non-Rhokiinsa (netarsudil) ocular hypotensive therapy in patients with elevated intraocular pressure due to primary open angle glaucoma or ocular hypertension] as per request for supplementary information (RSI) adopted in April 2022

Action: For adoption of advice to CHMP

7.2.14. Setmelanotide - IMCIVREE (CAP) - EMEA/H/C/005089/MEA 001.1

Applicant: Rhythm Pharmaceuticals Netherlands B.V.,

PRAC Rapporteur: Anna Mareková

Scope: MAH's response to MEA 001 [protocol for study RM-IMC-901 (listed as a category 3 study in the RMP): a registry of patients with biallelic homozygous pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency obesity treated with setmelanotide (from initial opinion/marketing authorisation)]

as per the request for supplementary information (RSI) adopted in February 2022

Action: For adoption of advice to CHMP

7.2.15. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 015.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Amendment to a protocol previously agreed in November 2020 for study A3921334 (listed as a category 3 study in the RMP): a non-interventional PASS to evaluate the effectiveness of additional risk minimisation measures (aRMM) materials for Xeljanz (tofacitinib) in Europe via a survey of healthcare professionals (HCPs), as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019

Action: For adoption of advice to CHMP

7.2.16. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 017.4

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 017.2 [protocol previously agreed in June 2021 for study C4591021 (previously known as vACcine Covid-19 monitoring readinESS/Vaccine monitoring Collaboration for Europe (ACCESS/VAC4EU)): an assessment of potential increased risk of adverse events of special interest (AESI), including myocarditis/pericarditis after being vaccinated with COVID-19 messenger ribonucleic acid (mRNA) vaccine estimating the time trend, in relation to DHPC letter dissemination, of the proportion of individuals who received real-world clinical assessments for myocarditis/pericarditis following Comirnaty (tozinameran) vaccination] together with a statistical analysis plan (SAP) as per request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.2.17. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/MEA 013.1

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Revised protocol for study P20-390: a cohort study of long-term safety of upadacitinib in the treatment of atopic dermatitis in Denmark and Sweden

Action: For adoption of advice to CHMP

7.2.18. Vosoritide - VOXZOGO (CAP) - EMEA/H/C/005475/MEA 005.1

Applicant: BioMarin International Limited

PRAC Rapporteur: Zane Neikena

Scope: MAH's response to MEA 005.1 [protocol for study 111-603: a multicentre, non-

interventional study to evaluate long-term safety in patients with achondroplasia treated with Voxzogo (vosoritide)]

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[17]

None

7.4. Results of PASS non-imposed in the marketing authorisation(s)[18]

7.4.1. Autologous CD34+ enriched cell fraction that contains CD34+ cells transduced with retroviral vector that encodes for the human adenosine deaminase (ADA) complementary deoxyribonucleic acid (cDNA) sequence - STRIMVELIS (CAP) - EMEA/H/C/003854/II/0033, Orphan

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP[19]

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study STRIM-001 (listed as a category 3 study in the RMP): a cross-sectional study evaluating referring healthcare providers' and parents/carers' understanding of specific risks associated with Strimvelis treatment. The RMP (version 6.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - JCOVDEN (CAP) - EMEA/H/C/005737/II/0048/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final reports from four exploratory studies conducted to further characterise the potential mechanisms underlying the important identified risk of thrombosis with thrombocytopenia syndrome (TTS). These studies evaluated the levels of anti-PF4 antibodies using clinical samples, both from Ad26.COV2.S and other non-COVID-19 Ad26-based vaccine clinical studies. Interim results from an additional exploratory study are provided and the submission milestone for the final results has been updated. The RMP version 4.1 has been submitted and updated in line with this procedure and the ongoing procedure EMEA/H/C/005737/II/0047/G. In addition, the MAH removed the important identified risk of anaphylaxis from the list of safety concerns (PSUSA/00010916/202108), updated the routine pharmacovigilance activities section and took the opportunity to implement other administrative updates in the RMP in alignment with procedure EMEA/H/C/005737/II/033

Action: For adoption of PRAC Assessment Report

[17] In accordance with Article 107p-q of Directive 2001/83/EC
[18] 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
[19] Advanced therapy medicinal product

7.4.3. Dasabuvir - EXVIERA (CAP) - EMEA/H/C/003837/WS2216/0052; glecaprevir, pibrentasvir - MAVIRET (CAP) - EMEA/H/C/004430/WS2216/0049; ombitasvir, paritaprevir, ritonavir - VIEKIRAX (CAP) - EMEA/H/C/003839/WS2216/0064

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study B20-146 listed as a category 3 study in the RMP. This is a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS)

Action: For adoption of PRAC Assessment Report

7.4.4. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0058/G, Orphan

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variation consisting of: 1) submission of the final study report of the DEFIFrance registry (listed as category 3 study in the RMP): a national, post-registration observational study of the long-term safety and health outcome of patients treated with Defitelio, including patients with severe hepatic veno-occlusive disease (VOD) after haematopoietic stem cell transplantation (HSC T). The submission of the study report addresses LEG/011.3. In addition, the MAH took the opportunity to provide two errata to the clinical study reports of studies #R09-1425 and #2006-05. Consequential changes to RMP version 9.2 have been implemented; 2) submission of the updated RMP version 9.2 in order to remove reproductive toxicity as a potential risk

Action: For adoption of PRAC Assessment Report

7.4.5. Elbasvir, grazoprevir - ZEPATIER (CAP) - EMEA/H/C/004126/II/0033

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report for study B20-146 (listed as a category 3 study in the RMP): a non-imposed joint PASS to evaluate the risk of de novo hepatocellular carcinoma (HCC) in patients with compensated cirrhosis treated with direct-acting antivirals (DAA) for chronic hepatitis C (HCC de novo PASS)

Action: For adoption of PRAC Assessment Report

7.4.6. Idebenone - RAXONE (CAP) - EMEA/H/C/003834/II/0031, Orphan

Applicant: Santhera Pharmaceuticals (Deutschland) GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Update of sections 4.2, 4.4, 4.9 and 5.1 of the SmPC based on the final study report from study SNT-IV-003 (PAROS) (listed as a category 2 study in the RMP and Annex II (SOB003)): a non-interventional study of clinical experience in patients prescribed Raxone

(idebenone) for the treatment of Leber's hereditary optic neuropathy (LHON). Annex II and the RMP (version 1.14) are updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.7. Sapropterin - KUVAN (CAP) - EMEA/H/C/000943/II/0073

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final report from study BMN 162-501 KAMPER (formerly EMR700773-001) (listed as a category 3 study in the RMP): an observational drug registry to assess the long-term safety in subjects treated with Kuvan (in fulfilment of MEA 020). The RMP version 15.1 has also been submitted

Action: For adoption of PRAC Assessment Report

7.4.8. Sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS2222/0077; sofosbuvir, ledipasvir - HARVONI (CAP) - EMEA/H/C/003850/WS2222/0104; sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS2222/0064; sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/WS2222/0054

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of the final report from study B20-146 (listed as a category 3 study in the RMP): a non-imposed joint post-authorisation safety study to evaluate the risk of de novo hepatocellular carcinoma (HCC) in patients with compensated cirrhosis treated with direct-acting antivirals for chronic hepatitis C (HCC De Novo PASS)

Action: For adoption of PRAC Assessment Report

7.4.9. Tafamidis - VYNDAQEL (CAP) - EMEA/H/C/002294/II/0081, Orphan

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Update of section 5.1 of the SmPC in order to update information based on final results from study B3461029 listed as a Specific Obligation in the Annex II of the Product Information. This is a non-interventional PASS sub-study evaluating effects of tafamidis on disease progression in patients with non-Val30Met mutations and symptomatic neuropathy. Consequently, the MAH proposes a switch from marketing authorisation under exceptional circumstances to full marketing authorisation given the fulfilment of the SOB. The Annex II and Package Leaflet are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet

Action: For adoption of PRAC Assessment Report

7.4.10. Velaglucerase alfa - VPRIV (CAP) - EMEA/H/C/001249/II/0049, Orphan

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Martin Huber

Scope: Submission of final physician data study results for study EUPASS 14255: an evaluation of the effectiveness of risk minimisation measures - a survey among healthcare professionals (HCPs) and patient/caregivers to assess their knowledge and attitudes on prescribing and home administration conditions of velaglucerase alfa (Vpriv) in 6 European countries. Annex II was updated in order to to include new agreed key elements for the educational material. The RMP (version 11.0) was updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.11. Vortioxetine - BRINTELLIX (CAP) - EMEA/H/C/002717/II/0037

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study PASS 16034N (listed as a category 3 study in the RMP): a non-interventional post-authorisation safety study (PASS) of vortioxetine in Europe - An analysis of European automated healthcare databases. The RMP version 4.0 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. Arsenic trioxide - TRISENOX (CAP) - EMEA/H/C/000388/MEA 050.4

Applicant: Teva B.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Second interim report for study PASS C18477-ONC-50025: a post-authorisation long term safety cohort study in acute promyelocytic leukaemia (APL) patients treated with Trisenox (arsenic trioxide) to assess the long-term safety of all-trans retinoic acid (ATRA) + arsenic trioxide (ATO) in newly-diagnosed low to intermediate risk APL patients in a real-world clinical practice setting *

Action: For adoption of advice to CHMP

7.5.2. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 007.6

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: First interim report for study D8111R00006: a post-authorisation/post-marketing observational study using existing secondary health data sources to evaluate the association between exposure to AZD1222 and safety concerns

Action: For adoption of advice to CHMP

7.5.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 006.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Third Quarterly Report for study D8110C00003: COVID-19 Vaccines International Pregnancy Registry of Women Exposed to AZD1222 Immediately Before or During Pregnancy (C-VIPER)

Action: For adoption of advice to CHMP

7.5.4. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 003.6

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Fifth interim report for a study (listed as a category 3 study in the RMP): a post authorisation safety of Spikevax (elasomeran) in the US - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals [P903]

Action: For adoption of advice to CHMP

7.5.5. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 004.6

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Second interim report for study mRNA-1273-P904 (study 1) (listed as a category 3 study in the RMP): a post-authorisation active surveillance safety study using secondary data to monitor real-world safety of Spikevax (COVID-19 mRNA-1273 vaccine) in Europe - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals in European populations and electronic database assessment of use in pregnant women

Action: For adoption of advice to CHMP

7.5.6. Elasomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 034.3

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: First interim report for study mRNA-1273-P905 [study monitoring the safety of Spikevax (COVID-19 vaccine) in pregnancy: an observational study using routinely collected health data in five European countries]

Action: For adoption of advice to CHMP

7.5.7. Ertugliflozin - STEGLATRO (CAP) - EMEA/H/C/004315/MEA 002.4

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002.3 [first 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] as per the request for supplementary information adopted in March 2022

Action: For adoption of advice to CHMP

7.5.8. Ertugliflozin, metformin hydrochloride - SEGLUROMET (CAP) - EMEA/H/C/004314/MEA 002.4

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002.3 [first 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] as per the request for supplementary information adopted in March 2022

Action: For adoption of advice to CHMP

7.5.9. Ertugliflozin, sitagliptin - STEGLUJAN (CAP) - EMEA/H/C/004313/MEA 002.4

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 002.3 [first 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] as per the request for supplementary information adopted in March 2022

Action: For adoption of advice to CHMP

7.5.10. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 003.1

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a study (listed as a category 3 study in the RMP): a national prospective, observational, uncontrolled cohort study whose objectives are to evaluate the risk of selected adverse events (AEs) in rheumatoid arthritis (RA), juvenile idiopathic arthritis, and other rheumatic disease patients treated with infliximab using the Anti-Rheumatic Therapies in Sweden (ARTIS) national surveillance programme [final clinical study report (CSR) expected in 2027]

Action: For adoption of advice to CHMP

7.5.11. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 002.3

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a prospective study (listed as a category 3 study in the RMP) to treat patients with rheumatological disorders with biological agents to assess long-term toxicity of these agents in routine clinical practice using the British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (BSRBR-RA): an established nationwide register [final clinical study report (CSR) expected in 2027]

Action: For adoption of advice to CHMP

7.5.12. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 005.3

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a study (listed as a category 3 study in the RMP): a prospective, observational cohort study whose objectives are to evaluate the long-term effectiveness, safety, and costs associated with tumour necrosis factor (TNF)-inhibitor therapies in the treatment of rheumatoid arthritis (RA) and to compare this to a cohort of RA patients who are treated with non-biologic disease-modifying antirheumatic drugs (DMARDs) [final clinical study report (CSR) expected in 2027]

Action: For adoption of advice to CHMP

7.5.13. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 006.3

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual interim report for a study (listed as a category 3 in the RMP) conducted in the Spanish register of adverse events of biological therapies in rheumatic diseases (BIOBADASER) to identify relevant adverse events occurring during treatment of rheumatic diseases with biological therapies, to estimate the frequency of their occurrence; to identify unexpected adverse events; to identify relevant adverse events that occur following the suspension of the treatment, to estimate the relative risk of occurrence of adverse events with biological therapies in patients with rheumatoid arthritis (RA) compared to those not exposed to these treatments; to identify risk factors for suffering adverse reactions with these treatments; to evaluate, under non-experimental conditions, the treatment duration before the biological medications had been suspended in patients with rheumatic diseases, as well as the reasons for the interruption of the treatment [final clinical study report (CSR) expected in 2027]

Action: For adoption of advice to CHMP

7.5.14. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 009.2

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for the Chronisch Entzündliche Darmerkrankungen, ein Unabhängiges Register (CEDUR) to describe the long-term effectiveness of treatment with inflammatory bowel disease (IBD)

Action: For adoption of advice to CHMP

7.5.15. Infliximab - FLIXABI (CAP) - EMEA/H/C/004020/MEA 010.2

Applicant: Samsung Bioepis NL B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim report for the Czech Register of inflammatory bowel disease (IBD) Patients on Biological Therapy (CREDIT) to monitor effectiveness of total population of IBD patients on biological medication in the Czech Republic and regular analytical evaluation of the effectiveness

Action: For adoption of advice to CHMP

7.5.16. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/MEA 002.4

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 002.3 [first annual interim report for study VX20-445-120: a five year-registry based study to assess real-world effects and utilisation patterns of elexacaftor/tezacaftor/ivacaftor combination therapy (ELX/TEZ/IVA) in patients with cystic fibrosis (CF)] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.5.17. Mexiletine - NAMUSCLA (CAP) - EMEA/H/C/004584/MEA 001.3

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Interim report for study LUP/MEX/2018/001: registry study to determine the long-term safety and tolerability of Namuscla for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorder

Action: For adoption of advice to CHMP

7.5.18. Pegfilgrastim - NEULASTA (CAP) - EMEA/H/C/000420/MEA 059.3

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study 20170701 (listed as category 3 study in the RMP): an observational study to assess the effectiveness of the Neulasta (pegfilgrastim) patient alert card (PAC) and to measure medication errors related to the use of the On-Body injector (OBI) to assess respondent awareness of key safety messages and behavioural intent to

carry out recommended actions as described in the PAC and to estimate the proportion of OBI administrations associated with medication error

Action: For adoption of advice to CHMP

7.5.19. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 003.4

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 003.3 [first interim report for study 165-501: a multicentre, prospective global observational study to evaluate the long-term safety of subcutaneous injections of pegvaliase in patients with phenylketonuria] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.5.20. Pegvaliase - PALYNZIQ (CAP) - EMEA/H/C/004744/MEA 005.3

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: First interim report for study 165-504: a prospective global multicentre observational safety surveillance study to assess maternal, foetal and infant outcomes of exposure to Palynziq (pegvaliase) during pregnancy and breastfeeding

Action: For adoption of advice to CHMP

7.5.21. Prasterone - INTRAROSA (CAP) - EMEA/H/C/004138/ANX 001.1

Applicant: Endoceutics S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study ERC-243: a non-interventional PASS - Drug Utilisation Study (DUS) to describe the baseline characteristics, utilisation patterns of EU postmenopausal women initiating treatment with Intrarosa and to assess whether EU prescribers abide by the contraindications stated in the EU SmPC (protocol previously agreed in July 2021)

Action: For adoption of advice to CHMP

7.5.22. Tildrakizumab - ILUMETRI (CAP) - EMEA/H/C/004514/MEA 003.5

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: MAH's response to MEA 003.4 [annual progress report 2021 for study M-14745-40: a European psoriasis registry to collect long-term safety data for tildrakizumab and to further characterise the long-term safety profile of tildrakizumab in the treatment of psoriasis under conditions of routine clinical practice] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.5.23. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 054

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study C4591022: Pfizer-BioNTech COVID-19 Vaccine Exposure during Pregnancy: A Non-Interventional Post-Approval Safety Study of Pregnancy and Infant Outcomes in the Organization of Teratology Information Specialists (OTIS)/MotherToBaby Pregnancy Registry

Action: For adoption of advice to CHMP

7.5.24. Ulipristal acetate - ESMYA (CAP) - EMEA/H/C/002041/MEA 018.6

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Sixth yearly progress report for study PGL14-001: a prospective, multinational, multicentre, non-interventional study to evaluate the long-term safety of Esmya (ulipristal acetate) in particular the endometrial safety and the current prescription and management patterns of Esmya (ulipristal acetate) in a long-term treatment setting

Action: For adoption of advice to CHMP

7.5.25. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 044.14

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Fourth interval safety registry for study CNTO1275PSO4056: an observational PASS of ustekinumab in the treatment of paediatric patients aged 12 years and older with moderate to severe plaque psoriasis (adolescent registry)

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/MEA 002.4

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: MAH's responses to MEA 002.2 [protocol for study D8220C00008 (listed as a category 3 study in the RMP): a phase 3b, multicentre, open-label, single-arm study in subjects with chronic lymphocytic leukaemia (ASSURE) to address missing information around moderate to severe cardiac impaired patients in subjects treated with Calquence (acalabrutinib)] as per the request for supplementary information (RSI) adopted in February 2022

Action: For adoption of advice to CHMP

7.6.2. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/REC 004

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Submission of an addendum to the final clinical report for study (17712): efficacy and safety study of darolutamide (ODM-201) in men with high-risk non-metastatic castration-resistant prostate cancer (ARAMIS)

Action: For adoption of advice to CHMP

7.6.3. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 005.3

Applicant: TEVA GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Protocol synopsis for a multi-country retrospective database study TV48125-MH-40217: 'A Long-Term Observational, Retrospective Cohort Study to Evaluate the Safety Including Cardiovascular Safety, of Fremanezumab in Patients with Migraine in Routine Clinical Practice in the United States and Europe' to replace the current ongoing prospective PASS (TV48125-MH-50039)

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. Amifampridine - FIRDAPSE (CAP) - EMEA/H/C/001032/S/0073 (without RMP)

Applicant: SERB SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/004061/S/0020 (without RMP)

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Clofarabine - EVOLTRA (CAP) - EMEA/H/C/000613/S/0076 (without RMP)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0099 (without RMP)

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.5. Zanamivir - DECTOVA (CAP) - EMEA/H/C/004102/S/0013 (without RMP)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ulla Wändel Liminga

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. Amivantamab - RYBREVANT (CAP) - EMEA/H/C/005454/R/0002 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/R/0040 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/R/0006 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/R/0044 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Bevacizumab - MVASI (CAP) - EMEA/H/C/004728/R/0025 (without RMP)

Applicant: Amgen Technology (Ireland) Unlimited Company

PRAC Rapporteur: Anette Kirstine Stark

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Budesonide - JORVEZA (CAP) - EMEA/H/C/004655/R/0016 (without RMP)

Applicant: Dr. Falk Pharma GmbH

PRAC Rapporteur: Zane Neikena

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/R/0032 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Human fibrinogen, human thrombin - VERASEAL (CAP) - EMEA/H/C/004446/R/0018 (without RMP)

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Amelia Cupelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Hydrocortisone - ALKINDI (CAP) - EMEA/H/C/004416/R/0014 (without RMP)

Applicant: Diurnal Europe BV

PRAC Rapporteur: Annika Folin

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Miglustat - MIGLUSTAT GEN.ORPH (CAP) - EMEA/H/C/004366/R/0022 (with RMP)

Applicant: Gen.Orph

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Naloxone - NYXOID (CAP) - EMEA/H/C/004325/R/0014 (without RMP)

Applicant: Mundipharma Corporation (Ireland) Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Ocrelizumab - OCREVUS (CAP) - EMEA/H/C/004043/R/0033 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Padeliporfin - TOOKAD (CAP) - EMEA/H/C/004182/R/0019 (without RMP)

Applicant: STEBA Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. Prasterone - INTRAROSA (CAP) - EMEA/H/C/004138/R/0022 (with RMP)

Applicant: Endoceutics S.A.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.12. Rurioctocog alfa pegol - ADYNOVI (CAP) - EMEA/H/C/004195/R/0033 (with RMP)

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/R/0030 (without RMP)

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

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. Ibuprofen (NAP) - DE/H/0392/II/032/G

Applicant: Johnson & Johnson GmbH (Dolormin für Kinder Ibuprofensaft 20 mg/mL)

PRAC Lead: Martin Huber

Scope: Second PRAC consultation on a grouped type II variations (DE/H/0392/II/032/G) on the use of ibuprofen during pregnancy, on request of Germany (first PRAC consultation concluded in April 2022)

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

12.8.1. Marketing authorisation applications (MAA) forecast for 2022 – planning update dated Q2 2022

Action: For discussion

12.8.2. European Commission (EC) report on performance of pharmacovigilance tasks - third three-yearly report – status update

Action: For discussion

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance inspections

None

12.9.3. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

None

12.21. Others

12.21.1. EMA records management system – update on Sharepoint migration

Action: For discussion

13. Any other business

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/