27 September 2021
EMA/PRAC/483204/2021
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 27-30 September 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

27 September 2021, 10:30 – 19:30, via teleconference

28 September 2021, 08:30 – 19:30, via teleconference

29 September 2021, 08:30 – 19:30, via teleconference

30 September 2021, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

14 October 2021, 09:00 – 12:00, via teleconference

Disclaimers

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

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

Note on access to documents

Some documents mentioned in the agenda cannot be released at present following a request for access to documents within the framework of Regulation (EC) No 1049/2001 as they are subject to on-going procedures for which a final decision has not yet been adopted. They will become public when adopted or considered public according to the principles stated in the Agency policy on access to documents (EMA/127362/2006, Rev. 1).

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 27-30 September 2021. See October 2021 PRAC minutes (to be published post November 2021 PRAC meeting).

1.2. Agenda of the meeting on 27-30 September 2021

Action: For adoption

1.3. Minutes of the previous meeting on 30 August-02 September 2021

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

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

Applicants: Theramex Ireland Limited (Zoely), various

PRAC Rapporteur: To be appointed; PRAC Co-rapporteur: To be appointed

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

Action: For adoption of a list of questions (LoQ)

3.2. Ongoing procedures

3.2.1. Amfepramone (NAP) - EMEA/H/A-31/1501

Applicant(s): Artegodan GmbH, Temmler Pharma GmbH

PRAC Rapporteur: Anette Kirstine Stark; PRAC Co-rapporteur: Eva Jirsová

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

Action: For adoption of a list of experts for the ad-hoc expert group (AHEG) meeting

3.3. Procedures for finalisation

None

3.4. Re-examination procedures[1]

None

3.5. Others

None

4. Signals assessment and prioritisation[2]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Enzalutamide – XTANDI (CAP)

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Signal of erythema multiforme

Action: For adoption of PRAC recommendation

[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

EPITT 19734 – New signal

Lead Member State(s): ES

4.2. New signals detected from other sources

4.2.1. Sorafenib – NEXAVAR (CAP)

Applicant: Bayer AG

PRAC Rapporteur: Annika Folin

Scope: Signal of tumour lysis syndrome (TLS)

Action: For adoption of PRAC recommendation

EPITT 19733 – New signal

Lead Member State(s): SE

4.3. Signals follow-up and prioritisation

4.3.1. Coronavirus (COVID-19) mRNA[3] vaccine (nucleoside-modified) - COMIRNATY (CAP) – EMEA/H/C/005735/SDA/034

Applicant(s): BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of erythema multiforme

Action: For adoption of PRAC recommendation

EPITT 19721 – Follow-up to July 2021

4.3.2. Coronavirus (COVID-19) mRNA[4] vaccine (nucleoside-modified) - COMIRNATY (CAP) – EMEA/H/C/005735/SDA/035

Applicant(s): BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of glomerulonephritis and nephrotic syndrome

Action: For adoption of PRAC recommendation

EPITT 19722 – Follow-up to July 2021

4.3.3. Coronavirus (COVID-19) mRNA[5] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/036

Applicant(s): Moderna Biotech Spain, S.L.

[3] Messenger ribonucleic acid
[4] Messenger ribonucleic acid
[5] Messenger ribonucleic acid

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of erythema multiforme

Action: For adoption of PRAC recommendation

EPITT 19720 – Follow-up to July 2021

4.3.4. Coronavirus (COVID-19) mRNA[6] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/037

Applicant(s): Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of glomerulonephritis and nephrotic syndrome

Action: For adoption of PRAC recommendation

EPITT 19724 – Follow-up to July 2021

4.3.5. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/034.2

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of immune thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19678 - Follow-up to July 2021

4.3.6. Piperacillin (NAP); piperacillin, tazobactam (NAP)

Applicant(s): various

PRAC Rapporteur: Marek Juračka

Scope: Signal of hemophagocytic lymphohistiocytosis (HLH)

Action: For adoption of PRAC recommendation

EPITT 19676 – Follow-up to April 2021

4.3.7. Warfarin (NAP)

Applicant(s): various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Signal of anticoagulant-related nephropathy

Action: For adoption of PRAC recommendation

EPITT 19652 – Follow-up to May 2021

[6] Messenger ribonucleic acid

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) - EMEA/H/C/005754

Scope: Active immunisation to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus), in individuals 18 years of age and older

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

5.1.2. Metformin hydrochloride, sitagliptin hydrochloride monohydrate - EMEA/H/C/005678

Scope: Treatment of type 2 diabetes mellitus (T2DM)

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

5.1.3. Sapropterin - EMEA/H/C/005646

Scope: Treatment of hyperphenylalaninemia (HPA)

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

5.1.4. Semaglutide - EMEA/H/C/005422

Scope: Treatment for weight loss and weight maintenance

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

5.1.5. Voxelotor - EMEA/H/C/004869, Orphan

Applicant: Global Blood Therapeutics Netherlands

Scope: Treatment of haemolytic anaemia in adults and paediatric patients 12 years of age and older with sickle cell disease (SCD)

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. Benralizumab - FASENRA (CAP) - EMEA/H/C/004433/II/0036

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Submission of an updated RMP (version 4.0) to remove long term use of benralizumab, serious hypersensitivity, loss of/reduction of long-term efficacy as safety concerns and to change the risk categorisation of helminth infection from an important identified risk to an important potential one, as requested in the conclusions of the last PSUR single assessment (PSUSA) procedure (PSUSA/00010661/202005) finalised in May 2021 and variation II/031 finalised in July 2021

Action: For adoption of PRAC Assessment Report

5.2.2. Cladribine - MAVENCLAD (CAP) - EMEA/H/C/004230/II/0015

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of an updated RMP (version 1.5.2) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template). In addition, the MAH took the opportunity to include long-term safety data from the completed PREMIERE registry: a prospective observational long-term safety registry of multiple sclerosis patients who have participated in cladribine clinical studies; and to remove it from the pharmacovigilance plan. Furthermore, the status of the post-approval safety study MS 700568-0002: a long term, prospective, observational cohort study evaluating the safety profile in patients with highly active relapsing multiple sclerosis (RMS) newly started on oral cladribine (CLARION); and study MS 700568-0004: pregnancy outcomes in women exposed to oral cladribine: a multi-country cohort database study (CLEAR) are updated. Finally, the RMP is updated in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010634/201907) adopted in January 2020

Action: For adoption of PRAC Assessment Report

5.2.3. Coronavirus (COVID-19) mRNA[7] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/II/0059

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 2.3) in order to add myocarditis/pericarditis as an important identified risk as per the outcome of the signal procedure (SDA/032) (EPITT: 19712) dated July 2021. This includes an update of the risk minimisation measures related to myocarditis/pericarditis. The MAH took the opportunity to update the RMP in line with exposure data, information on planned/ongoing safety studies and inclusion of two new non-interventional US PASS, namely study C4591009: a non-interventional post-approval safety study of COVID-19 mRNA vaccine (Comirnaty) in the United States; and study C4591036: a prospective cohort study with at least 5 years of follow-up for potential long-term sequelae of myocarditis after vaccination (Pediatric Heart Network)

Action: For adoption of PRAC Assessment Report

[7] Messenger ribonucleic acid

5.2.4. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/II/0018

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of an updated RMP (version 2.2) in order to include thrombocytopenia as an important potential risk as per the outcome of the signal procedure on embolic and thrombotic events (SDA/018.1 - EPITT 19689) in May 2021 and the outcome of variation II/0006/G dated July 2021, to propose studies aimed at further characterisation of thrombosis with thrombocytopenia syndrome (TTS) and thrombocytopenia, following the outcome of the signal procedure on embolic and thrombotic events (SDA/018.1 - EPITT 19689) in May 2021, to include Guillain-Barré syndrome as an important identified risk as per the outcome of variation II/0012 dated July 2021. In addition, the MAH took the opportunity to update in the RMP to include the submission milestone dates for study VAC31518COV4001: a post-authorisation, observational study to assess the safety of Ad26.COV2.S (COVID-19 Vaccine Janssen) using health insurance claims and/or electronic health record (EHR) database(s) in the United States, and study VAC31518COV4002: a post-authorisation, observational study to assess the effectiveness of Ad26.COV2.S (COVID-19 Vaccine Janssen) using health insurance claims and/or electronic health record (EHR) database(s) in the United States

Action: For adoption of PRAC Assessment Report

5.2.5. Emtricitabine, tenofovir disoproxil - TRUVADA (CAP) - EMEA/H/C/000594/II/0173

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Submission of an updated RMP (version 17.2) to remove the additional risk minimisation measures (aRMMs) for the pre-exposure prophylaxis (PrEP) indication risks. Annex II of the product information is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.6. Fentanyl - EFFENTORA (CAP) - EMEA/H/C/000833/WS2127/0058; NAP

Applicant: Teva B.V.

PRAC Rapporteur: Martin Huber

Scope: Submission of an updated RMP (version 5.0) to bring it in line with revision 2 of GVP module V on 'Risk management systems' and to update the list of safety concerns in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/201704) adopted in February 2018. In addition, the key messages of the educational materials are updated in line with the conclusions of the PSUSA procedure (PSUSA/00001369/202004) adopted in January 2021

Action: For adoption of PRAC Assessment Report

5.2.7. Filgrastim - NIVESTIM (CAP) - EMEA/H/C/001142/II/0063

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kirsti Villikka

Scope: Submission of an updated RMP (version 10.0) in order to update the RMP in accordance with revision 2 of GVP module V on 'Risk management systems' and revision 2.0.1 of the guidance on the format of RMP in the EU (template) and to propose deletion of selected safety concerns listed as important identified risks, important potential risks and missing information

Action: For adoption of PRAC Assessment Report

5.2.8. Ivabradine - CORLENTOR (CAP) - EMEA/H/C/000598/WS2050/0056/G; PROCORALAN (CAP) - EMEA/H/C/000597/WS2050/0055/G

Applicant: Les Laboratoires Servier

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) submission of an updated RMP (version 7.0) in line with the changes approved for Ivabradine Anpharm (R/0014) finalised in March 2020.; 2) product information is brought in line with the latest quality review of documents (QRD) template (version 10.2)

Action: For adoption of PRAC Assessment Report

5.2.9. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/WS2157/0102; sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS2157/0076; sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS2157/0062; sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/WS2157/0049

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' to amend the study milestone due date from 'Q3 2021' to 'Q4 2021' for the PASS to evaluate the recurrence of hepatocellular carcinoma (HCC)

Action: For adoption of PRAC Assessment Report

5.2.10. Obeticholic acid - OCALIVA (CAP) - EMEA/H/C/004093/II/0026, Orphan

Applicant: Intercept Pharma International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of an updated RMP (version 1.2) in order to bring it in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template) and to add clinical studies (listed as specific obligations in Annex II-E on 'Specific obligation to complete post-authorisation measures for the conditional marketing authorisation') to the pharmacovigilance plan, namely study 747-302: a phase 4, double-blind, randomized, placebo-controlled, multicentre study evaluating the effect of obeticholic acid on clinical

outcomes in patients with primary biliary cholangitis; and study 747-401: a phase 4, double-blind, randomized, placebo-controlled study evaluating the pharmacokinetics and safety of obeticholic acid in patients with primary biliary cholangitis and moderate to severe hepatic impairment; as agreed in the conclusions of the conditional renewal procedure (R/0023) finalised in November 2020. Other changes also include an update to the exposure data from clinical studies, addition of data on post-marketing experience and addition of some specific relevant SmPC wording in the risk minimisation measures

Action: For adoption of PRAC Assessment Report

5.2.11. Tivozanib - FOTIVDA (CAP) - EMEA/H/C/004131/II/0018

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Submission of an updated RMP (version 4.0) in order to include data from study TIVO-3: a randomised, controlled, multicentre, open-label phase 3 study to compare tivozanib with sorafenib in subjects with advanced renal cell carcinoma. Additional updates to the RMP include new information from clinical studies and post-marketing exposure

Action: For adoption of PRAC Assessment Report

5.2.12. Vildagliptin - GALVUS (CAP) - EMEA/H/C/000771/WS1970/0067; JALRA (CAP) - EMEA/H/C/001048/WS1970/0069; XILIARX (CAP) - EMEA/H/C/001051/WS1970/0067; vildagliptin, metformin hydrochloride - EUCREAS (CAP) - EMEA/H/C/000807/WS1970/0081; ICANDRA (CAP) - EMEA/H/C/001050/WS1970/0084; ZOMARIST (CAP) - EMEA/H/C/001049/WS1970/0083

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Submission of an updated RMP (version 15.0) in order to bring it in line with revision II of GVP module V on 'Risk management systems' and aligned with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00003113/201802) adopted in October 2018. Annex II-D on 'conditions or restrictions with regard to the safe and effective use of the medicinal product' of the product information is updated to remove the statement on submission of an RMP update every 3 years

Action: For adoption of PRAC Assessment Report

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

5.3.1. Anakinra - KINERET (CAP) - EMEA/H/C/000363/II/0086

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Extension of indication to include treatment of coronavirus disease 2019 (COVID-19) in adult patients with pneumonia who are at risk of developing severe respiratory failure. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package

leaflet and the RMP (version 5.7) are updated in accordance

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

5.3.2. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0064

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include adjuvant treatment of non-small cell lung cancer (NSCLC) following resection and platinum-based chemotherapy for adult patients whose tumours have programmed death-ligand 1 (PD-L1) expression on ≥ 1% of tumour cells (TC) for Tecentriq (atezolizumab) as monotherapy based on the results from pivotal study GO29527 (IMpower010): a phase 3, open-label, randomized study to investigate the efficacy and safety of atezolizumab compared with best supportive care following adjuvant cisplatin-based chemotherapy in patients with completely resected stage IB-IIIA NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of Tecentriq (atezolizumab) 840 mg concentrate for solution for infusion SmPC and Tecentriq (atezolizumab) 1,200 mg concentrate for solution for infusion SmPC are updated. The package leaflet and the RMP (version 21.0) are updated. The MAH took the opportunity to introduce minor editorial updates throughout the product information

Action: For adoption of PRAC RMP AR, PRAC RMP assessment overview and advice to 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. Beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium - TRYDONIS (CAP) - EMEA/H/C/004702/X/0015

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Extension application to add a new pharmaceutical form (inhalation powder) associated with new strength (88 µg / 5 µg / 9 µg). The RMP (version 7.1) is updated in accordance

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

5.3.5. Bictegravir, 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 extended 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

5.3.6. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/II/0093, Orphan

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.8, 5.1, 5.2, and 6.6 of the SmPC based on results from study C25004: an open-label study in order to assess the safety and tolerability, of brentuximab vedotin when combined with multiagent chemotherapy regimen for first-line treatment of advanced-stage Hodgkin lymphoma in paediatric patients. The RMP (version 16.0) is updated in accordance

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

5.3.7. Brigatinib - ALUNBRIG (CAP) - EMEA/H/C/004248/II/0037

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Update of section 5.1 of the SmPC in order to update efficacy information based on final results from study AP26113-13-301 (listed as a post-authorisation efficacy study (PAES) in Annex II): a randomised, open-label, multicentre phase 3 study comparing brigatinib versus crizotinib in patients with advanced anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) who have not previously received ALK-directed therapy. The RMP (version 5.4) is updated in accordance

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

5.3.8. Ceftolozane, tazobactam - ZERBAXA (CAP) - EMEA/H/C/003772/II/0036

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to include treatment of paediatric patients aged from birth to less than 18 years based on final results from: 1) study MK-7625A-034: a phase 2, randomized, active comparator-controlled, double-blind clinical trial to study the safety and efficacy of ceftolozane/tazobactam versus meropenem in paediatric subjects with complicated urinary tract infection, including pyelonephritis; 2) study MK-7625A-035: a

phase 2, randomized, active comparator-controlled, double-blind clinical trial to study the safety and efficacy of ceftolozane/tazobactam plus metronidazole versus meropenem in paediatric subjects with complicated intra-abdominal infection. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 3.1) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.9. Coronavirus (COVID-19) mRNA[8] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/X/0044/G

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Extension application to add a new pharmaceutical form (dispersion for injection) with a new strength (0.1 mg/mL). The RMP (version 2.4) is updated accordingly

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

5.3.10. Dapagliflozin - EDISTRIDE (CAP) - EMEA/H/C/004161/WS1952/0042; FORXIGA (CAP) - EMEA/H/C/002322/WS1952/0060

Applicant: AstraZeneca AB

PRAC Rapporteur: Annika Folin

Scope: Extension of indication for Forxiga and Edistride (dapagliflozin) to include treatment of children aged 10 years and adolescents with type 2 diabetes mellitus (T2DM) based on the results from studies: 1) study MB10209/D1690C000016: a randomised, multicentre, parallel, single-dose study to explore the pharmacokinetics and pharmacodynamics of dapagliflozin in children, 10 to less than 18 years of age with T2DM receiving one of three dose levels of dapagliflozin: 2.5, 5 or 10 mg; 2) study MB102-138/D1690C00017: a randomised, double-blind, placebo-controlled, 24 week efficacy and safety study of dapagliflozin 10 mg as compared to placebo with a 28-week open label safety extension phase, in patients aged from 10 to less than 18 years (and young adults from 18 to less than 25 years) with T2DM who have inadequate glycaemic control on diet and exercise with: either metformin only, or insulin only or with metformin and insulin. 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 21.0) are updated in accordance

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

5.3.11. Deferiprone - FERRIPROX (CAP) - EMEA/H/C/000236/X/0145

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension application to introduce a new pharmaceutical form (gastro-resistant tablets). The RMP (version 14.0) is updated in accordance

[8] Messenger ribonucleic acid

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

5.3.12. Evolocumab - REPATHA (CAP) - EMEA/H/C/003766/II/0049/G

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped variations consisting of: 1) extension of indication to include a new paediatric indication in paediatric patients aged 10 years and over with heterozygous familial hypercholesterolaemia as an adjunct to diet, alone or in combination with other lipid-lowering therapy, to reduce low-density lipoprotein cholesterol (LDL-C) based on results of study 20120123 (HAUSER-RCT): a randomized, multicentre, placebo-controlled, double blind, parallel group, 24-week trial in 158 paediatric patients aged 10 to > 18 years with heterozygous familial hypercholesterolaemia. As a consequence, sections 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.0) are updated in accordance; 2) extension of indication to modify the existing indication for treatment of adults and paediatric patients aged 10 years and over with homozygous familial hypercholesterolaemia in combination with other lipid-lowering therapies based on interim results from study 20120124 (HAUSER-OLE): an open label, single arm, multicentre, 80-week trial to evaluate the safety, tolerability and efficacy of Repatha (evolocumab) for LDL-C reduction in paediatric patients from aged ≥ 10 to < 18 years of age with homozygous familial hypercholesterolaemia. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated accordingly

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

5.3.13. Febuxostat - ADENURIC (CAP) - EMEA/H/C/000777/II/0061

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final results from study FAST (Febuxostat versus Allopurinol Streamlined Trial) (listed as a category 3 study in the RMP): an interventional study investigating the cardiovascular safety of febuxostat in comparison with allopurinol in patients with chronic symptomatic hyperuricaemia. The package leaflet and the RMP (version 8.0) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet and to update the warning relevant to the content of sodium according to the Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use'

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

5.3.14. Guselkumab - TREMFYA (CAP) - EMEA/H/C/004271/II/0028

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC to reflect 5 years data from the final study reports of pivotal psoriasis studies (listed as category 3 studies in the RMP), namely:

1) study PSO3001: a phase 3, multicentre, randomized, double-blind, placebo and active comparator-controlled study evaluating the efficacy and safety of guselkumab in the treatment of subjects with moderate to severe plaque-type psoriasis; 2) study PSO3002: a phase 3, multicentre, randomized, double-blind, placebo and active comparator-controlled study evaluating the efficacy and safety of guselkumab for the treatment of subjects with moderate to severe plaque-type psoriasis with randomized withdrawal and retreatment. In the long-term extension part of these studies subjects received open-label guselkumab every 8 weeks (q8w) starting at week 52 in PSO3001 and at week 76 in PSO3002, with the last dose at week 252 and the last safety follow-up visit at week 264. The RMP (version 8.1) is 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 RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.15. Human normal immunoglobulin - HIZENTRA (CAP) - EMEA/H/C/002127/II/0129

Applicant: CSL Behring GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication in order to expand the approved secondary immunodeficiencies (SID) indications to any symptomatic SID in accordance with the 'guideline on core SmPC for human normal immunoglobulin for intravenous administration' (EMA/CHMP/BPWP/94038/ 2007 Rev 5; CHMP, 2018). As a consequence, sections 4.1 and 4.2 of the SmPC are updated. The package leaflet and the RMP (version 4.6) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.16. Ibalizumab - TROGARZO (CAP) - EMEA/H/C/004961/II/0015

Applicant: Theratechnologies Europe Limited

PRAC Rapporteur: David Olsen

Scope: Updated timelines for the post-authorisation efficacy study (PAES) to further characterise the efficacy of ibalizumab in combination with other anti-retroviral medicinal products, for the treatment of adults infected with multidrug resistant human immunodeficiency virus-1 (HIV-1) infection for whom it is otherwise not possible to construct a suppressive antiviral regimen (PROMISE study) to provide the final study report from October 2025 to October 2026. Annex II of the product information is updated accordingly. The RMP (version 2.0) is updated accordingly and in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010797/202009) adopted in April 2021

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

5.3.17. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0068, Orphan

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Update of section 4.4 of the SmPC in order to add baseline monitoring in in addition to the current warnings for periodic monitoring of cardiac failure and cardiac arrhythmias in patients receiving ibrutinib. The package leaflet and the RMP (version 18.1) are updated accordingly

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

5.3.18. Insulin lispro - LYUMJEV (CAP) - EMEA/H/C/005037/X/0010

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Annika Folin

Scope: Extension application to change the insulin lispro master cell bank (MCB) and related process steps. The RMP is updated (version 11.1) accordingly

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

5.3.19. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/II/0096, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Extension of indication for Kalydeco (ivacaftor) tablets in combination regiment with Kaftrio (ivacaftor/tezacaftor/elexacaftor) to include the treatment of adults, adolescents and children aged 6 years and older with cystic fibrosis who are homozygous for the F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene or heterozygous for F508del and have a minimal function (MF) mutation in the CFTR gene. This application is based on the results of study VX18-445-106: a phase 3, open-label, multicentre study in subjects 6 through 11 years of age, with F/MF and F/F genotypes. As a consequence, sections 4.1, 4.2, 5.1, and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. The RMP (version 12.0) are updated in accordance

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

5.3.20. Ivacaftor - KALYDECO (CAP) - EMEA/H/C/002494/WS2048/0101; tezacaftor, ivacaftor - SYMKEVI (CAP) - EMEA/H/C/004682/WS2048/0030

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Update of sections 4.2, 4.5, 4.8 and 5.1 of the SmPC to reflect the final clinical study report (CSR) part A of study VX17-661-116: a phase 3, open-label, rollover study to evaluate the safety and efficacy of long-term treatment with tezacaftor in combination with ivacaftor in subjects with cystic fibrosis aged 6 years and older, homozygous or heterozygous for the F508del-cystic fibrosis transmembrane conductance regulator (CFTR) mutation. The package leaflet and the RMP (version 3.1 for Symkevi) 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/X/0008/G, Orphan

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Grouped applications consisting of: 1) extension application to introduce a new strength of 37.5 mg/25 mg/50 mg film-coated tablets; 2) extension of indication to include paediatric use aged from 6 to 11 years. The RMP (version 3.0) is updated accordingly

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

5.3.22. Lipegfilgrastim - LONQUEX (CAP) - EMEA/H/C/002556/II/0058/G

Applicant: Teva B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Grouped variations consisting of an extension of indication to include treatment of the paediatric population and introduction of an age appropriate presentation in vials. 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 12.0) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.1)

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

5.3.23. Migalastat - GALAFOLD (CAP) - EMEA/H/C/004059/II/0034, Orphan

Applicant: Amicus Therapeutics Europe Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.8, 5.1 and 5.2 of the SmPC based on final results from study AT1001-020 (listed as category 3 in the RMP): a phase 3b, 2-stage, open-label, uncontrolled, multicentre study to evaluate the safety, pharmacokinetic, pharmacodynamic and efficacy of migalastat treatment in paediatric subjects 12 to < 18 years of age and weighing ≥ 45 kg with Fabry disease and with amenable galactosidase alfa (GLA) variants. The RMP (version 7.0) is updated accordingly (in fulfilment of Article 46 of Regulation 1901/2006 as amended). In addition, the MAH took the opportunity to introduce some minor editorial changes to the SmPC and package leaflet and to bring the product information 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 CHMP

5.3.24. Niraparib - ZEJULA (CAP) - EMEA/H/C/004249/X/0029, Orphan

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Extension application to introduce a new pharmaceutical form (100 mg film-coated

tablet). The RMP (version 5.1) is updated in accordance

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

5.3.25. Nitisinone - NITISINONE MDK (CAP) - EMEA/H/C/004281/X/0007

Applicant: MendeliKABS Europe Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: Extension application to add a new strength of 20 mg (hard capsule). The RMP (version 2.0) is updated accordingly

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

5.3.26. Ospemifene - SENSHIO (CAP) - EMEA/H/C/002780/II/0041

Applicant: Shionogi B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Extension of indication to delete information on specific subset of patients, based on the final study report of the imposed non-interventional PASS (listed in Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product'): an observational retrospective cohort study of ospemifene to assess the incidence of venous thromboembolism (VTE) and other safety concerns as agreed in the RMP in vulvar and vaginal atrophy (VVA) patients treated with ospemifene compared to: 1) patients newly prescribed selective estrogen receptor modulators (SERMs) for oestrogen-deficiency conditions or breast cancer prevention, and 2) the incidence in untreated VVA patients. As a consequence, sections 4.1 and 4.4 of the SmPC are updated. The package leaflet and Annex II-D are updated in accordance. The RMP (version 2) is 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 RMP AR, PRAC RMP assessment overview and advice to CHMP

5.3.27. Ozanimod - ZEPOSIA (CAP) - EMEA/H/C/004835/II/0002/G

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Grouped variation consisting of: 1) extension of indication to include the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic agent for Zeposia (ozanimod). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.2 and 5.1 of the SmPC and Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' are updated. The package leaflet and the RMP (version 1.1) are updated in accordance. In addition, the MAH took the opportunity to implement editorial changes throughout the product information; 2) update of sections 4.4 and 4.5 of the SmPC in order to update the current SmPC description about pharmacokinetic (PK) interaction with breast cancer resistance protein (BCRP) inhibitors based on study RPC-1063-CP-001: a phase 1, randomized, parallel-group, open-label study to evaluate the effect of cyclosporine on the single-dose pharmacokinetics of ozanimod and

major active metabolites in healthy adult subjects

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

5.3.28. Padeliporfin - TOOKAD (CAP) - EMEA/H/C/004182/II/0015

Applicant: STEBA Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Submission of the clinical study report for study CLIN1001 PCM301FU5 (listed as a post-authorisation efficacy study (PAES), category 1 study in Annex II): a European randomised phase 3 study to assess the efficacy and safety of Tookad (padeliporfin) soluble for localised prostate cancer compared to active surveillance. Annex II is updated to remove reference to this study. The RMP (version 8.0) is updated accordingly

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

5.3.29. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0108

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include the adjuvant treatment in monotherapy of adults with renal cell carcinoma (RCC) at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions. As a consequence, sections 4.1, 4.2 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 35.1) are updated accordingly

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

5.3.30. Pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/II/0109

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication for Keytruda (pembrolizumab) as monotherapy in the treatment of unresectable or metastatic microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) colorectal, endometrial, gastric, small intestine, biliary, or pancreatic cancer in adults who have received prior therapy, based on the results from: 1) study KEYNOTE-164 (KN164): a phase 2 study of pembrolizumab as monotherapy in subjects with previously treated locally advanced unresectable or metastatic (stage IV) dMMR or MSI-H colorectal carcinoma; 2) study KEYNOTE-158 (KN158): a clinical trial of pembrolizumab evaluating predictive biomarkers in subjects with advanced solid tumours. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 34.1) are updated in accordance

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

5.3.31. Risankizumab - SKYRIZI (CAP) - EMEA/H/C/004759/II/0014

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of indication to include the treatment of active psoriatic arthritis in adults. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated accordingly. Additionally, Annex II is also updated

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

5.3.32. Secukinumab - COSENTYX (CAP) - EMEA/H/C/003729/II/0079

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Extension of indication to include treatment of juvenile idiopathic arthritis (enthesitis-related arthritis and juvenile psoriatic arthritis) in patients 2 years and older whose disease has responded inadequately to, or who cannot tolerate, conventional therapy. 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 10.0) are updated in accordance

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

5.3.33. Semaglutide - OZEMPIC (CAP) - EMEA/H/C/004174/X/0021

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Extension application to add a new strength of 2 mg solution for injection. The RMP (version 6.0) is updated accordingly

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

5.3.34. Somapacitan - SOGROYA (CAP) - EMEA/H/C/005030/X/0001/G, Orphan

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Martin Huber

Scope: Grouped application consisting of: extension application to add a new strength of 5 mg/1.5 mL (3.3 mg/mL). The RMP is updated (version 2.0) accordingly; alignment of the endotoxin release acceptance for Sogroya (somapacitan) 10 mg, to the narrower limit proposed limit for the 5 mg strength (<16 EU/mL). At the same time, the units for endotoxin are changed from EU/mg to EU/mL

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

5.3.35. Tocilizumab - ROACTEMRA (CAP) - EMEA/H/C/000955/II/0101

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include the treatment of coronavirus disease 2019 (COVID-19) in hospitalised adults who are receiving systemic corticosteroids and require

supplemental oxygen or mechanical ventilation. As a consequence, sections 4.1, 4.2, 4.3, 4.4, 4.8, 5.1 and 5.2 of the SmPC for RoActemra (tocilizumab) 20 mg/mL concentrate for solution for infusion are updated. The package leaflet and the RMP (version 27.0) are updated in accordance. Furthermore, the product information is brought in line with the latest quality review of documents (QRD) template (version 10.2 rev. 1)

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

5.3.36. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0035

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Extension of indication to include treatment of adult patients with active ankylosing spondylitis (AS) who have responded inadequately to conventional therapy for Xeljanz (tofacitinib) film-coated tablets. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 17.1) are updated in accordance

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

5.3.37. Vedolizumab - ENTYVIO (CAP) - EMEA/H/C/002782/II/0061

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Adam Przybylkowski

Scope: Extension of indication to add treatment of adult patients with pouchitis, who have undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis, and have had an inadequate response with, lost response to, or were intolerant to antibiotic therapy for Entyvio (vedolizumab) 300 mg powder for concentrate for solution for infusion, based on final results from study Vedolizumab-4004 (ERNEST): an interventional, randomized, double-blind, placebo-controlled, multicentre study to evaluate the efficacy and safety of Entyvio intravenous (vedolizumab) in the treatment of chronic pouchitis. As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 5.2 of the SmPC for Entyvio (vedolizumab) 300 mg are updated. The package leaflet and the RMP (version 7.0) are updated in accordance

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Agomelatine - THYMANAX (CAP); VALDOXAN (CAP) - PSUSA/00000071/202102 (with RMP)

Applicant(s): Les Laboratoires Servier (Valdoxan), Servier (Ireland) Industries Ltd. (Thymanax)

PRAC Rapporteur: Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Apalutamide - ERLEADA (CAP) - PSUSA/00010745/202102

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. Baloxavir marboxil - XOFLUZA (CAP) - PSUSA/00010895/202102

Applicant: Roche Registration GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Baricitinib - OLUMIANT (CAP) - PSUSA/00010578/202102

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Belimumab - BENLYSTA (CAP) - PSUSA/00009075/202103

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Bempedoic acid - NILEMDO (CAP); bempedoic acid, ezetimibe - NUSTENDI (CAP) - PSUSA/00010841/202102

Applicant(s): Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Bevacizumab - AVASTIN (CAP); AYBINTIO (CAP); EQUIDACENT (CAP); MVASI (CAP); ONBEVZI (CAP); ZIRABEV (CAP) - PSUSA/00000403/202102

Applicant(s): Amgen Technology (Ireland) Unlimited Company (Mvasi), Centus Biotherapeutics Europe Limited (Equidacent), Pfizer Europe MA EEIG (Zirabev), Roche Registration GmbH (Avastin), Samsung Bioepis NL B.V. (Aybintio, Onbevzi)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Bosutinib - BOSULIF (CAP) - PSUSA/00010073/202103

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Brentuximab vedotin - ADCETRIS (CAP) - PSUSA/00010039/202102

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Brimonidine[9] - MIRVASO (CAP) - PSUSA/00010093/202102

Applicant: Galderma International

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Burosumab - CRYSVITA (CAP) - PSUSA/00010669/202102

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[9] Centrally authorised product(s) only

6.1.12. Cabotegravir - VOCABRIA (CAP) - PSUSA/00010900/202103

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Caplacizumab - CABLIVI (CAP) - PSUSA/00010713/202102

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Ceftazidime, avibactam - ZAVICEFTA (CAP) - PSUSA/00010513/202102

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Dabigatran - PRADAXA (CAP) - PSUSA/00000918/202103

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Elosulfase alfa - VIMIZIM (CAP) - PSUSA/00010218/202102

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Eravacycline - XERAVA (CAP) - PSUSA/00010718/202102

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Esketamine[10] - SPRAVATO (CAP) - PSUSA/00010825/202103

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - PSUSA/00010352/202102

Applicant: Holostem Terapie Avanzate s.r.l., ATMP[11]

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.20. Ferric maltol - FERACCRU (CAP) - PSUSA/00010476/202102

Applicant: Norgine B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Fluticasone furoate, umeclidinium, vilanterol - ELEBRATO ELLIPTA (CAP); TEMYBRIC ELLIPTA (CAP); TRELEGY ELLIPTA (CAP) - PSUSA/00010653/202103

Applicant(s): GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Fremanezumab - AJOVY (CAP) - PSUSA/00010758/202103

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[10] Centrally authorised product(s) only
[11] Advanced therapy medicinal product

6.1.23. Gimeracil, oteracil monopotassium, tegafur - TEYSUNO (CAP) - PSUSA/00002875/202101

Applicant: Nordic Group B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Guanfacine - INTUNIV (CAP) - PSUSA/00010413/202103

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Human coagulation factor X - COAGADEX (CAP) - PSUSA/00010481/202103

Applicant: BPL Bioproducts Laboratory GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Ibalizumab - TROGARZO (CAP) - PSUSA/00010797/202103

Applicant: Theratechnologies Europe Limited

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Imlifidase - IDEFIRIX (CAP) - PSUSA/00010870/202102

Applicant: Hansa Biopharma AB

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Influenza vaccine (surface antigen, inactivated, prepared in cell cultures) - FLUCELVAX TETRA (CAP) - PSUSA/00010737/202103

Applicant: Seqirus Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Isatuximab - SARCLISA (CAP) - PSUSA/00010851/202103

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Lefamulin - XENLETA (CAP) - PSUSA/00010872/202102

Applicant: Nabriva Therapeutics Ireland DAC

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Lenvatinib - KISPLYX (CAP); LENVIMA (CAP) - PSUSA/00010380/202102

Applicant(s): Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Meropenem, vaborbactam - VABOREM (CAP) - PSUSA/00010727/202102

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Nalmefene - SELINCRO (CAP) - PSUSA/00010120/202102

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Obiltoxaximab - OBILTOXAXIMAB SFL (CAP) - PSUSA/00010885/202103

Applicant: SFL Pharmaceuticals Deutschland GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Ospemifene - SENSHIO (CAP) - PSUSA/00010340/202102

Applicant: Shionogi B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Pirfenidone - ESBRIET (CAP) - PSUSA/00002435/202102

Applicant: Roche Registration GmbH

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[12]) - EMEA/H/W/002300/PSUV/0056

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.38. Pomalidomide - IMNOVID (CAP) - PSUSA/00010127/202102

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.39. Prasugrel - EFIENT (CAP) - PSUSA/00002499/202102

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

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

Action: For adoption of recommendation to CHMP

6.1.40. Pretomanid - DOVPRELA (CAP) - PSUSA/00010863/202102

Applicant: Mylan IRE Healthcare Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.41. Ranolazine - RANEXA (CAP) - PSUSA/00002611/202101

Applicant: Menarini International Operations Luxembourg S.A.

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Reslizumab - CINQAERO (CAP) - PSUSA/00010523/202102

Applicant: Teva B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Ribociclib - KISQALI (CAP) - PSUSA/00010633/202103 (with RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Rilpivirine[13] - REKAMBYS (CAP) - PSUSA/00010901/202103

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[13] Intramuscular use only

6.1.45. Ropeginterferon alfa-2b - BESREMI (CAP) - PSUSA/00010756/202102

Applicant: AOP Orphan Pharmaceuticals AG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Ruxolitinib - JAKAVI (CAP) - PSUSA/00010015/202102

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.47. Telotristat - XERMELO (CAP) - PSUSA/00010639/202102

Applicant: Ipsen Pharma

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.48. Tisagenlecleucel - KYMRIAH (CAP) - PSUSA/00010702/202102

Applicant: Novartis Europharm Limited, ATMP[14]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.49. Tivozanib - FOTIVDA (CAP) - PSUSA/00010636/202102

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.50. Trastuzumab emtansine - KADCYLA (CAP) - PSUSA/00010136/202102

Applicant: Roche Registration GmbH

PRAC Rapporteur: Anette Kirstine Stark

[14] Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.51. Ulipristal acetate[15] - ESMYA (CAP); ULIPRISTAL ACETATE GEDEON RICHTER[16] - PSUSA/00009325/202102

Applicant(s): Gedeon Richter Plc.

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.52. Upadacitinib - RINVOQ (CAP) - PSUSA/00010823/202102

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Atosiban - TRACTOCILE (CAP); NAP - PSUSA/00000264/202101

Applicants: Ferring Pharmaceuticals A/S (Tractocile), various

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Cladribine[17] - LITAK (CAP); NAP - PSUSA/00000787/202102

Applicants: Lipomed GmbH (Litak), various

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[15] Indication(s) for the treatment of moderate to severe symptoms of uterine fibroids only
[16] European Commission (EC) decision on the marketing authorisation (MA) withdrawal of Ulipristal acetate Gedeon Richter dated 13 July 2021
[17] Apart from medicinal product(s) with indication(s) for the treatment of multiple sclerosis

6.2.3. Dexmedetomidine - DEXDOR (CAP); NAP - PSUSA/00000998/202103 (with RMP)

Applicants: Orion Corporation (Dexdor), various

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Dexrazoxane - SAVENE (CAP); NAP - PSUSA/00001001/202102

Applicants: Clinigen Healthcare B.V. (Savene), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Estradiol, nomegestrol acetate - ZOELY (CAP); NAP - PSUSA/00002182/202101

Applicants: Theramex Ireland Limited (Zoely), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.6. Fingolimod - FINGOLIMOD ACCORD (CAP); GILENYA (CAP); NAP - PSUSA/00001393/202102

Applicants: Accord Healthcare S.L.U. (Fingolimod Accord), Novartis Europharm Limited (Gilenya), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.7. Influenza vaccine (surface antigen, inactivated, adjuvanted) - FLUAD TETRA (CAP); NAP - PSUSA/00010300/202103

Applicants: Seqirus Netherlands B.V. (Fluad Tetra), various

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.8. Nitisinone - NITISINONE MDK (CAP); NITYR (CAP); ORFADIN (CAP); NAP - PSUSA/00002169/202102

Applicants: Cycle Pharmaceuticals (Europe) Limited (Nityr), MendeliKABS Europe Limited

(Nitisinone MDK), Swedish Orphan Biovitrum International AB (Orfadin), various

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.9. Pemetrexed - ALIMTA (CAP); ARMISARTE (CAP); PEMETREXED ACCORD (CAP); PEMETREXED FRESENIUS KABI (CAP); NAP - PSUSA/00002330/202102

Applicants: Accord Healthcare S.L.U. (Pemetrexed Accord), Actavis Group PTC ehf (Armisarte), Eli Lilly Nederland B.V. (Alimta), Fresenius Kabi Deutschland GmbH (Pemetrexed Fresenius Kabi), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.3.1. Alprostadil[18] (NAP) - PSUSA/00000110/202101

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Amitriptyline hydrochloride, chlordiazepoxide (NAP) - PSUSA/00000171/202102

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Argatroban (NAP) - PSUSA/00009057/202101

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[18] Erectile dysfunction indication(s) only

6.3.4. Baclofen[19] (NAP) - PSUSA/00000293/202101

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Cilazapril (NAP); cilazapril, hydrochlorothiazide (NAP) - PSUSA/00000749/202102

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Cytomegalovirus immunoglobulin (NAP) - PSUSA/00000914/202101

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Dexamethasone[20] (NAP) - PSUSA/00000973/202101

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Eletriptan (NAP) - PSUSA/00001204/202102

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Granisetron[21] (NAP) - PSUSA/00001568/202102

Applicant(s): various

[19] Intrathecal use only
[20] Non-centrally authorised product(s) only
[21] All formulation(s) except transdermal patch

PRAC Lead: Marek Juracka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Human coagulation factor VIII[22] (NAP) - PSUSA/00009174/202102

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Hydroxyethyl starch (HES) (NAP) - PSUSA/00001694/202103

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Iloprost[23] (NAP) - PSUSA/00009190/202101

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Influenza vaccine[24] (split virion, inactivated) (NAP) - PSUSA/00010298/202103

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Influenza vaccine (surface antigen, inactivated) (NAP) - PSUSA/00001744/202103

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

[22] Inhibitor bypassing fraction only
[23] Intravenous (IV) use only
[24] Non-centrally authorised product(s) only

6.3.15. Lanthanum (NAP) - PSUSA/00003175/202103

Applicant(s): various

PRAC Lead: Roxana Dondera

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Lisdexamfetamine (NAP) - PSUSA/00010289/202102

Applicant(s): various

PRAC Lead: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Nafarelin (NAP) - PSUSA/00002105/202102

Applicant(s): various

PRAC Lead: Karen Pernille Harg

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Nomegestrol (NAP) - PSUSA/00002181/202101

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Propafenone (NAP) - PSUSA/00002550/202101

Applicant(s): various

PRAC Lead: Polona Golmajer

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. Valproic acid (NAP); sodium valproate (NAP); valproate pivoxil (NAP); valproate semisodium (NAP); valpriomide (NAP); valproate bismuth (NAP); calcium valproate (NAP); valproate magnesium (NAP) - PSUSA/00003090/202101

Applicant(s): various

PRAC Lead: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Leflunomide - ARAVA (CAP) - EMEA/H/C/000235/LEG 054

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Cumulative review of cases of serious infections, including opportunistic infections and varicella-zoster infections when leflunomide is used in combination with other immunosuppressant therapies in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001837/202009) adopted in May 2021

Action: For adoption of advice to CHMP

6.4.2. Leflunomide - ARAVA (CAP) - EMEA/H/C/000235/LEG 058

Applicant: Sanofi-Aventis Deutschland GmbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Cumulative review of cases of skin ulcer in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001837/202009) adopted in May 2021

Action: For adoption of advice to CHMP

6.4.3. Leflunomide - LEFLUNOMIDE MEDAC (CAP) - EMEA/H/C/001227/LEG 010

Applicant: medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Cumulative review of cases of skin ulcer in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001837/202009) adopted in May 2021

Action: For adoption of advice to CHMP

6.4.4. Leflunomide - LEFLUNOMIDE ZENTIVA (CAP) - EMEA/H/C/001129/LEG 026

Applicant: Zentiva, k.s.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Cumulative review of cases of skin ulcer in line with the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001837/202009) adopted in May 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/II/0020

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.4 and 4.8 of the SmPC to add a new warning on immune thrombocytopenia (ITP) and to add dizziness and ITP to the list of adverse drug reactions with frequencies uncommon and not know as per the conclusions of post-authorisation measure MEA 014.3 (monthly summary safety report (MSSR)) finalised in August 2021. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.5.2. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0046

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of section 4.8 of the SmPC to introduce facial rash with a frequency 'uncommon' related to the outcome of the PSUR single assessment (PSUSA) procedure (PSUSA/00010645/201909) finalised in April 2020. The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.5.3. Ravulizumab - ULTOMIRIS (CAP) - EMEA/H/C/004954/II/0016

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Update of sections 4.4 and 4.8 of the SmPC to add anaphylactic reaction, hypersensitivity and infusion-related reactions following the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA/00010787/202006) finalised in January 2021. The patient leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews[25]

6.6.1. Coronavirus (COVID-19) mRNA[26] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.8

Applicant: BioNTech Manufacturing GmbH

[25] 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

[26] Messenger ribonucleic acid

PRAC Rapporteur: Menno van der Elst

Scope: Ninth expedited monthly summary safety report (MSSR) for Comirnaty (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.2. Coronavirus (COVID-19) mRNA[27] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 011.7

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Eigth expedited monthly summary safety report (MSSR) for Spikevax (COVID-19 mRNA vaccine (nucleoside-modified)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.3. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/MEA 014.5

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Sixth expedited monthly summary safety report (MSSR) for COVID-19 Vaccine Janssen (COVID-19 vaccine (Ad26.COV2-S, recombinant)) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.4. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) – EMEA/H/C/005737/MEA 032

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Interim data from clinical study COV3009: a randomized, double-blind, placebo-controlled phase 3 study to assess the efficacy and safety of Ad26.COV2.S (COVID-19 Vaccine Janssen) for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older; and study COV3001: a randomized, double-blind, placebo-controlled phase 3 study to assess the efficacy and safety of Ad26.COV2.S for the prevention of SARS-CoV-2-mediated COVID-19 in adults aged 18 years and older, to assess the potential for a causal relationship between COVID-19 Vaccine Janssen (COVID-19 vaccine) and venous thromboembolism (VTE), as requested in the conclusions of post-authorisation measure MEA 014.4 (fifth monthly summary safety report (MSSR)) finalised in September 2021

Action: For adoption of PRAC Assessment Report

[27] Messenger ribonucleic acid

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[28]

7.1.1. Afamelanotide – SCENESSE (CAP) - EMEA/H/C/PSA/S/0076

Applicant: Clinuvel Europe Limited

PRAC Rapporteur: Martin Huber

Scope: 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)

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

7.1.2. Fenfluramine – FINTEPLA (CAP) - EMEA/H/C/PSP/S/0093.1

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to PSP/S/0093 [protocol for an observational registry to provide data on long-term safety of fenfluramine in routine practice, with a focus on characterising and quantifying the important potential risks of valvular heart disease (VHD) and pulmonary arterial hypertension (PAH) (primary objective), and growth retardation (secondary objective). In addition, data on the frequency of echocardiographic monitoring contribute to assess the effectiveness of risk minimisation measures] as per the request for supplementary information (RSI) adopted in May 2021

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

7.1.3. Valproate (NAP) - EMEA/H/N/PSP/J/0075.5

Applicant: Sanofi-Aventis Recherche & Développement

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0075.4 [interim report and substantial amendment to a protocol previously agreed in February 2020 for a joint drug utilisation study (DUS) to assess the effectiveness of the new risk minimisation measures (RMMs) and to further characterise the prescribing patterns for valproate as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454] as per the request for supplementary information (RSI) adopted in May 2021

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

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[29]

7.2.1. Berotralstat - ORLADEYO (CAP) - EMEA/H/C/005138/MEA 002

Applicant: BioCryst Ireland Limited

PRAC Rapporteur: Julia Pallos

Scope: Protocol for study BCX7353-401: a non-interventional post-authorisation study to evaluate safety, tolerability and effectiveness of berotralstat for patients with hereditary angioedema in a real-world setting (from initial opinion/marketing authorisation (MA))

Action: For adoption of advice to CHMP

7.2.2. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/MEA 010

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study VAC31518COV4001 (listed as a category 3 study in the RMP): a post-authorisation, observational study to assess the safety of Ad26.COV2.S (COVID-19 Vaccine Janssen) using health insurance claims and/or electronic health record (EHR) database(s) in the United States [final study report expected in December 2024]

Action: For adoption of advice to CHMP

7.2.3. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/MEA 051

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Protocol for study 1160.307: a European non-interventional cohort study based on new data collection to measure the safety of dabigatran etexilate for the treatment of venous thromboembolism (VTE) and prevention of recurrent VTE in paediatric patients from birth to less than 2 years of age [final clinical study report (CSR) expected in Q2 2025] (from X/0122/G)

Action: For adoption of advice to CHMP

7.2.4. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 005.1

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 005 [protocol for study ZX008-2102: a drug utilisation study (DUS) in Europe to describe fenfluramine use in routine clinical practice [final report expected in August 2025] (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in May 2021

[29] 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

Action: For adoption of advice to CHMP

7.2.5. Fenfluramine - FINTEPLA (CAP) - EMEA/H/C/003933/MEA 006

Applicant: Zogenix ROI Limited

PRAC Rapporteur: Martin Huber

Scope: Protocol for study ZX008-2104: a European study of the effectiveness of risk minimisation measures for fenfluramine in Dravet syndrome [final report expected in October 2023] (from initial opinion/marketing authorisation (MA))

Action: For adoption of advice to CHMP

7.2.6. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - EMEA/H/C/005269/MEA 002.2

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: MAH Response to MEA 002.1 [protocol 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 June 2021

Action: For adoption of advice to CHMP

7.2.7. Risdiplam - EVRYSDI (CAP) - EMEA/H/C/005145/MEA 007

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Protocol for study BN42833 - Risdiplam pregnancy surveillance study: a phase 4, non-interventional surveillance study [final study report expected in Q4/2031] (from initial opinion/marketing authorisation (MA))

Action: For adoption of advice to CHMP

7.2.8. Sotagliflozin - ZYNQUISTA (CAP) - EMEA/H/C/004889/MEA 004.4

Applicant: Guidehouse Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 004.3 [protocol for study LX4211.1-401-MAL: a nested, case-control study to evaluate the risk of malignancies (bladder, renal, breast, Leydig cell, pancreatic, thyroid and prostate cancers) in adult patients with type 1 diabetes mellitus (T1DM) using sotagliflozin in existing healthcare databases in Europe and in the United States [final clinical study report (CSR) expected in April 2030] as per the request for supplementary information (RSI) adopted in April 2021

Action: For adoption of advice to CHMP

7.2.9. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 030.2

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: MAH's response to MEA 030.1 [protocol for study F506-PV-0001: a non-interventional PASS on outcomes associated with the use of tacrolimus around conception, or during pregnancy or lactation using data from the Transplant Pregnancy Registry International (TPRI) registry] as per the request for supplementary information (RSI) adopted in May 2021

Action: For adoption of advice to CHMP

7.2.10. Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 022.2

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to MEA 022.1 [protocol for study F506-PV-0001: a non-interventional PASS on outcomes associated with the use of tacrolimus around conception, or during pregnancy or lactation using data from the Transplant Pregnancy Registry International (TPRI) registry] as per the request for supplementary information (RSI) adopted in May 2021

Action: For adoption of advice to CHMP

7.2.11. Vonicog alfa - VEYVONDI (CAP) - EMEA/H/C/004454/MEA 001.4

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Amendment to a protocol previously agreed in June 2019 for study ON (BAX0111) VWF-500 COL (also called ATHN-9 study) (listed as a category 3 study in the RMP): a real world safety and effectiveness study of factor replacement for clinically severe von Willebrand disease (VWD)

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[30]

7.3.1. Hydroxyethyl starch (HES) (NAP) - EMEA/H/N/PSR/J/0031

Applicant(s): Fresenius Kabi Deutschland GmbH (Volulyte, Voluven), B. Braun Melsungen AG (Tetraspan, Venofundin)

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to PSR/J/0031 [results for a joint retrospective, multinational, drug utilisation study (DUS) to assess the non-adherence of physicians in hydroxyethyl starch (HES) accredited hospitals to the approved European product information [regarding

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

indication for use, contraindications and posology (dosage)] for HES 130-containing medicinal products in clinical routine after implementation of a set of risk minimisation measures as required in the outcome of the referral procedure under Article 107i of Directive 2001/83/EC for HES completed in 2018 (EMEA/H/A-107i/1457)] as per the request for supplementary information (RSI) adopted in May 2021

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

7.3.2. Nomegestrol, estradiol - ZOELY (CAP) - EMEA/H/C/PSR/S/0032

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to PSR/S/0032 [results for a prospective observational study to assess in particular the risk of venous thromboembolic events (VTE) and arterial thromboembolic events (ATE) in nomegestrel/oestradiol users compared with the VTE risk in users of combined oral contraceptives (COCs)-containing levonorgestrel] as per the request for supplementary information (RSI) adopted in July 2021

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

7.3.3. Radium (Ra^{223}) – XOFIGO (CAP) - EMEA/H/C/PSR/S/0034

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Results for study PRECISE: an observational, non-randomised, retrospective study evaluating the rates of bone fractures and survival in metastatic castration-resistant prostate cancer (mCRPC) patients treated with radium-223 in routine clinical practice in Sweden, as required in the outcome of the referral procedure under Article 20 of Regulation (EC) No 726/2004 completed in 2018 (EMEA/H/A-20/1459]

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

7.3.4. Rivaroxaban – XARELTO (CAP) - EMEA/H/C/PSR/S/0027

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to PSR/S/0027 [final study report comprising the pharmaco-epidemiological study programme of rivaroxaban use and potential adverse outcomes in routine clinical practice in the UK, Germany, the Netherlands and Sweden] as per the request for supplementary information (RSI) adopted in March 2021

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[31]

7.4.1. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/II/0038

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final study report (CSR) from PsOBest registry (listed as a category 3 study in the RMP): an observational study to assess the long-term safety and effectiveness of apremilast in routine clinical practice in Germany. The RMP (version 14.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.2. Apremilast - OTEZLA (CAP) - EMEA/H/C/003746/II/0039

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Segovia

Scope: Submission of the final study report (CSR) from the UK Clinical Practice Research Database (CPRD) (listed as a category 3 study in the RMP): an observational study to assess the long-term data of apremilast in patients with psoriasis and psoriatic arthritis. The RMP (version 14.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.3. Brolucizumab - BEOVU (CAP) - EMEA/H/C/004913/II/0008

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.8 of the SmPC in order to include the description of intraocular inflammation, based on the final results from a non-interventional retrospective real-world evidence study conducted in patients with neovascular (wet) age-related macular degeneration (nAMD) to better understand the incidence of adverse events/safety signal after initiating treatment with brolucizumab for up to 6 months

Action: For adoption of PRAC Assessment Report

7.4.4. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/II/0126/G

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Grouped variation consisting of: 1) submission of the final report from drug utilisation study 1160.129 (GLORIA AF): a three-phase, international, multicentre, prospective, observational registry programme in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke in order to investigate patient

[31] In accordance with Article 61a (6) of Regulation (EC) No 726/2004, in line with the revised variations regulation for any submission as of 4 August 2013

characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients globally and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke; 2) submission of the final report from drug utilisation study 1160.136 (EU GLORIA AF) (listed as a category 3 study in the RMP): a three-phase, international, multicentre, prospective, observational registry programme in patients with newly diagnosed non-valvular atrial fibrillation (NV AF) at risk for stroke in order to investigate patient characteristics influencing the choice of antithrombotic treatment for the prevention of stroke in NV AF patients from participating countries in EU/EEA Member States and to collect data from clinical practice settings on important outcome events of antithrombotic treatments for the prevention of stroke. The RMP (version 39) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.5. Edoxaban - LIXIANA (CAP) - EMEA/H/C/002629/WS2078/0034; ROTEAS (CAP) - EMEA/H/C/004339/WS2078/0020

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report from study ETNA-VTE-EUROPE (DSE-EDO-05-14-EU), (listed as a category 3 study in the RMP): a non-interventional study on edoxaban treatment in routine clinical practice in patients with venous thromboembolism in Europe. The RMP (version 12.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Infliximab - INFLECTRA (CAP) - EMEA/H/C/002778/II/0100/G

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped variations consisting of the submission of the final clinical study reports (CSRs) for CT-P13 registry studies in inflammatory bowel disease (IBD), ankylosing spondylitis (AS) and rheumatoid arthritis (RA) initiated with the objective of assessing long-term safety in these indications, namely: 1) study CT-P13 4.3: EU and Korean IBD registry; 2) CT-P13 4.4: EU and Korean AS registry; 3) study from the British Society for Rheumatology Biologicals Register (BSRBR)-RA; 4) study from the German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT)

Action: For adoption of PRAC Assessment Report

7.4.7. Infliximab - REMSIMA (CAP) - EMEA/H/C/002576/II/0103/G

Applicant: Celltrion Healthcare Hungary Kft.

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped variations consisting of the submission of the final clinical study reports (CSRs) for CT-P13 registry studies in inflammatory bowel disease (IBD), ankylosing spondylitis (AS) and rheumatoid arthritis (RA) initiated with the objective of assessing long-term safety in these indications, namely: 1) study CT-P13 4.3: EU and Korean IBD registry;

2) CT-P13 4.4: EU and Korean AS registry; 3) study from the British Society for Rheumatology Biologicals Register (BSRBR)-RA; 4) study from the German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT)

Action: For adoption of PRAC Assessment Report

7.4.8. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/II/0024

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final clinical study report (CSR) of study INSLIC08571 (listed as a category 3 study in the RMP): a survey to evaluate the knowledge and understanding of the key safety messages in the healthcare professional guide and the patient guide (in fulfilment of MEA 002). The RMP (version 6.0) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.9. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/II/0038

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: Submission of the final study report for study OBS12753 (listed as a category 3 study in the RMP): a prospective cohort study of long-term safety of teriflunomide in multiple sclerosis patients in Europe. The RMP (version 7.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 024.15

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 024.14 [annual report 2020 on adverse events and/or lack of efficacy, immunological data, follow-up growth disturbances in children and data on urinary hexose tetrasaccharide (Hex4) from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status [final clinical study report expected in Q4 2021]] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.5.2. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/MEA 025.15

Applicant: Genzyme Europe BV

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 025.14 [annual report 2020 on data on patients with renal or hepatic insufficiency from the Pompe registry: a global, multicentre, observational and voluntary programme designed to collect uniform and meaningful clinical data related to the onset, progression, and treated course of patients with Pompe disease irrespective of treatment status [final clinical study report expected in Q4 2021]] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.5.3. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/MEA 019.7

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 019.6 [second interim report for drug utilisation survey OBS14697: a drug utilisation study to assess the effectiveness of dosing recommendation of Praluent (alirocumab) as per the product information to avoid very low-density lipoprotein (LDL)-C levels [final results expected in Q3 2021]] as per the request for supplementary information (RSI) adopted in May 2021

Action: For adoption of advice to CHMP

7.5.4. Coronavirus (COVID-19) mRNA[32] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 003.2

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Interim report for an enhanced pharmacovigilance study (listed as a category 3 study in the RMP) to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals - post authorisation safety of SARS-CoV-2 mRNA-1273 vaccine in the US [final clinical study report (CSR) expected in June 2023] (from initial opinion/marketing authorisation (MA))

Action: For adoption of advice to CHMP

7.5.5. Coronavirus (COVID-19) mRNA[33] vaccine (nucleoside-modified) - SPIKEVAX (CAP) - EMEA/H/C/005791/MEA 005.2

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Interim report for a study (listed as a category 3 study in the RMP): Moderna mRNA-1273 observational pregnancy outcome study to evaluate outcomes of pregnancies in females exposed to mRNA-1273 vaccine (Spikevax) during pregnancy [final clinical study report (CSR) expected in June 2024]

Action: For adoption of advice to CHMP

[32] Messenger ribonucleic acid
[33] Messenger ribonucleic acid

7.5.6. Elosulfase alfa - VIMIZIM (CAP) - EMEA/H/C/002779/ANX 005.6

Applicant: BioMarin International Limited

PRAC Rapporteur: Rhea Fitzgerald

Scope: Seventh annual report (reporting period: 14 February 2020 to 12 February 2021) for the multicentre, multinational, observational Morquio A registry study (MARS): a voluntary observational registry study to characterise and describe the mucopolysaccharidosis IV type A (MPS IVA) population and to evaluate the long-term effectiveness and safety of Vimizim (elosulfase alfa) [final clinical study report (CSR) expected by March 2025]

Action: For adoption of advice to CHMP

7.5.7. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/MEA 010.4

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Fifth monitoring interim report for study 1245.97: a non-interventional PASS assessing the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study [final clinical study report (CSR) expected in June 2021]

Action: For adoption of advice to CHMP

7.5.8. Empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/MEA 006.6

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Fifth monitoring interim report for study 1245.97: a non-interventional PASS assessing the risk of urinary tract malignancies in relation to empagliflozin exposure in patients with type 2 diabetes mellitus (T2DM): a multi-database European study [final clinical study report (CSR) expected in June 2021]

Action: For adoption of advice to CHMP

7.5.9. Eribulin - HALAVEN (CAP) - EMEA/H/C/002084/MEA 024.1

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: MAH's response to MEA 024 [interim results for study E7389-M044-504 (IRENE): an observational, post-authorisation, single-arm, prospective, multicentre cohort study to characterise and determine the incidence of eribulin-induced peripheral neuropathy (PN), and the frequency and time to resolution of eribulin-induced PN in adult patients treated with eribulin in a real-life setting with locally advanced or metastatic breast cancer who have progressed after at least one chemotherapeutic regimen for advanced disease] as per the request for supplementary information (RSI) adopted in March 2020

Action: For adoption of advice to CHMP

7.5.10. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[34]) - EMEA/H/W/002300/MEA 003.5

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Fourth annual progress report for study EPI-MAL-003 (listed as a category 3 study in the RMP): a phase 4 prospective observational study to evaluate the safety, effectiveness and impact of Mosquirix (plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted)) in young children in sub-Saharan Africa in order to estimate the incidence of potential adverse events of special interest (AESI) and other adverse events leading to hospitalisation or death, in children vaccinated with the vaccine, together with MAH's response to MEA 003.4 [third annual progress report] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.5.11. Umeclidinium - ROLUFTA ELLIPTA (CAP) - EMEA/H/C/004654/ANX 003.1

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: MAH's response to ANX 003 [interim report for study 201038 (EU PASS 10316): non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with umeclidinium/vilanterol (UMEC/VI) combination, or inhaled UMEC versus tiotropium] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

7.5.12. Umeclidinium, vilanterol - ANORO ELLIPTA (CAP) - EMEA/H/C/002751/ANX 001.3

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: MAH's response to ANX 001.2 [interim report for study 201038 (EU PASS 10316): non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with umeclidinium/vilanterol (UMEC/VI) combination, or inhaled UMEC versus tiotropium] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

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

7.5.13. Umeclidinium, vilanterol - LAVENTAIR ELLIPTA (CAP) - EMEA/H/C/003754/ANX 001.3

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: MAH's response to ANX 001.2 [interim report for study 201038 (EU PASS 10316): non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with umeclidinium/vilanterol (UMEC/VI) combination, or inhaled UMEC versus tiotropium] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

7.5.14. Umeclidinium bromide - INCRUSE ELLIPTA (CAP) - EMEA/H/C/002809/ANX 001.3

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ilaria Baldelli

Scope: MAH's response to ANX 001.2 [interim report for study 201038 (EU PASS 10316): non-interventional post-authorisation safety (PAS) observational cohort study to quantify the incidence and comparative safety of selected cardiovascular and cerebrovascular events in chronic obstructive pulmonary disease (COPD) patients with umeclidinium/vilanterol (UMEC/VI) combination, or inhaled UMEC versus tiotropium] as per the request for supplementary information (RSI) adopted in June 2021

Action: For adoption of advice to CHMP

7.5.15. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 022.23

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 022.22 [tenth annual report for study C0168Z03 (PSOLAR: PSOriasis Longitudinal Assessment and Registry): an international prospective cohort study/registry programme designed to collect data on psoriasis (PSO) patients that are eligible to receive systemic therapies, including generalised phototherapy and biologics] as per the request for supplementary information (RSI) adopted in May 2021

Action: For adoption of advice to CHMP

7.6. Others

7.6.1. Acalabrutinib - CALQUENCE (CAP) - EMEA/H/C/005299/MEA 002.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: MAH's response to MEA 002 [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 April 2021

Action: For adoption of advice to CHMP

7.6.2. Plasmodium falciparum and hepatitis B vaccine (recombinant, adjuvanted) - MOSQUIRIX (Art 58[35]) - EMEA/H/W/002300/MEA 019

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Jean-Michel Dogné

Scope: Statistical report on the results of the 'Malaria Vaccine Program Evaluation' (MVPE) led by WHO[36] - Mosquirix (plasmodium falciparum and hepatitis B vaccine - RTS,S/AS01) MVPE 24 months after the vaccination with Mosquirix (plasmodium falciparum and hepatitis B vaccine) was introduced by national immunisation programmes

Action: For adoption of advice to CHMP

7.6.3. Sacubitril, valsartan - ENTRESTO (CAP) - EMEA/H/C/004062/MEA 004.10

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Statistical analysis plan for CLCZ696B2015 (PASS 3) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of Entresto/Neparvis (sacubitril/valsartan) [final study report expected in December 2022]

Action: For adoption of advice to CHMP

7.6.4. Sacubitril, valsartan - NEPARVIS (CAP) - EMEA/H/C/004343/MEA 003.7

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Statistical analysis plan for CLCZ696B2015 (PASS 3) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to assess the risk of myotoxicity, hepatotoxicity and acute pancreatitis in statin-exposed heart failure patients with or without concomitant use of Entresto/Neparvis (sacubitril/valsartan) [final study report expected in December 2022]

Action: For adoption of advice to CHMP

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

7.6.5. Tacrolimus - ADVAGRAF (CAP) - EMEA/H/C/000712/MEA 032

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ronan Grimes

Scope: Submission of a critical analysis of the feasibility of using alternative data sources to complement the Transplantation Pregnancy Registry International (TPRI) study outcomes on pregnancy and breastfeeding

Action: For adoption of advice to CHMP

7.6.6. Tacrolimus - MODIGRAF (CAP) - EMEA/H/C/000954/MEA 024

Applicant: Astellas Pharma Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of a critical analysis of the feasibility of using alternative data sources to complement the Transplantation Pregnancy Registry International (TPRI) study outcomes on pregnancy and breastfeeding

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

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

7.8. Ongoing Scientific Advice

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

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. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/004061/S/0017 (without RMP)

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.2. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/S/0028 (without RMP)

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Ebola vaccine (rDNA[37], replication-incompetent) - MVABEA (CAP) - EMEA/H/C/005343/S/0006 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.4. Ebola vaccine (rDNA[38], replication-incompetent) - ZABDENO (CAP) - EMEA/H/C/005337/S/0005 (without RMP)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Jean-Michel Dogné

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. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/R/0026 (without RMP)

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Coronavirus (COVID-19) mRNA[39] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/R/0046 (without RMP)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

[37] Ribosomal deoxyribonucleic acid
[38] Ribosomal deoxyribonucleic acid
[39] Messenger ribonucleic acid

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/R/0037 (without RMP)

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.4. Ex vivo expanded autologous human corneal epithelial cells containing stem cells - HOLOCLAR (CAP) - EMEA/H/C/002450/R/0039 (without RMP)

Applicant: Holostem Terapie Avanzate s.r.l., ATMP[40]

PRAC Rapporteur: Rhea Fitzgerald

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CAT and CHMP

8.2.5. Polatuzumab vedotin - POLIVY (CAP) - EMEA/H/C/004870/R/0008 (without RMP)

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.6. Selpercatinib - RETSEVMO (CAP) - EMEA/H/C/005375/R/0008 (without RMP)

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Adalimumab - AMGEVITA (CAP) - EMEA/H/C/004212/R/0029 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

[40] Advanced therapy medicinal product

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Chenodeoxycholic acid - CHENODEOXYCHOLIC ACID LEADIANT (CAP) - EMEA/H/C/004061/R/0018 (without RMP)

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Edoxaban - ROTEAS (CAP) - EMEA/H/C/004339/R/0021 (with RMP)

Applicant: Berlin Chemie AG

PRAC Rapporteur: Tiphaine Vaillant

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Tenofovir alafenamide - VEMLIDY (CAP) - EMEA/H/C/004169/R/0035 (without RMP)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/R/0040 (without RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Umeclidinium - ROLUFTA ELLIPTA (CAP) - EMEA/H/C/004654/R/0019 (without RMP)

Applicant: GlaxoSmithKline Trading Services Limited

PRAC Rapporteur: Ilaria Baldelli

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. Fluconazole (NAP) - DE/H/xxxx/WS/926

Applicant(s): Pfizer Pharma PFE GmbH

PRAC Lead: Martin Huber

Scope: PRAC consultation on a worksharing variation procedure (DE/H/xxxx/WS/926) for fluconazole-containing medicinal products on the product information wording on congenital malformations and low-dose fluconazole treatment, related to the wording agreed in the recommendation of PSUR single assessment (PSUSA) procedure (PSUSA/00001404/202003) concluded in November 2020, on request of Germany

Action: For adoption of advice to Member States

11.2. Other requests

11.2.1. Irinotecan[41] (NAP) - FR/H/PSUFU/00001783/202005

Applicant(s): Pfizer Healthcare Ireland (Campto), Sun Pharmaceutical Industries Europe B.V (Irinotecan), Aurovitas Spain, S.A.U (Irinotecan Aurovitas)

PRAC Lead: Tiphaine Vaillant

Scope: PRAC consultation on a PSUR follow-up (PSU FU) procedure evaluating analyses relating to irinotecan starting dose in patients with reduced uridine diphosphate glucuronosyltransferase (UGT1A1) activity and possible risk minimisation measures, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUR single assessment (PSUSA) procedure (PSUSA/00001783/202005) concluded in January 2021, on request of France

Action: For adoption of advice to Member States

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

[41] Except liposomal formulation(s)

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

12.4.2. Coronavirus (COVID-19) pandemic - EMA lessons learned

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 2021 – planning update dated Q3 2021

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: Sabine Straus

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

12.20.1. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact – draft decision aid for PRAC stakeholder engagement

PRAC lead: Daniel Morales

Action: For discussion

12.21. Others

12.21.1. EMA new emergency notification system

Action: for discussion

12.21.2. EU pharmaceutical legislation – revision of Directive 2001/83/EC and Regulation (EC) No 726/2004

Action: For discussion

12.21.3. Good Pharmacovigilance Practice (GVP) – planning for 2022

PRAC lead: Sabine Straus

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/