05 July 2021
EMA/PRAC/379709/2021
Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 05-08 July 2021

Chair: Sabine Straus – Vice-Chair: Martin Huber

05 July 2021, 10:30 – 19:30, via teleconference

06 July 2021, 08:30 – 19:30, via teleconference

07 July 2021, 08:30 – 19:30, via teleconference

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

Organisational, regulatory and methodological matters (ORGAM)

22 July 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).

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1. Introduction

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

Pre-meeting list of participants and restrictions in relation to declarations of interests applicable to the items of the agenda for the PRAC plenary session to be held 05-08 July 2021. See July 2021 PRAC minutes (to be published post September 2021 PRAC meeting).

1.2. Agenda of the meeting on 05-08 July 2021

Action: For adoption

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

None

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 outstanding issues (LoOI)

3.3. Procedures for finalisation

3.3.1. Betibeglogene autotemcel – ZYNTEGLO (CAP) – EMEA/H/A-20/1504

Applicant: Bluebird bio (Netherlands) B.V.; ATMP[1]

PRAC Rapporteur: Brigitte Keller-Stanislawski; PRAC Co-rapporteur: Menno van der Elst

Scope: Review of the benefit-risk balance following notification by the European Commission of a referral under Article 20 of Regulation (EC) No 726/2004 based on pharmacovigilance data

Action: For adoption of a recommendation to CAT and CHMP

3.4. Re-examination procedures[2]

None

3.5. Others

None

4. Signals assessment and prioritisation[3]

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Atezolizumab – TECENTRIQ (CAP)

Applicant(s): Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

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

Scope: Signal of cholangitis sclerosing

Action: For adoption of PRAC recommendation

EPITT 19708 – New signal

Lead Member State(s): PT

4.1.2. Ertapenem – INVANZ (CAP); NAP

Applicant(s): Merck Sharp & Dohme B.V., various

PRAC Rapporteur: To be appointed

Scope: Signal of toxic encephalopathy in patients with renal impairment

Action: For adoption of PRAC recommendation

EPITT 19498 – New signal

Lead Member State(s): PT

4.1.3. Propylthiouracil (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

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

Action: For adoption of PRAC recommendation

EPITT 19692 – New signal

Lead Member State(s): EE

4.2. New signals detected from other sources

None

4.3. Signals follow-up and prioritisation

4.3.1. Coronavirus (COVID-19) mRNA[4] vaccine (nucleoside-modified) - COMIRNATY (CAP) – EMEA/H/C/005735/SDA/032

Applicant(s): BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Signal of myocarditis and pericarditis

Action: For adoption of PRAC recommendation

EPITT 19712 – Follow-up to June 2021

[4] Messenger ribonucleic acid

4.3.2. Coronavirus (COVID-19) mRNA[5] vaccine (nucleoside-modified) - SPIKEVAX (previously COVID-19 VACCINE MODERNA) (CAP) - EMEA/H/C/005791/SDA/026.1

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

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of immune thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19679 – Follow-up to May 2021

4.3.3. Coronavirus (COVID-19) mRNA[6] vaccine (nucleoside-modified) - SPIKEVAX (previously COVID-19 VACCINE MODERNA) (CAP) – EMEA/H/C/005791/SDA/033

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

PRAC Rapporteur: Hans Christian Siersted

Scope: Signal of myocarditis and pericarditis

Action: For adoption of PRAC recommendation

EPITT 19713 – Follow-up to June 2021

4.3.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/SDA/034.1

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 May 2021

4.3.5. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) – EMEA/H/C/005675/SDA/065

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Signal of acute macular outer retinopathy

Action: For adoption of PRAC recommendation

EPITT 19703 - Follow-up to May 2021

4.3.6. Donepezil (NAP)

Applicant(s): various

[5] Messenger ribonucleic acid
[6] Messenger ribonucleic acid

PRAC Rapporteur: Martin Huber

Scope: Signal of cardiac conduction disorders including QT prolongation and Torsade de Pointes

Action: For adoption of PRAC recommendation

EPITT 19667 – Follow-up to March 2021

4.3.7. Immune checkpoint inhibitors: atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/SDA/021.1; avelumab - BAVENCIO (CAP) - EMEA/H/C/004338/SDA/007.1; cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/SDA/007.1; durvalumab - IMFINZI (CAP) - EMEA/H/C/004771/SDA/007.1; ipilimumab - YERVOY (CAP) - EMEA/H/C/002213/SDA/041.1; pembrolizumab - KEYTRUDA (CAP) - EMEA/H/C/003820/SDA/029.1; nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/SDA/042.1

Applicant(s): AstraZeneca AB (Imfinzi), Bristol-Myers Squibb Pharma EEIG (Opdivo, Yervoy), Merck Europe B.V. (Bavencio), Merck Sharp & Dohme B.V. (Keytruda), Regeneron Ireland Designated Activity Company (DAC) (Libtayo), Roche Registration GmbH (Tecentriq)

PRAC Rapporteur: Menno van der Elst

Scope: Signal of immune-mediated cystitis

Action: For adoption of PRAC recommendation

EPITT 19610 – Follow-up to May 2021

4.3.8. Octreotide (NAP)

Applicant(s): various

PRAC Rapporteur: Ronan Grimes

Scope: Signal of pancreatic exocrine insufficiency

Action: For adoption of PRAC recommendation

EPITT 19661 – Follow-up to March 2021

4.3.9. Olaparib – LYNPARZA (CAP) - EMEA/H/C/003726/SDA/017

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Signal of Pneumocystis jirovecii pneumonia

Action: For adoption of PRAC recommendation

EPITT 19651 – Follow-up to February 2021

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/II/0006/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped variations consisting of: 1) update of section 4.4 of the SmPC to add a warning for individuals who have experienced a previous cerebral venous sinus thrombosis (CVST) with thrombocytopenia or heparin-induced thrombocytopenia (HIT) to outweigh the potential risks before the administration of COVID-19 Vaccine Janssen. The package leaflet and the RMP (version 2.1) are updated accordingly; 2) update to the RMP (version 2.1) for COVID-19 Vaccine Janssen to include thrombosis with thrombocytopenia syndrome (TTS) in the list of the safety concerns as an important identified risk as per the outcome adopted in May 2021 in the context of the signal procedure on embolic and thrombotic events (with COVID-19 Vaccine Janssen (Ad26.COV2-S [recombinant]) (SDA 018.1). In addition, the MAH took the opportunity to update the RMP with the milestone date for the submission of the protocol for study VAC31518COV4003: a post-authorisation observational study to assess the safety of Ad26.COV2.S using electronic health record (EHR) database(s) in Europe. Finally, the MAH proposed a revised frequency of data mining from the EudraVigilance database and to correct the long-term follow-up time in study VAC31518COV4001: a post-authorisation observational study to assess the safety of Ad26.COV2.S using health insurance claims and/or EHR database(s) in the United States

Action: For adoption of PRAC Assessment Report

4.4.2. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/II/0010

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of section 4.3 of the SmPC in order to add a contraindication related to the administration of Ad26.COV2.S to individuals with a history of capillary leak syndrome (CLS) reported following administration of this vaccine in the Global Medical Safety (GMS) and related to the signal procedure on CLS (with vaccine (ChAdOx1-S [recombinant])) (SDA 047) in June 2021. In addition, the company proposed to include CLS as an important potential risk in the EU-RMP

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Adalimumab - EMEA/H/C/005548

Scope: Treatment of rheumatoid arthritis, psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis, treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis

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

5.1.2. Adalimumab - EMEA/H/C/005947

Scope: Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, paediatric Crohn's disease, ulcerative colitis, uveitis, paediatric uveitis

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

5.1.3. Aducanumab - EMEA/H/C/005558

Scope: Treatment of Alzheimer's disease

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

5.1.4. Anifrolumab - EMEA/H/C/004975

Scope: Add-on therapy for the treatment of adult patients with moderate to severe systemic lupus erythematosus (SLE) despite standard therapy

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

5.1.5. Arachis hypogaea extract - EMEA/H/C/004810

Scope: Treatment of peanut allergy

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

5.1.6. Artesunate - EMEA/H/C/005718, Orphan

Applicant: B And O Pharm

Scope: Treatment of severe malaria

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

5.1.7. Autologous glioma tumour cells (inactivated), autologous glioma tumour cell lysates, (inactivated), allogeneic glioma tumour cells (inactivated), allogeneic glioma tumour cell lysates (inactivated) - EMEA/H/C/003693, Orphan

Applicant: Epitopoietic Research Corporation-Belgium (E.R.C.), ATMP[7]

Scope: Treatment of glioma

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

5.1.8. Avacopan - EMEA/H/C/005523, Orphan

Applicant: Vifor Fresenius Medical Care Renal Pharma France

Scope: Treatment of granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA)

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

5.1.9. Bamlanivimab - EMEA/H/C/005836

Scope: Treatment of coronavirus (COVID-19) in combination with etesevimab

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

5.1.10. Diroximel fumarate - EMEA/H/C/005437

Scope: Treatment of relapsing remitting multiple sclerosis

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

5.1.11. Etesevimab - EMEA/H/C/005837

Scope: Treatment of coronavirus (COVID-19) in combination with bamlanivimab

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

5.1.12. Lasmiditan - EMEA/H/C/005332

Scope: Acute treatment of migraine with or without aura in adults

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

5.1.13. Opicapone - EMEA/H/C/005782

Scope: Treatment of Parkinson’s disease and motor fluctuations

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

[7] Advanced therapy medicinal product

5.1.14. Rivaroxaban - EMEA/H/C/005600

Scope: Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and prevention of recurrent DVT and PE in adults; prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery

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

5.1.15. Sitagliptin fumarate - EMEA/H/C/005741

Scope: Treatment of type 2 diabetes mellitus (T2DM)

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

5.1.16. Sotrovimab - EMEA/H/C/005676

Scope: Treatment of coronavirus disease 2019 (COVID-19)

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

5.1.17. Tecovirimat - EMEA/H/C/005248

Scope: Treatment of Orthopoxvirus disease

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. Atezolizumab - TECENTRIQ (CAP) - EMEA/H/C/004143/II/0061

Applicant: Roche Registration GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of an updated RMP (version 20.0) in order to add severe cutaneous adverse reactions (SCARs) as an important identified risk and its associated risk minimisation measure: a dear healthcare professional communication (DHPC) following the addition of SCARs to the product information as an outcome of variation II/0054 finalised in February 2021. In addition, the MAH took the opportunity to update the due dates of final clinical study reports (CSR) of two post-authorisation efficacy studies (PAES)

Action: For adoption of PRAC Assessment Report

5.2.2. 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

Action: For adoption of PRAC Assessment Report

5.2.3. Brinzolamide, timolol - AZARGA (CAP) - EMEA/H/C/000960/II/0045

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Submission of an updated RMP (version 3.0) to remove important identified risks (respiratory disorders, cardiovascular disorders, corneal decompensation and metabolic acidosis), important potential risk (long term use of preserved eye drops) and missing information (use in paediatric patients)

Action: For adoption of PRAC Assessment Report

5.2.4. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0015

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of an updated RMP (version 3.1) in order to update the safety concerns to add 'thrombosis in combination with thrombocytopenia' as an important identified risk and 'thrombosis' as an important potential risk, with consequential changes in the RMP. Updates to the pharmacovigilance plan have also been implemented. These changes are implemented in line with the recommendation of the signal procedure on 'embolic and thrombotic events' (EPITT 19683) adopted in April 2021. The MAH took the opportunity to further update the RMP to reclassify 'anaphylaxis' as an important identified risk, already reflected in the product information as an adverse drug reaction

Action: For adoption of PRAC Assessment Report

5.2.5. Emicizumab - HEMLIBRA (CAP) - EMEA/H/C/004406/II/0021

Applicant: Roche Registration GmbH

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of an updated RMP (version 2.5) in order to add thromboembolic events without concomitant activated prothrombin complex concentrate (aPCC) as an important potential risk in the safety specifications and to update the milestones of study BO40853 (listed as a category 3 study in the RMP): a PASS based on healthcare professional (HCP) and patient/carer survey to evaluate awareness, knowledge and compliance of HCPs and patients/carers to additional risk minimisation measures (guide for HCPs, patient/carer guide, patient alert card), in relation to the safety concerns of thromboembolic events, thrombotic microangiopathy and life-threatening bleeding due to misinterpretation of the standard coagulation tests in line with the approved substantial amended protocol in December 2020 (MEA 002.2)

Action: For adoption of PRAC Assessment Report

5.2.6. Epoetin alfa - ABSEAMED (CAP) - EMEA/H/C/000727/WS2013/0092; BINOCRIT (CAP) - EMEA/H/C/000725/WS2013/0091; EPOETIN ALFA HEXAL (CAP) - EMEA/H/C/000726/WS2013/0091

Applicant: Sandoz GmbH

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of an updated RMP (version 18) for Abseamed, Binocrit, Epoetin Alfa Hexal (epoetin alfa) in line with the RMP of the medicinal product of reference consisting of: 1) replacement of the term 'tumour growth potential' with 'disease progression' and 'premature death' with 'survival impact'; 2) clinical study data on these two topics were shortened; 3) removal of TRIGONS study proposal (MEA18; HX575-502) as additional pharmacovigilance activity. The risks of disease progression and survival impact will be monitored by routine pharmacovigilance and continue to be reviewed in PSURs

Action: For adoption of PRAC Assessment Report

5.2.7. Ledipasvir, sofosbuvir - HARVONI (CAP) - EMEA/H/C/003850/WS2086/0097; sofosbuvir - SOVALDI (CAP) - EMEA/H/C/002798/WS2086/0071; sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/WS2086/0059

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Updated Annex II to revise the study milestone from 'Q2 2023' to 'Q3 2021' for the hepatocellular carcinoma (HCC) recurrence PASS as per the outcome of the imposed PASS protocol procedure (PSA/J/0055) adopted in June 2020. In addition, the MAH took the opportunity to update the list of local representatives 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 Assessment Report

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

5.3.1. 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

5.3.2. Cabotegravir - VOCABRIA (CAP) - EMEA/H/C/004976/II/0004

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC based on week 124 results from the FLAIR study: a phase 3, randomized, open-label study to evaluate the efficacy, safety and tolerability of the combined treatment cabotegravir and rilpivirine. The package leaflet and the RMP (version 2) are updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet, to introduce editorial changes and corrections throughout the product information 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

5.3.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0026

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to include updated efficacy and safety information based on primary analysis from study D8110C00001 (listed as a specific obligation in Annex II): a phase 3 randomised, double-blind, placebo-controlled, multicentre study in adults to determine the safety, efficacy and immunogenicity of Vaxzevria (COVID-19 vaccine). The package leaflet and Annex II are updated accordingly. The RMP (version 3 succession 2) is updated in accordance

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

5.3.4. Coronavirus (COVID-19) mRNA[8] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/II/0036

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.8 and 5.1 of the SmPC to include new information based on updated interim results from study C4591001: a phase 1/2/3, placebo-controlled, observer-blind, interventional, dose-finding, study to evaluate the safety, tolerability, immunogenicity and efficacy of SARS-CoV-2 RNA vaccine candidates against COVID-19 in healthy individuals. The package leaflet and the RMP (version 2.1) are updated accordingly

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

5.3.5. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/II/0056, Orphan

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 15-007 (listed as a specific obligation in Annex II): a phase 3, randomised, adaptive study of defibrotide vs. best supportive care in the prevention of hepatic veno-occlusive disease in adult and paediatric patients undergoing

[8] Messenger ribonucleic acid

hematopoietic stem cell transplant (HSCT). The RMP (version 9) is updated accordingly. The MAH took the opportunity to bring the product information in line with the latest quality review of documents (QRD) (template 10.2). In addition, the MAH introduced some minor correction throughout the product information

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

5.3.6. Delamanid - DELTYBA (CAP) - EMEA/H/C/002552/X/0046/G, Orphan

Applicant: Otsuka Novel Products GmbH

PRAC Rapporteur: Laurence de Fays

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form (dispersible tablets) associated with a new strength (25 mg); 2) extension of indication to include the treatment of children of at least 10 kg of body weight for Deltyba (delamanid) 50 mg film-coated tablets. As a consequence, sections 3, 4.1, 4.2, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet, labelling and the RMP (version 3.3) are updated accordingly. Annex II is updated to remove the specific obligation related to an in vitro study using the hollow fibre system model of tuberculosis (HFS-TB)

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

5.3.7. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/II/0069/G

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Grouped variations consisting of: 1) update of section 4.8 of the SmPC in order to add rhinorrhoea to the list of adverse drug reactions (ADRs) with frequency not known based on a systematic review of information from clinical and non-clinical studies, post-marketing data and scientific literature. The package leaflet has been updated accordingly; 2) update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 109MS303 (ENDORSE) (listed as a category 3 study in the RMP): a dose-blind, multicentre, extension study to determine the long-term safety and efficacy of two doses of BG00012 (dimethyl fumarate) monotherapy in subjects with relapsing-remitting multiple sclerosis. The RMP (version 11.1) is updated accordingly

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

5.3.8. Dinutuximab beta - QARZIBA (CAP) - EMEA/H/C/003918/II/0027/G, Orphan

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Grouped variations consisting of: 1) anatomical therapeutic chemical (ATC) code change to L01XC16 according to the World Health Organization (WHO); 2) update of section 4.8 of the SmPC in order to include changes to the overall incidence of reported adverse reactions based on post marketing data. In addition, minor changes are introduced in the SmPC, package leaflet and labelling in order to harmonise the product information with other regulatory regions; 3) submission of an updated RMP (version 10.00) in order to include an alignment to post marketing data (PSUR#6) and to introduce updates on the

important identified risks and important potential risks. In addition, the MAH took the opportunity to introduce some linguistic corrections on Swedish, Finnish, Italian, Spanish, and Portuguese EMA annexes

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

5.3.9. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/X/0045/G

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Grouped applications consisting of: 1) extension of application to add a new strength (100 mg solution for injection) consisting of: one presentation containing 2 pre-filled syringes and one presentation containing 6 pre-filled syringes (multipack of 3 packs of 2); 2) extension of indication to include treatment of paediatric patients with severe asthma with type 2 inflammation aged 6 to 11 years old. The RMP (version 6.0) are updated accordingly

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

5.3.10. 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

5.3.11. 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

5.3.12. 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

5.3.13. Lenvatinib - LENVIMA (CAP) - EMEA/H/C/003727/II/0045

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: Update of section 5.1 of the SmPC with additional efficacy and safety data from study E7080-G000-211: a phase 2 multicentre, randomised, double-blind, non-inferiority trial in subjects with ^{131}I-refractory differentiated thyroid cancer to evaluate whether an oral starting dose of 18 mg daily will provide comparable efficacy to a 24 mg starting dose with an improved safety profile. The RMP (version 12.3) is updated accordingly. In addition, the MAH took the opportunity to update the details of local representatives of Bulgaria, Croatia, Estonia, Hungary, Lithuania, Latvia, Malta, Poland, Romania, Slovenia

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

5.3.14. Lenvatinib - KISPLYX (CAP) - EMEA/H/C/004224/II/0048

Applicant: Eisai GmbH

PRAC Rapporteur: David Olsen

Scope: Submission of the final report from study E7080-G000-211 (listed as a category 3 study in the RMP): a multicentre, randomised, double-blind phase 2 trial of lenvatinib (E7080) in subjects with ^{131}I-refractory differentiated thyroid cancer to evaluate whether an oral starting dose of 18 mg daily will provide comparable efficacy to a 24 mg starting dose, but have a better safety profile. The RMP (version 12.3) is updated accordingly

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

5.3.15. Lomitapide - LOJUXTA (CAP) - EMEA/H/C/002578/II/0046

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an alternative study: an evaluation of the effect of lomitapide treatment on major adverse cardiovascular events (MACE) in patients with homozygous familial hypercholesterolemia (LILITH) to the currently agreed protocol for study on the effects of lomitapide on carotid and aortic atherosclerosis in patients treated with lomitapide in usual care (CAPTURE) in order to propose an evaluation of the effect of lomitapide treatment on MACE in patients with homozygous familial hypercholesterolemia. As a

consequence, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' and the RMP (version 6.4) are updated accordingly. In addition, the MAH took the opportunity 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

5.3.16. Mecasermin - INCRELEX (CAP) - EMEA/H/C/000704/II/0067

Applicant: Ipsen Pharma

PRAC Rapporteur: Kirsti Villikka

Scope: Update of the conditions of the non-interventional PASS (listed as a specific obligation in Annex II) by using different criteria of patient exposure and long term follow up to assess the relevant safety data, with consequential amendment of the study completion date. The RMP (version 13) is updated accordingly and submitted together with an amended global registry protocol (amendment 8). The package leaflet is updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the 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

5.3.17. 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

5.3.18. Paliperidone - PALIPERIDONE JANSSEN-CILAG INTERNATIONAL (CAP) - EMEA/H/C/005486/X/0002/G

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Grouped applications consisting of: 1) extension application to introduce two new

strengths of 700 mg and 1000 mg prolonged-release suspension for injection. The RMP (version 10.1) is updated accordingly; 2) change of the (invented) name of the medicinal product from Paliperidone Janssen-Cilag International to Byannli; 3) deletion of the 25 mg, 50 mg, 75 mg, 100 mg and 150 mg/100 mg strengths from the Paliperidone Janssen-Cilag marketing authorisation (EU/1/20/1453/001-006)

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

5.3.19. Pandemic influenza vaccine (H5N1) (split virion, inactivated, adjuvanted) - ADJUPANRIX (CAP) - EMEA/H/C/001206/II/0074

Applicant: GlaxoSmithkline Biologicals SA

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include use in children from 6 months to <18 years for Adjupanrix (pandemic influenza vaccine (H5N1)) based on the results of the following studies: 1) study H5N1-013: a phase 2, non-randomised, open-label study to evaluate the safety and immunogenicity in children aged 6 to 35 months; 2) study H5N1-032: a phase 3, randomised, open, active-controlled study to evaluate the safety and immunogenicity in children aged 3 to 17 years. As a consequence, sections 4.1, 4.2, 4.8, 5.1 and 6.6 of the SmPC are updated. The package leaflet and the RMP (version 13) are updated in accordance. Further, the MAH proposed to update section 4.4 with information on sodium and potassium content in line with the excipients guideline, as well as to add some wording on traceability. 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 10.2). Finally, the MAH introduced minor editorial changes throughout the product information

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

5.3.20. Posaconazole - NOXAFIL (CAP) - EMEA/H/C/000610/II/0062

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Extension of indication to include primary treatment of invasive aspergillosis in adults and adolescents from 13 years of age for Noxafil (posaconazole) gastroresistant tablet and concentrate for solution for infusion based on the results of study P069: a phase 3 randomized study of the efficacy and safety of posaconazole versus voriconazole for the treatment of invasive aspergillosis. 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 16.2) are updated in accordance

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

5.3.21. Posaconazole - NOXAFIL (CAP) - EMEA/H/C/000610/X/0063/G

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Grouped applications consisting of: 1) extension application to introduce a new

pharmaceutical form (gastro-resistant powder and solvent for oral suspension); 2) extension of indication to the paediatric population. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 17.1) are updated in accordance

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

5.3.22. Raltegravir - ISENTRESS (CAP) - EMEA/H/C/000860/II/0093

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Update of section 4.6 of the SmPC in order to update safety information following pregnancy outcome data for raltegravir 400 mg film-coated tablet from prospective reports of pregnancy data with known outcome and time of raltegravir exposure. The RMP (version 15.1) is updated accordingly. In addition, the MAH took the opportunity to introduce some minor changes agreed in previous procedures in the product information and to update the list of local representatives for Germany. Finally, 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. Rilpivirine - REKAMBYS (CAP) - EMEA/H/C/005060/II/0004

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC to update safety and efficacy information based on week 124 results from the FLAIR study: a phase 3, randomised, open-label study to evaluate the efficacy, safety and tolerability of the combined treatment cabotegravir and rilpivirine. The package leaflet and the RMP (version 3.1) are updated accordingly. The MAH took the opportunity to introduce editorial changes and corrections throughout the product information

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

5.3.24. 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

5.3.25. Selinexor - NEXPOVIO (CAP) - EMEA/H/C/005127/II/0001/G

Applicant: Karyopharm Europe GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) extension of indication for Nexpovio (selinexor) in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have received at least one prior therapy; 2) addition of a new pack size (8 tablets) to align with the dose modification guidance for the new indication. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 6.5 of the SmPC are updated accordingly. Annex II is updated to reflect the completion of the specific obligation. The labelling, package leaflet and RMP (version 1.1) are updated in accordance

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

5.3.26. Sofosbuvir, velpatasvir - EPCLUSA (CAP) - EMEA/H/C/004210/X/0056/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped applications consisting of: 1) extension application to introduce a new pharmaceutical form (coated granules in sachet) associated with strengths 200mg/50mg and 150mg/37.5mg. The new presentations are indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients 3 years of age and older; 2) inclusion of paediatric use in patients 3 years of age and older to the existing presentations of the film-coated tablets. 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 7.1) are updated accordingly. In addition, the MAH took the opportunity to implement minor updates and corrections throughout the product information

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

5.3.27. Sofosbuvir, velpatasvir, voxilaprevir - VOSEVI (CAP) - EMEA/H/C/004350/X/0045/G

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Grouped application consisting of: 1) extension application to introduce a new strength (200 mg /50 mg /50 mg film-coated tablets). The new presentation is indicated for the treatment of chronic hepatitis C virus (HCV) infection in patients aged 12 years and older or weighing at least 30 kg. In addition, the MAH took the opportunity to implement minor editorial updates in module 3.2.P; 2) extension of indication to include paediatric use in patients aged 12 years and older or weighing at least 30 kg to the existing presentation. 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 3.2) are updated in accordance

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

5.3.28. Tenofovir alafenamide - VEMLIDY (CAP) - EMEA/H/C/004169/II/0030

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ilaria Baldelli

Scope: Submission of the final report from study GS-US-320-4018 (listed as a category 3

study in the RMP): a phase 3, randomised, double blind study to evaluate the efficacy and safety of switching from tenofovir disoproxil fumarate 300 mg once daily to tenofovir alafenamide 25 mg once daily in subjects with chronic hepatitis B who are virologically suppressed. The RMP (version 6.1) is updated accordingly

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

5.3.29. Tenofovir disoproxil - VIREAD (CAP) - EMEA/H/C/000419/II/0204

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of final study report for study GS-US-174-0144 (listed as category 3 study in the RMP): a randomised, double-blind evaluation of the antiviral efficacy, safety and tolerability of tenofovir disporoxil fumarate. This application fulfils the Article 46 commitment to provide the final week 192 study results for clinical measure 'study 5' (study GS_US_174-0144) listed in the paediatric investigation plan (PIP). As a consequence, section 5.1 of the SmPC is updated accordingly. Additionally, the risk minimisation measures for paediatrics are removed from the RMP and Annex II of the product information. The package leaflet and the RMP (version 25.1) are updated accordingly. In addition, the MAH took the opportunity to implement minor linguistic amendments throughout the product information. Furthermore, the expression of lactose content in Annex I for the tablets was changed to refer to lactose base (not as monohydrate) in line with current practice

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

5.3.30. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0028

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Submission of the final report on Biospecimen testing study (listed as a category 3 study in the RMP): an exploratory study to assess biomarkers related to venous thromboembolism (VTE) events in study A3921133 (a phase 3b/4 randomised safety endpoint study of 2 doses of tofacitinib in comparison to a tumour necrosis factor (TNF) inhibitor in subjects with rheumatoid arthritis). The RMP (version 14.1) is updated accordingly

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

6. Periodic safety update reports (PSURs)

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

6.1.1. Angiotensin II - GIAPREZA (CAP) - PSUSA/00010785/202012

Applicant: Paion Deutschland GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Betibeglogene autotemcel - ZYNTEGLO (CAP) - PSUSA/00010769/202011

Applicant: bluebird bio (Netherlands) B.V, ATMP[9]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.3. Blinatumomab - BLINCYTO (CAP) - PSUSA/00010460/202012

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. Cannabidiol[10] - EPIDYOLEX (CAP) - PSUSA/00010798/202012

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. Cholera vaccine (recombinant, live, oral) - VAXCHORA (CAP) - PSUSA/00010862/202012

Applicant: Emergent Netherlands B.V.

PRAC Rapporteur: Jean-Michel Dogné

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

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. Crisaborole - STAQUIS (CAP) - PSUSA/00010842/202012

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.7. Darunavir - PREZISTA (CAP) - PSUSA/00000934/202012

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.8. Delafloxacin - QUOFENIX (CAP) - PSUSA/00010822/202012

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

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Dengue tetravalent vaccine (live, attenuated) - DENGVAXIA (CAP) - PSUSA/00010740/202012

Applicant: Sanofi Pasteur

PRAC Rapporteur: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Elotuzumab - EMPLICITI (CAP) - PSUSA/00010500/202011

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Encorafenib - BRAFTOVI (CAP) - PSUSA/00010719/202012

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Entrectinib - ROZLYTREK (CAP) - PSUSA/00010874/202012

Applicant: Roche Registration GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.13. Eribulin - HALAVEN (CAP) - PSUSA/00001254/202011

Applicant: Eisai GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. Follitropin delta - REKOVELLE (CAP) - PSUSA/00010554/202011

Applicant: Ferring Pharmaceuticals A/S

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. Formoterol fumarate dihydrate, glycopyrronium bromide, budesonide - TRIXEO AEROSPHERE (CAP) - PSUSA/00010908/202012

Applicant: AstraZeneca AB

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. Indacaterol, mometasone furoate - ATECTURA BREEZHALER (CAP); BEMRIST BREEZHALER (CAP) - PSUSA/00010850/202011

Applicant(s): Novartis Europharm Limited

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. Inotuzumab ozogamicin - BESPONSA (CAP) - PSUSA/00010659/202012

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. Levodopa - INBRIJA (CAP) - PSUSA/00107800/202012

Applicant: Acorda Therapeutics Ireland Limited

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Luspatercept - REBLOZYL (CAP) - PSUSA/00010860/202012

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Laurence de Fays

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Lutetium (^{177}Lu) oxodotreotide - LUTATHERA (CAP) - PSUSA/00010643/202012

Applicant: Advanced Accelerator Applications

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Mexiletine[11] - NAMUSCLA (CAP) - PSUSA/00010738/202012

Applicant: Lupin Europe GmbH

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[11] Centrally authorised product(s) only

6.1.22. Netarsudil - RHOKIINSA (CAP) - PSUSA/00107812/202012

Applicant: Aerie Pharmaceuticals Ireland Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Olaparib - LYNPARZA (CAP) - PSUSA/00010322/202012

Applicant: AstraZeneca AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Pertuzumab, trastuzumab - PHESGO (CAP) - PSUSA/00010906/202012

Applicant: Roche Registration GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Polatuzumab vedotin - POLIVY (CAP) - PSUSA/00010817/202012

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Ponatinib - ICLUSIG (CAP) - PSUSA/00010128/202012

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Ravulizumab - ULTOMIRIS (CAP) - PSUSA/00010787/202012

Applicant: Alexion Europe SAS

PRAC Rapporteur: Kimmo Jaakkola

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Reteplase - RAPILYSIN (CAP) - PSUSA/00002623/202011

Applicant: Actavis Group PTC ehf

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Rotavirus vaccine pentavalent (live, oral) - ROTATEQ (CAP) - PSUSA/00002666/202011

Applicant: MSD Vaccins

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Rucaparib - RUBRACA (CAP) - PSUSA/00010694/202012

Applicant: Clovis Oncology Ireland Limited

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Saquinavir - INVIRASE (CAP) - PSUSA/00002684/202012

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Secukinumab - COSENTYX (CAP) - PSUSA/00010341/202012

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Selexipag - UPTRAVI (CAP) - PSUSA/00010503/202012

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Adrien Inoubli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Semaglutide - OZEMPIC (CAP); RYBELSUS (CAP) - PSUSA/00010671/202011

Applicant(s): Novo Nordisk A/S

PRAC Rapporteur: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Sofosbuvir - SOVALDI (CAP) - PSUSA/00010134/202012

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.36. Sonidegib - ODOMZO (CAP) - PSUSA/00010408/202012

Applicant: Sun Pharmaceutical Industries Europe B.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.37. Treosulfan[12] - TRECONDI (CAP) - PSUSA/00010777/202012

Applicant: Medac Gesellschaft fur klinische Spezialpraparate mbH

PRAC Rapporteur: Julia Pallos

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.38. Turoctocog alfa pegol - ESPEROCT (CAP) - PSUSA/00010782/202012

Applicant: Novo Nordisk A/S

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

[12] Centrally authorised product(s) only

6.1.39. Venetoclax - VENCLYXTO (CAP) - PSUSA/00010556/202012

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

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

6.2.1. Clofarabine - EVOLTRA (CAP); IVOZALL (CAP); NAP - PSUSA/00000805/202012

Applicants: Genzyme Europe BV (Evoltra), Orphelia Pharma SAS (Ivozall), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Edotreotide - SOMAKIT TOC (CAP); NAP - PSUSA/00010552/202012

Applicants: Advanced Accelerator Applications (SomaKit TOC), various

PRAC Rapporteur: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Human hepatitis B immunoglobulin - ZUTECTRA (CAP); NAP - PSUSA/00001631/202011

Applicants: Biotest Pharma GmbH (Zutectra), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Lenalidomide - LENALIDOMIDE ACCORD (CAP); LENALIDOMIDE MYLAN (CAP); REVLIMID (CAP); NAP - PSUSA/00001838/202012

Applicants: Accord Healthcare S.L.U. (Lenalidomide Accord), Bristol-Myers Squibb Pharma EEIG (Revlimid), Mylan Ireland Limited (Lenalidomide Mylan), various

PRAC Rapporteur: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Lutetium (^{177}Lu) chloride - ENDOLUCINBETA (CAP); LUMARK (CAP); NAP - PSUSA/00010391/202012

Applicants: I.D.B. Holland B.V. (Lumark), ITM Medical Isotopes GmbH (EndolucinBeta), various

PRAC Rapporteur: Ronan Grimes

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. Benazepril (NAP) - PSUSA/00000313/202011

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Ciprofloxacin hydrochloride, hydrocortisone (NAP) - PSUSA/00000774/202011

Applicant(s): various

PRAC Lead: Ilaria Baldelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Diphtheria, tetanus, pertussis (acellular, component), poliomyelitis (inactivated), haemophilus type b conjugate vaccine (adsorbed) (NAP) - PSUSA/00001124/202011

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Ethanol extracts: Iberis amara L., planta tota recens; Angelica archangelica L., radix; Matricaria recutita L., flos; Carum carvi L., fructus; Silybum marianum (L.) Gaertn., fructus; Melissa officinalis L., folium; Mentha piperita L., folium; Chelidonium majus L., herba; Glycyrrhiza glabra L., radix (NAP) - PSUSA/00010800/202011

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Glatiramer (NAP) - PSUSA/00001529/202011

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Hydroxycarbamide[13] (NAP) - PSUSA/00009182/202012

Applicant(s): various

PRAC Lead: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Indapamide (NAP) - PSUSA/00001731/202011

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Methylprednisolone (NAP) - PSUSA/00002026/202011

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.9. Phenylephrine, tropicamide (NAP) - PSUSA/00010430/202011

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

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

6.3.10. Sultamicillin (NAP) - PSUSA/00002829/202011

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Tafluprost, timolol (NAP) - PSUSA/00010324/202012

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Vecuronium bromide (NAP) - PSUSA/00003102/202011

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Yellow fever vaccine (live) (NAP) - PSUSA/00003135/202012

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Dexmedetomidine - DEXDOR (CAP) - EMEA/H/C/002268/LEG 016.3

Applicant: Orion Corporation

PRAC Rapporteur: Ulla Wändel Liminga

Scope: MAH's response to LEG 016.2 [analysis of available mortality data from controlled clinical trials in the dexmedetomidine development programme as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00000998/201903) adopted in November 2019] as per the request for supplementary information (RSI) adopted in May 2021

Action: For adoption of advice to CHMP

6.4.2. Fentanyl - EFFENTORA (CAP) - EMEA/H/C/000833/LEG 019

Applicant: Teva B.V.

PRAC Rapporteur: Martin Huber

Scope: Review of the current labelling for fentanyl transmucosal route of administration regarding off-label use, misuse and accidental exposure as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/202004) adopted in January 2021

Action: For adoption of advice to CHMP

6.4.3. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 030

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Review of the current labelling for fentanyl transmucosal route of administration regarding off-label use, misuse and accidental exposure as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/202004) adopted in January 2021

Action: For adoption of advice to CHMP

6.4.4. Fentanyl - PECFENT (CAP) - EMEA/H/C/001164/LEG 021

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Martin Huber

Scope: Review of the current labelling for fentanyl transmucosal route of administration regarding off-label use, misuse and accidental exposure as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/202004) adopted in January 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Coronavirus (COVID-19) mRNA[14] vaccine (nucleoside-modified) - SPIKEVAX (previously COVID-19 VACCINE MODERNA) (CAP) - EMEA/H/C/005791/II/0015/G

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Grouped variations to address PRAC requests raised as per the conclusions of the second and third monthly safety summary report (MSSR) procedures (MEA/011.1 and MEA/011.2) respectively: 1) update of sections 4.4 of the SmPC to provide additional safety information regarding hypersensitivity and anaphylaxis, as requested by the PRAC in the second MSSR. The package leaflet is updated accordingly; 2) update of section 4.8 of the

[14] Messenger ribonucleic acid

SmPC to include 'delayed injection site reaction' as an adverse reaction with a frequency 'common', as requested by the PRAC in the third MSSR. The package leaflet is updated accordingly. In addition, the MAH submitted a justification for not adding diarrhoea to the product information as an adverse reaction as requested by the PRAC in the third MSSR and took the opportunity to introduce minor editorial changes in the product information

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. Fampridine - FAMPYRA (CAP) - EMEA/H/C/002097/II/0049

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of section 4.8 of SmPC to include new symptoms of trigeminal neuralgia as per the outcome of the last PSUR single assessment (PSUSA) procedure (PSUSA/00001352/202001) finalised in September 2020. The package leaflet is updated accordingly. The MAH introduced further editorial updates including an update of the product information in line with the latest quality review of documents (QRD) template (version 10.2) and an update of the contact details of the local representatives

Action: For adoption of PRAC Assessment Report

6.5.4. 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[15]

6.6.1. Coronavirus (COVID-19) mRNA[16] vaccine (nucleoside-modified) - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 002.5

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Sixth expedited monthly summary safety report 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[17] vaccine (nucleoside-modified) - SPIKEVAX (previously COVID-19 VACCINE MODERNA) (CAP) - EMEA/H/C/005791/MEA 011.4

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Fifth expedited monthly summary safety report for Spikevax (previously COVID-19 Vaccine Moderna) (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 014.2

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Third expedited monthly summary safety report 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 (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 027.3

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Fourth expedited monthly summary safety report for Vaxzevria (COVID-19 vaccine (ChAdOx1-S [recombinant])) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

[15] 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
[16] Messenger ribonucleic acid
[17] Messenger ribonucleic acid

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)[18]

7.1.1. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSP/S/0087.2

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to PSP/S/0087.1 [protocol for a non-interventional PASS to investigate the risk of mortality in patients prescribed Lemtrada (alemtuzumab) relative to comparable patients using other disease modifying therapies: a cohort study] as per the request for supplementary information (RSI) adopted in February 2021

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

7.1.2. Alemtuzumab – LEMTRADA (CAP) - EMEA/H/C/PSP/S/0088.2

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to PSP/S/0088.1 [protocol for a non-interventional PASS to investigate drug utilisation and safety monitoring patterns for Lemtrada (alemtuzumab)] as per the request for supplementary information (RSI) adopted in February 2021

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

7.1.3. Cabotegravir – VOCABRIA (CAP); rilpivirine – REKAMBYS (CAP) - EMEA/H/C/PSP/J/0092.1

Applicant(s): Janssen-Cilag International N.V. (Rekambys), ViiV Healthcare B.V. (Vocabria)

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSP/J/0092 [protocol for a joint drug utilisation study (DUS) to assess adherence, effectiveness and resistance: a prospective observational cohort study in people living with human immunodeficiency virus (HIV) (PLWH) initiating antiretroviral (ARV) regimen of cabotegravir (CAB) + rilpivirine (RPV) long-acting (LA) in collaboration with EuroSIDA[19]] as per the request for supplementary information (RSI) adopted in April 2021

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

7.1.4. Chlormadinone acetate, ethinylestradiol (NAP) – EMEA/H/N/PSA/J/0072

Applicant: Gedeon Richter PLC

PRAC Rapporteur: Martin Huber

[18] In accordance with Article 107n of Directive 2001/83/EC
[19] Prospective observational pan-European cohort study

Scope: Substantial amendment to a protocol previously agreed in October 2018 for a case control study comparing levonorgestrel and chlormadinone acetate to compare the risk of venous thromboembolism (VTE) of combined hormonal contraceptives (COCs) containing chlormadinone (CMA) 2mg / ethinylestradiol (EE) 30 µg, compared to COCs containing levonorgestrel (LNG) 0.15mg, both combined with 30 µg ethinylestradiol (EE)

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

7.1.5. Lenalidomide – REVLIMID (CAP) - EMEA/H/C/PSA/S/0067.1

Applicant: Bristol-Myers Squibb Pharma

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to PSA/S/0067 [substantial amendment to a protocol previously agreed in September 2016 (PSP/0020.3) for study CC-5013-MM-034: a prospective non-interventional PASS of lenalidomide in previously untreated adult multiple myeloma patients who are not eligible for transplant (Revlimid TNE NDMM PASS)] as per the request for supplementary information (RSI) adopted in March 2021

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

7.1.6. Prasterone – INTRAROSA (CAP) - EMEA/H/C/PSA/S/0070

Applicant: Endoceutics S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Substantial amendment to a protocol previously agreed for a non-interventional PASS: a drug utilisation study (DUS) to describe the baseline characteristics, utilisation patterns of EU postmenopausal women initiating treatment with Intrarosa (prasterone) and to assess whether EU prescribers abide by the contraindications stated in the EU SmPC

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

7.1.7. Valproate (NAP) - EMEA/H/N/PSA/J/0071

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

PRAC Rapporteur: Jean-Michel Dogné

Scope: Substantial amendment to a protocol previously agreed for an observational study to evaluate and identify the best practices for switching of valproate in clinical practice

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)[20]

7.2.1. Autologous peripheral blood T cells CD[21]4 and CD8 selected and CD3 and CD28 activated transduced with retroviral vector expressing anti-CD19 CD28/CD3-zeta

[20] 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

[21] Cluster of differentiation

chimeric antigen receptor and cultured - TECARTUS (CAP) - EMEA/H/C/005102/MEA 005

Applicant: Kite Pharma EU B.V., ATMP[22]

PRAC Rapporteur: Menno van der Elst

Scope: Protocol for study KT-EU-472-5966: a prescriber survey to assess prescribers' understanding of the risks of Tecartus (KTE-X19) to evaluate the effectiveness of risk minimisation activities, namely healthcare professional (HCP) educational materials and patient alert card (PAC) [final study report expected in September 2023] (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CAT and CHMP

7.2.2. Beclometasone, formoterol, glycopyrronium bromide - TRIMBOW (CAP) - EMEA/H/C/004257/MEA 002

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

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

Action: For adoption of advice to CHMP

7.2.3. Canagliflozin - INVOKANA (CAP) - EMEA/H/C/002649/MEA 009.3

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 009.2 consisting in an amended protocol for a drug utilisation study (DUS) to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in type 1 diabetes mellitus (T1DM) and the risk of diabetic ketoacidosis (DKA) using EU databases on market uptake and exposure within the European Union as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.4. Canagliflozin, metformin - VOKANAMET (CAP) - EMEA/H/C/002656/MEA 008.3

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 008.2 consisting in an amended protocol for a drug utilisation study (DUS) to evaluate the drug utilisation patterns of canagliflozin-containing medicines including off-label usage in type 1 diabetes mellitus (T1DM) and the risk of

[22] Advanced therapy medicinal product

diabetic ketoacidosis (DKA) using EU databases on market uptake and exposure within the European Union as per the request for supplementary information (RSI) adopted in October 2020

Action: For adoption of advice to CHMP

7.2.5. Cannabidiol - EPIDYOLEX (CAP) - EMEA/H/C/004675/MEA 007.2

Applicant: GW Pharma (International) B.V.

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: MAH's response to MEA 007.1 [protocol for study GWEP19022 (listed as a category 3 study in the RMP): a prospective, observational cohort long-term safety study to assess the potential for chronic liver injury in patients treated with Epidyolex (cannabidiol oral solution) when used under conditions of routine clinical care] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

7.2.6. Coronavirus (COVID-19) mRNA[23] vaccine (nucleoside-modified) - SPIKEVAX (previously COVID-19 VACCINE MODERNA) (CAP) - EMEA/H/C/005791/MEA 004.2

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Protocol for a study (listed as a category 3 study in the RMP): a post-authorisation active surveillance safety study using secondary data to monitor real-world safety of the COVID-19 mRNA-1273 vaccine in Europe [final clinical study report (CSR) expected in December 2023]

Action: For adoption of advice to CHMP

7.2.7. Coronavirus (COVID-19) mRNA[24] vaccine (nucleoside-modified) - SPIKEVAX (previously COVID-19 VACCINE MODERNA) (CAP) - EMEA/H/C/005791/MEA 034

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Hans Christian Siersted

Scope: Protocol for a study monitoring the safety of Spikevax (previously COVID-19 Vaccine Moderna) in pregnancy: an observational study using routinely collected health data in five European countries

Action: For adoption of advice to CHMP

7.2.8. Coronavirus (COVID-19) vaccine (Ad26.COV2-S, recombinant) - COVID-19 VACCINE JANSSEN (CAP) - EMEA/H/C/005737/MEA 008

Applicant: Janssen-Cilag International N.V.

[23] Messenger ribonucleic acid
[24] Messenger ribonucleic acid

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study VAC31518COV4003 (listed as a category 3 study in the RMP): a post-authorisation, observational study to assess the safety of Ad26.COV2.S using electronic health record (EHR) database(s) in Europe (from initial opinion/marketing authorisation(s) (MA))

Action: For adoption of advice to CHMP

7.2.9. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 007.1

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 007 [protocol for study D8111R00006: a post-authorisation/post-marketing observational study using existing secondary health data sources to evaluate the association between exposure to COVID-19 vaccine (ChAdOx1-S [recombinant] (AZD1222 / Vaxzevria) and safety concerns (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in May 2021

Action: For adoption of advice to CHMP

7.2.10. Dabigatran etexilate - PRADAXA (CAP) - EMEA/H/C/000829/MEA 050

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Anette Kirstine Stark

Scope: Protocol for a human factors study to assess effectiveness of a training video to mitigate potential medication errors during the reconstitution and dosing of the dabigatran etexilate paediatric oral solution [final clinical study report (CSR) expected in January 2022] (from X/0122/G)

Action: For adoption of advice to CHMP

7.2.11. Dimethyl fumarate - TECFIDERA (CAP) - EMEA/H/C/002601/MEA 008.6

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 008.5 [amendment to a protocol previously agreed in September 2020 for study 109MS402: Biogen multiple sclerosis (MS) pregnancy exposure registry to prospectively evaluate pregnancy outcomes in women with MS who were exposed to a registry-specified Biogen MS product during the eligibility window for that product] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.2.12. Dulaglutide - TRULICITY (CAP) - EMEA/H/C/002825/MEA 006.3

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: MAH's response to MEA 006.2 [protocol for study H9X-MC-B013 (listed as a category 3 study in the RMP): a non-interventional retrospective study to estimate the incidence rates of events of interest among type 2 diabetes mellitus (T2DM) patients treated with dulaglutide compared to other glucagon-like peptide 1 (GLP-1) receptor agonists in order to better characterise the safety profile of dulaglutide in terms of acute pancreatitis, pancreatic and thyroid malignancies] as per the request for supplementary information (RSI) adopted in February 2020

Action: For adoption of advice to CHMP

7.2.13. Esketamine - SPRAVATO (CAP) - EMEA/H/C/004535/MEA 002.2

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Kirsti Villikka

Scope: MAH's response to MEA 002.1 [protocol for a pregnancy registry study (listed as a category 3 study in the RMP) using the National Pregnancy Registry for Psychiatric Medications (NPRPM) in order to further characterise the impact of the missing information of use during pregnancy on the safety profile of esketamine nasal spray and obtain information on the frequency of major malformations (from initial opinion/marketing authorisation) [final report expected in Q4 2024]] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.2.14. Fremanezumab - AJOVY (CAP) - EMEA/H/C/004833/MEA 005.2

Applicant: Teva GmbH

PRAC Rapporteur: Kirsti Villikka

Scope: Substantial amendment to a protocol previously agreed in March 2020 for study TV48125-MH-50039: a long-term, prospective, phase 4, observational study to evaluate the safety, including cardiovascular safety, of fremanezumab in patients with migraine in routine clinical practice

Action: For adoption of advice to CHMP

7.2.15. Naloxegol - MOVENTIG (CAP) - EMEA/H/C/002810/MEA 006.10

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 006.9 [substantial amendment to a protocol previously agreed in December 2018 for study D3820R00009 (previously study D2288R00084): an observational PASS of Moventig (naloxegol) among patients aged 18 years and older treated with opioids chronically] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.2.16. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/MEA 014.3

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to MEA 014.2 [protocol for study A3921321: a drug utilisation study (DUS) on the utilisation and prescribing patterns of Xeljanz (tofacitinib) in two European countries using administrative claims databases and national registries for assessment, as requested in the conclusions of the referral procedure under Article 20 of Regulation (EC) No 726/2004 (EMEA/H/A-20/1485) finalised in November 2019] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

7.2.17. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 047.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 047.1 [protocol for study SWIBREG-UST UC: an observational PASS to describe the safety of ustekinumab and other ulcerative colitis treatments in a cohort of patients with ulcerative colitis using the Swedish Inflammatory Bowel Disease Register (SWIBREG) as requested in the conclusions of variation II/071 finalised in July 2019 [final clinical study report (CSR) expected in May 2027]] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

7.2.18. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 048.2

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 048.1 [protocol for study SNDS-UST UC: an observational PASS to describe the safety of ustekinumab and other ulcerative colitis treatments in a cohort of patients with ulcerative colitis using the French administrative healthcare database (SNDS) as requested in the conclusions of variation II/071 finalised in July 2019 [final clinical study report (CSR) expected in May 2027]] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)[25]

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

Applicant: Theramex Ireland Limited

PRAC Rapporteur: Adrien Inoubli

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

Scope: 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

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

7.4. Results of PASS non-imposed in the marketing authorisation(s)[26]

7.4.1. Alglucosidase alfa - MYOZYME (CAP) - EMEA/H/C/000636/II/0079

Applicant: Genzyme Europe BV

PRAC Rapporteur: Adrien Inoubli

Scope: Submission of the final report from study ALGMYC07390: a prevalence study of immunology testing in patients treated with alglucosidase alfa with significant hypersensitivity/anaphylactic reactions to test the effectiveness of the approved safety information packet (SIP)

Action: For adoption of PRAC Assessment Report

7.4.2. Aripiprazole - ABILIFY MAINTENA (CAP) - EMEA/H/C/002755/II/0040

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Submission of the final report from study 15893N (listed as a category 3 study in the RMP): a non-interventional PASS related to extrapyramidal symptoms - a cohort study with a 2-year follow-up using European longitudinal electronic medical records or claims databases

Action: For adoption of PRAC Assessment Report

7.4.3. Bazedoxifene - CONBRIZA (CAP) - EMEA/H/C/000913/II/0052

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final clinical study report (CSR) for study B1781044 (listed as a category 3 study in the RMP): a non-interventional cohort study to characterise the risk of venous thromboembolic events (VTE) and selected clinical endpoints of interest among a patient population prescribed bazedoxifine, raloxifene, or a bisphosphonate in Europe in usual clinical care setting

Action: For adoption of PRAC Assessment Report

[26] 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

7.4.4. Daunorubicin, cytarabine - VYXEOS LIPOSOMAL (CAP) - EMEA/H/C/004282/II/0017, Orphan

Applicant: Jazz Pharmaceuticals Ireland Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Submission of the final clinical study report (CSR) for a post-marketing observational study to assess the nature, incidence and severity of infusion-related reactions in adult patients treated with Vyxeos liposomal (daunorubicin/cytarabine)

Action: For adoption of PRAC Assessment Report

7.4.5. Estrogens conjugated, bazedoxifene - DUAVIVE (CAP) - EMEA/H/C/002314/II/0030

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study B2311060 (listed as a category 3 study in the RMP): a non-interventional, post-authorisation safety study of conjugated estrogens/bazedoxifene (CE/BZA) in the US, with the aim to monitor the safety profile of Duavive (CE/BZA) in comparison to oestrogen and progestin combination hormone therapy (E+P HT)

Action: For adoption of PRAC Assessment Report

7.4.6. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/II/0070/G

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped variations consisting of: 1) submission of non-interventional final study report D2403: a long-term, prospective, multinational, parallel-cohort study monitoring safety in patients with multiple sclerosis (MS) newly started on fingolimod once daily or treated with another approved disease-modifying therapy; 2) submission of non-interventional final study report D2406/D2409: a long-term, prospective, non-interventional, multinational, parallel-cohort study monitoring safety in patients with MS newly initiated on fingolimod once daily or treated with another approved disease-modifying therapy (including cardiac sub-study D2409)). As a consequence, Annex II-D on 'Conditions or restrictions with regard to the safe and effective use of the medicinal product' is updated to remove the obligation to perform study PASS D2409. The RMP (version 19.0) is updated accordingly. In addition, the MAH took the opportunity to implement some minor editorial changes

Action: For adoption of PRAC Assessment Report

7.4.7. Glycerol phenylbutyrate - RAVICTI (CAP) - EMEA/H/C/003822/II/0038/G, Orphan

Applicant: Immedica Pharma AB

PRAC Rapporteur: Ilaria Baldelli

Scope: Grouped variations consisting of: 1) submission of the final report for study HPN-

100-014: a non-interventional registry study - a long-term registry of patients with urea cycle disorders (UCDs) conducted in the US; 2) submission of an updated RMP (version 7) to remove the important potential risks of carcinogenicity and peracetic acid (PAA) toxicity. The update to the RMP is based on the review of new and available data including the study report for HPN-100-014 and a new toxicological expert examination of pre-clinical carcinogenicity findings as well as a cumulative review of literature and post marketing data. In accordance with the proposed changes to the RMP, an update of Annex II is requested to waive the imposed condition related to the non-interventional PASS on 'European post-authorization registry for Ravicti (glycerol phenylbutyrate) oral liquid in partnership with the European registry and network for intoxication type metabolic diseases (E-IMD)'. The SmPC and package leaflet have been updated to delete the information on additional monitoring (including the black triangle)

Action: For adoption of PRAC Assessment Report

7.4.8. Isavuconazole - CRESEMBA (CAP) - EMEA/H/C/002734/II/0035/G, Orphan

Applicant: Basilea Pharmaceutica Deutschland GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Grouped variations consisting of: 1) submission of the final report from study WSA-REG-001 (listed as a category 3 study in the RMP): a retrospective case-collection study, in which cases of invasive mucormycosis treated with isavuconazole were compared to cases treated with other systemic antifungals. The RMP (version 8.2) is updated accordingly; 2) remove study AK1820-301 (listed as a category 3 study in the RMP): a phase 3 multicentre, open-label study to evaluate safety and efficacy of 200 mg intravenous or oral isavuconazole for the treatment of adult Japanese patients with deep mycosis, with the primary endpoint of safety (proportion of patients with adverse events), and secondary endpoints of efficacy outcomes

Action: For adoption of PRAC Assessment Report

7.4.9. Talimogene laherparepvec - IMLYGIC (CAP) - EMEA/H/C/002771/II/0044

Applicant: Amgen Europe B.V., ATMP[27]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study 20180099 (listed as a category 3 study in the RMP): a cross-sectional survey to evaluate physician knowledge of safety messages included in the physician education booklet (PEB) for Imlygic (talimogene laherparepvec)

Action: For adoption of PRAC Assessment Report

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

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of final physician data study results for study EUPASS 14255: an

[27] Advanced therapy medicinal product

evaluation of the effectiveness of risk minimisation measures - a survey among healthcare professionals (HCPs) and patient/caregivers to assess their knowledge and attitudes on prescribing and home administration conditions of velaglucerase alfa (Vpriv) in 6 European countries

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. Ataluren - TRANSLARNA (CAP) - EMEA/H/C/002720/MEA 002.7

Applicant: PTC Therapeutics International Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Five-year interim report for study PTC124-GD-0250-DMD (listed as a category 3 study in the RMP): a post-approval registry observational study exploring the long-term of ataluren safety and effectiveness in usual care setting [final clinical study report (CSR) expected in April 2023] together with MAH's response to MEA 002.6 [four-year interim report for study PTC124-GD-0250-DMD] as per the request for supplementary information (RSI) adopted in January 2020

Action: For adoption of advice to CHMP

7.5.2. Baricitinib - OLUMIANT (CAP) - EMEA/H/C/004085/MEA 009.2

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: First interim report for study I4V-MC-B0166: a PASS to assess off-label use in paediatric patients in the UK using the Clinical Practice Research Datalink (CPRD) database

Action: For adoption of advice to CHMP

7.5.3. Belimumab - BENLYSTA (CAP) - EMEA/H/C/002015/MEA 003.15

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Eighth annual interim report for study BEL116543/HGS1006-C1124 (SABLE): a long-term controlled safety registry evaluating the incidence of all-cause mortality and adverse events of special interest (AESIs) in patients with systemic lupus erythematosus followed for a minimum of 5 years

Action: For adoption of advice to CHMP

7.5.4. Cabozantinib - CABOMETYX (CAP) - EMEA/H/C/004163/MEA 001.5

Applicant: Ipsen Pharma

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 001.4 [interim report for study F-FR-60000-001 (CASSIOPE): a prospective non-interventional study of the utilisation of cabozantinib tablets in adults with advanced renal cell carcinoma (RCC) following prior vascular endothelial growth factor (VEGF)-targeted therapy in real life settings in terms of dose modifications due to adverse events (AEs) when used as a second line therapy or third and later line therapy] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

7.5.5. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/MEA 002.3

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Ilaria Baldelli

Scope: First interim report for study DFIDM-1801 (ARCANGELO (itAlian pRospective study on CANGrELOr)): a multicentre prospective observational study of acute coronary syndrome patients undergoing percutaneous coronary intervention (PCI) who receive cangrelor and transition to either clopidogrel, prasugrel or ticagrelor

Action: For adoption of advice to CHMP

7.5.6. Defibrotide - DEFITELIO (CAP) - EMEA/H/C/002393/LEG 011.1

Applicant: Gentium S.r.l.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Second interim report for a national, post-registration observational study of the long-term safety and health outcome of patients treated with Defitelio (defibrotide), including patients with severe hepatic veno-occlusive disease (VOD) after hematopoietic stem-cell transplantation (HSCT) (DEFIFRANCE registry)

Action: For adoption of advice to CHMP

7.5.7. Flutemetamol (^{18}F) - VIZAMYL (CAP) - EMEA/H/C/002557/MEA 002.5

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: Second recruitment report for study GE067-027 CPR: a post-authorisation study to assess the frequency of Vizamyl (flutemetamol (^{18}F)) image classification errors in clinical practice in Europe and to evaluate the effectiveness of Vizamyl (flutemetamol (^{18}F)) educational training programme/reader training in Europe [final study report expected in Q1 2021]

Action: For adoption of advice to CHMP

7.5.8. Rivastigmine - EXELON (CAP) - EMEA/H/C/000169/MEA 036.7

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual report (covering the period from 01 February 2020 to 31 January 2021) for a drug utilisation study (DUS) on the effectiveness of risk minimisation measures (RMM) for multiple patch use

Action: For adoption of advice to CHMP

7.5.9. Rivastigmine - PROMETAX (CAP) - EMEA/H/C/000255/MEA 037.7

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: Annual report (covering the period from 01 February 2020 to 31 January 2021) for a drug utilisation study (DUS) on the effectiveness of risk minimisation measures (RMM) for multiple patch use

Action: For adoption of advice to CHMP

7.5.10. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 001.2

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: First interim report for study OP0005: a European non-interventional PASS to study the adherence to the risk minimisation measures (RMMs) in the product information by estimating the compliance with contraindications and target indication(s) amongst incident romosozumab users, and analysing the utilisation pattern using the EU-adverse drug reactions (EU-ADR) Alliance [final study results expected in March 2026]

Action: For adoption of advice to CHMP

7.5.11. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 002.2

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Comparative interim report for study OP0004: a European non-interventional PASS to evaluate potential differences in terms of serious cardiovascular adverse events between romosozumab and currently available therapies used in comparable patients in real-world conditions using the EU-adverse drug reactions (EU-ADR) Alliance [final study results expected in December 2026]

Action: For adoption of advice to CHMP

7.5.12. Teduglutide - REVESTIVE (CAP) - EMEA/H/C/002345/ANX 003.8

Applicant: Shire Pharmaceuticals Ireland Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 003.6 [third biennial interim results for study TED-R-13-002: an international short bowel syndrome registry - a prospective, long-term observational cohort study of patients with short bowel syndrome] as per the request for

supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.5.13. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/ANX 003.6

Applicant: Novartis Europharm Limited, ATMP[28]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to ANX 003.4 [annual safety reports and first five-yearly interim report for a study based on disease registry CCTL019B2401 (listed as a category 1 study in Annex II and the RMP): a non-interventional PASS in acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL) patients in order to further characterise the safety, including long-term safety, of Kymriah (tisagenlecleucel) [final study report expected in December 2038] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CAT and CHMP

7.5.14. Tisagenlecleucel - KYMRIAH (CAP) - EMEA/H/C/004090/MEA 005.1

Applicant: Novartis Europharm Limited, ATMP[29]

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 005 [first five-yearly interim report for study CCTL019A2205B (listed as a category 3 study in the RMP): a long-term follow-up of patients exposed to lentiviral-based CD19 directed chimeric antigen receptor T (CAR-T)-cell therapy in order to describe selected, delayed adverse events (AEs) suspected to be related to previous CD19 CAR-T-cell therapy as outlined in current Health Authority guidelines [final study report expected in December 2037] (from opinion/marketing authorisation (MA))] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CAT and CHMP

7.5.15. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 024.16

Applicant: Janssen-Cilag International NV

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 024.15 [tenth annual interim report for study CNTO1275PSO4007 (Nordic pregnancy research initiative) (C0743T): exposure to ustekinumab during pregnancy in patients with psoriasis: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers] as per the request for supplementary information (RSI) adopted in February 2021

Action: For adoption of advice to CHMP

[28] Advanced therapy medicinal product
[29] Advanced therapy medicinal product

7.6. Others

7.6.1. Avatrombopag - DOPTELET (CAP) - EMEA/H/C/004722/MEA 003

Applicant: Swedish Orphan Biovitrum AB (publ)

PRAC Rapporteur: Eva Segovia

Scope: Feasibility assessment for a study to further characterise the long-term safety profile of avatrombopag in patients with primary chronic immune thrombocytopenia in European patient registers and electronic health care databases as requested in the conclusions of variation II/0004/G finalised in December 2020

Action: For adoption of advice to CHMP

7.6.2. Fingolimod - GILENYA (CAP) - EMEA/H/C/002202/MEA 038.3

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Tiphaine Vaillant

Scope: MAH's response to MEA 038.2 [First interim report for open-label extension phase of study CFTY720D2311: a phase 3, two-year, double-blind, double dummy, randomised, multicentre, active controlled study evaluating efficacy and safety of fingolimod once daily versus interferon β-1a once weekly in paediatric patients with multiple sclerosis (MS) aged 10 to <18 years old] as per the request for supplementary information (RSI) adopted in March 2021

Action: For adoption of advice to CHMP

7.6.3. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/MEA 049

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: From X/074/G: Feasibility report on conducting a study in children from birth to less than 2 years diagnosed with VTE and treated with rivaroxaban in comparison to children with VTE treated with other anticoagulants. [Due date: 31/03/2021]

Action: For adoption of advice to CHMP

7.7. New Scientific Advice

None

7.8. Ongoing Scientific Advice

None

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

None

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

8.1. Annual reassessments of the marketing authorisation

8.1.1. Amifampridine - FIRDAPSE (CAP) - EMEA/H/C/001032/S/0071 (without RMP)

Applicant: SERB SA

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Leadiant GmbH

PRAC Rapporteur: Adam Przybylkowski

Scope: Annual reassessment of the marketing authorisation

Action: For adoption of advice to CHMP

8.1.3. Idursulfase - ELAPRASE (CAP) - EMEA/H/C/000700/S/0092 (without RMP)

Applicant: Shire Human Genetic Therapies AB

PRAC Rapporteur: Liana Gross-Martirosyan

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. Brentuximab vedotin - ADCETRIS (CAP) - EMEA/H/C/002455/R/0090 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Crizanlizumab - ADAKVEO (CAP) - EMEA/H/C/004874/R/0003 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Laurence de Fays

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.3. Ixazomib - NINLARO (CAP) - EMEA/H/C/003844/R/0030 (without RMP)

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Annika Folin

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Bezlotoxumab - ZINPLAVA (CAP) - EMEA/H/C/004136/R/0029 (without RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Darunavir - DARUNAVIR MYLAN (CAP) - EMEA/H/C/004068/R/0014 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Emtricitabine, tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL KRKA (CAP) - EMEA/H/C/004215/R/0018 (without RMP)

Applicant: Krka, d.d., Novo mesto

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Emtricitabine, tenofovir disoproxil - EMTRICITABINE/TENOFOVIR DISOPROXIL MYLAN (CAP) - EMEA/H/C/004050/R/0016 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.5. Etelcalcetide - PARSABIV (CAP) - EMEA/H/C/003995/R/0017 (without RMP)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ilaria Baldelli

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.6. Insulin glargine, lixisenatide - SULIQUA (CAP) - EMEA/H/C/004243/R/0022 (with RMP)

Applicant: Sanofi-aventis groupe

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Ivabradine - IVABRADINE ZENTIVA (CAP) - EMEA/H/C/004117/R/0008 (with RMP)

Applicant: Zentiva k.s.

PRAC Rapporteur: Menno van der Elst

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Mercaptamine - CYSTADROPS (CAP) - EMEA/H/C/003769/R/0022 (without RMP)

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Simoctocog alfa - VIHUMA (CAP) - EMEA/H/C/004459/R/0026 (without RMP)

Applicant: Octapharma AB

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.10. Tadalafil - TALMANCO (CAP) - EMEA/H/C/004297/R/0011 (without RMP)

Applicant: Mylan S.A.S

PRAC Rapporteur: Maria del Pilar Rayon

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.11. 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

8.3.12. Teriparatide - MOVYMIA (CAP) - EMEA/H/C/004368/R/0024 (with RMP)

Applicant: Stada Arzneimittel AG

PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.13. Teriparatide - TERROSA (CAP) - EMEA/H/C/003916/R/0020 (with RMP)

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Ronan Grimes

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

None

11.2. Other requests

11.2.1. Fentanyl (NAP) - FR/H/PSUFU/00001369/202004

Applicants: Angelini farmaceutica S.A., Aurobindo, Gedeon Richter PLC, Grünenthal, Kyowa Mylan, Sandoz, Stada, Teva B.V., Yes Pharmaceuticals

PRAC Lead: Tiphaine Vaillant

Scope: PRAC consultation on a PSUR follow-up (PSU FU) procedure evaluating off-label use, misuse and accidental exposure, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUR single assessment (PSUSA) procedure (PSUSA/00001369/202004) 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. Mandate of PRAC Chairperson - prolongation

Action: For discussion

12.1.2. PRAC working group - Best practice guide on using PRAC plenary time efficiently and effectively – update on the implementation of quantitative goals – Q2 2021

Action: For discussion

12.2. Coordination with EMA Scientific Committees or CMDh-v

None

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

12.3.1. Scientific Advice Working Party (SAWP)–PRAC interaction: process improvement - proposal

PRAC lead: Menno van der Elst, Adrien Inoubli, Martin Huber, Brigitte Keller-Stanislawski

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.5. Cooperation with International Regulators

12.5.1. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)-E19 on 'optimisation of safety data collection' – draft guideline - - A selective approach to safety data collection in specific late-stage pre-approval or post-approval studies

Action: For discussion

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 Q2 2021

Action: For discussion

12.8.2. PRAC workload statistics – Q2 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

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.15.3. Post-authorisation Safety Studies - non-imposed non-interventional PASS protocol & protocol amendment - assessment report (AR) template

Action: For discussion

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

12.18.3. COVID-19 safety updates – revised proposal

Action: For discussion

12.18.4. PRAC communication – call for expression of interest to review communication strategy and materials

PRAC lead: Sabine Straus

Action: For discussion

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

12.20.2. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact – study on codeine use and changes in alternative treatments for pain and cough in children after introduction of the risk minimisation measures following the completion of referral procedures for codeine-containing products

PRAC lead: David Olsen

Action: For discussion

12.20.3. Strategy on measuring the impact of pharmacovigilance - impact of regulatory actions – impact study

PRAC lead: Liana Gross-Martirosyan

Action: For adoption

12.20.4. Strategy on measuring the impact of pharmacovigilance – PRAC interest group (IG) Impact – impact study

Action: For discussion

12.21. Others

12.21.1. EMA-funded study after vaccination against SARS-CoV-2 – preliminary results

Action: For discussion

12.21.2. Questions and answers (Q&A) document on 'complex clinical trials' - draft

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/