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Human Medicines Division

Pharmacovigilance Risk Assessment Committee (PRAC)

Draft agenda for the meeting on 07-10 June 2022

Chair: Sabine Straus – Vice-Chair: Martin Huber

07 June 2022, 10:30 – 19:30, via teleconference

08 June 2022, 08:30 – 19:30, via teleconference

09 June 2022, 08:30 – 19:30, via teleconference

10 June 2022, 08:30 – 16:00, via teleconference

Organisational, regulatory and methodological matters (ORGAM)

21 June 2022, 09:00 - 11:00, via teleconference

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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 07-10 June 2022. See June 2022 PRAC minutes (to be published post July 2022 PRAC meeting).

1.2. Agenda of the meeting on 07-10 June 2022

Action: For adoption

1.3. Minutes of the previous meeting on 02-05 May 2022

Action: For adoption

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

2.1. Newly triggered procedures

None

2.2. Ongoing procedures

None

2.3. Procedures for finalisation

None

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

3.1. Newly triggered procedures

None

3.2. Ongoing procedures

3.2.1. Janus kinase (JAK) inhibitors¹: abrocitinib - CIBINQO (CAP); baricitinib - OLUMIANT (CAP); filgotinib - JYSELECA (CAP); tofacitinib - XELJANZ (CAP); upadacitinib - RINVOQ (CAP) – EMEA/H/A-20/1517

Applicant(s): AbbVie Deutschland GmbH & Co. KG (Rinvoq), Eli Lilly Nederland B.V. (Olumiant), Galapagos N.V. (Jyseleca), Pfizer Europe MA EEIG (Cibinqo, Xeljanz)

PRAC Rapporteur: Ulla Wändel Liminga; PRAC Co-rapporteur(s): Liana Gross-Martirosyan (Olumiant, Xeljanz), Nikica Mirošević Skvrce (Cibinqo, Jyseleca, Rinvoq)

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

Action: For adoption of PRAC list of outstanding issues (LoOI)

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

Applicant(s): various

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

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

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

3.3. Procedures for finalisation

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

Applicant(s): Artogodan 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 PRAC recommendation to CMDh

3.4. Re-examination procedures²

None

3.5. Others

None

¹ Indicated for the treatment of inflammatory disorders

² Re-examination of PRAC recommendation under Article 32 of Directive 2001/83/EC

4. Signals assessment and prioritisation³

4.1. New signals detected from EU spontaneous reporting systems

4.1.1. Adalimumab - AMGEVITA (CAP), AMSPARITY (CAP), HEFIYA (CAP), HUMIRA (CAP), HULIO (CAP), HUKYNDRA (CAP), HYRIMOZ (CAP), IDACIO (CAP), IMRALDI (CAP), LIBMYRIS (CAP), YUFLYMA (CAP)

Applicant(s): AbbVie Deutschland GmbH (Humria), Amgen Europe B.V.(Amgevita), Celltrion Healthcare Hungary Kft. (Yuflyma), Fresenius Kabi Deutschland GmbH (Idacio), Pfizer Europe MA EEIG (Amsparity), Sandoz GmbH (Hyrimoz, Hefiya), Samsung Bioepis NL B.V. (Imraldi), Stada Arzneimittel AG (Hukyndra, Libmyris), Viatriis Limited (Hulio)

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Signal of menstrual disorder

Action: For adoption of PRAC recommendation

EPITT 19812 – New signal

Lead Member State(s): SE

4.1.2. Codeine, ibuprofen (NAP)

Applicant(s): various

PRAC Rapporteur: To be appointed

Scope: Signal of renal tubular acidosis and hypokalaemia

Action: For adoption of PRAC recommendation

EPITT 19820 – New signal

Lead Member State(s): IE

4.1.3. Ipilimumab - YERVOY (CAP); nivolumab - OPDIVO (CAP)

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: To be appointed

Scope: Signal of pure red cell aplasia and aplastic anaemia

Action: For adoption of PRAC recommendation

EPITT 19804 – New signal

Lead Member State(s): DE, NL

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

4.1.4. Temozolomide – TEMODAL (CAP), TEMOMEDAC (CAP), TEMOZOLOMIDE ACCORD (CAP), TEMOZOLOMIDE HEXAL (CAP), TEMOZOLOMIDE SANDOZ (CAP), TEMOZOLOMIDE SUN (CAP), TEMOZOLOMIDE TEVA (CAP); NAP

Applicant(s): Accord Healthcare S.L.U. (Temozolomide Accord), Hexal AG (Temozolomide Hexal), medac Gesellschaft für klinische Spezialpräparate mbH (Temomedac), Merck Sharp & Dohme B.V. (Temodal), Sandoz GmbH (Temozolomide Sandoz), Sun Pharmaceutical Industries Europe B.V. (Temozolomide Sun), Teva B.V. (Temozolomide Teva)

PRAC Rapporteur: To be appointed

Scope: Signal of progressive multifocal leukoencephalopathy (PML)

Action: For adoption of PRAC recommendation

EPITT 19814 – New signal

Lead Member State(s): DE

4.1.5. Durvalumab - IMFINZI (CAP)

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Signal of myelitis transverse

Action: For adoption of PRAC recommendation

EPITT 19815 – New signal

Lead Member State(s): NO

4.2. New signals detected from other sources

4.2.1. Tildrakizumab – ILUMETRI (CAP)

Applicant: Almirall S.A

PRAC Rapporteur: Adam Przybylkowski

Scope: Signal of herpes zoster

Action: For adoption of PRAC recommendation

EPITT 19801 - New signal

Lead Member State(s): PL

4.3. Signals follow-up and prioritisation

4.3.1. Elasmomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/SDA/058

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of amenorrhea

Action: For adoption of PRAC recommendation

EPITT 19781 – Follow-up to February 2022

4.3.2. [Elasomeran - SPIKEVAX \(CAP\) - EMEA/H/C/005791/SDA/059](#)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of heavy menstrual bleeding

Action: For adoption of PRAC recommendation

EPITT 19780 – Follow-up to February 2022

4.3.3. [Gemtuzumab ozogamicin – MYLOTARG \(CAP\) - EMEA/H/C/004204/SDA/005](#)

Applicant(s): Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Signal of atypical haemolytic reactions

Action: For adoption of PRAC recommendation

EPITT 19788 – Follow-up to April 2022

4.3.4. [Human normal immunoglobulin⁴ – FLEBOGAMMA DIF \(CAP\) - EMEA/H/C/000781/SDA/025, KIOVIG \(CAP\) - EMEA/H/C/000628/SDA/042, PRIVIGEN \(CAP\) - EMEA/H/C/000831/SDA/033; NAP](#)

Applicant(s): Baxter AG (Kiovig), CSL Behring GmbH (Privigen), Instituto Grifols, S.A. (Flebogamma DIF), various

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Signal of thrombocytopenia

Action: For adoption of PRAC recommendation

EPITT 19764 – Follow-up to January 2022

4.3.5. [Tozinameran - COMIRNATY \(CAP\) - EMEA/H/C/005735/SDA/052](#)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: David Olsen

Scope: Signal of amenorrhea

Action: For adoption of PRAC recommendation

EPITT 19784 – Follow-up to February 2022

⁴ For intravenous use only

4.3.6. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/SDA/053

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: David Olsen

Scope: Signal of heavy menstrual bleeding

Action: For adoption of PRAC recommendation

EPITT 19783 – Follow-up to February 2022

4.4. Variation procedure(s) resulting from signal evaluation

4.4.1. Pregabalin - LYRICA (CAP) - EMEA/H/C/000546/WS2261/0118; pregabalin - PREGABALIN PFIZER (CAP) - EMEA/H/C/003880/WS2261/0047

Applicant: Upjohn EESV

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.4 and 4.8 of the SmPC with a warning regarding Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) as severe cutaneous adverse reactions as requested in the conclusions of the signal procedure (EPITT 19723) adopted in January 2022 (SDA 055). The package leaflet is updated accordingly

Action: For adoption of PRAC Assessment Report

4.4.2. Tofacitinib - XELJANZ (CAP) - EMEA/H/C/004214/II/0044

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.4, 4.8 and 5.1 to add warnings and safety data on serious infections, viral reactivation, non-melanoma skin cancer and fractures. This is based on the final results from study A3921133 (listed as a category 3 study in the RMP): a PASS conducted to evaluate the safety of tofacitinib 5 mg and 10 mg compared to tumour necrosis factor inhibitor (TNFi) in adult subjects aged ≥ 50 years with moderately or severely active rheumatoid arthritis (RA) and with at least 1 additional cardiovascular (CV) risk factor, as requested in the outcome of the signal procedure (EPITT 19382) adopted in June 2021 (SDA 016). The package leaflet is updated accordingly. The RMP (version 21.1) is also updated in accordance. In addition, the MAH took the opportunity to update the outer carton (section 4 for oral solution) to include a total volume of 240 mL as requested in the conclusions of procedure X/0024/G adopted in June 2021

Action: For adoption of PRAC Assessment Report

5. Risk management plans (RMPs)

5.1. Medicines in the pre-authorisation phase

5.1.1. Coronavirus (COVID-19) vaccine (inactivated, adjuvanted, adsorbed) - EMEA/H/C/006019

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

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

5.1.2. Coronavirus (COVID-19) vaccine (recombinant) - EMEA/H/C/005754

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

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

5.1.3. Iodine (¹³¹I) omburtamab - EMEA/H/C/005499, Orphan

Applicant: Y-Mabs Therapeutics A/S

Scope: Treatment of neuroblastoma

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

5.1.4. Maralixibat - EMEA/H/C/005857, Orphan

Applicant: Mirum Pharmaceuticals International B.V.

Scope: Treatment of cholestatic liver disease in patients with Alagille syndrome (ALGS) 1 year of age and older

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

5.1.5. Ranibizumab - EMEA/H/C/005617

Scope: Treatment of neovascular age-related macular degeneration (AMD)

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

5.1.6. Sutimlimab - EMEA/H/C/005776, Orphan

Applicant: Genzyme Europe BV

Scope: Treatment of haemolysis in adult patients with cold agglutinin disease (CAD)

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

5.1.7. Teriflunomide - EMEA/H/C/005962

Scope: Treatment of multiple sclerosis (MS)

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

5.1.8. Teriparatide - EMEA/H/C/005793

Scope: Treatment of osteoporosis

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

5.1.9. Tirzepatide - EMEA/H/C/005620

Scope: Treatment of adults with type 2 diabetes mellitus

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. Alogliptin - VIPIDIA (CAP) - EMEA/H/C/002182/WS2191/0029; alogliptin, metformin - VIPDOMET (CAP) - EMEA/H/C/002654/WS2191/0036; alogliptin, pioglitazone - INCRESYNC (CAP) - EMEA/H/C/002178/WS2191/0040

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Menno van der Elst

Scope: Submission of an updated RMP (version 11) in order to consolidate it within a single RMP for Vipidia (alogliptin), Vipdomet (alogliptin/metformin) and Incresync (alogliptin/pioglitazone) as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010061/202104) finalised in November 2021. The consolidated RMP is also updated in line with revision 2 of GVP module V on 'Risk management systems' and the targeted follow up questionnaires (FUQ) of severe hypersensitivity and skin reactions, pancreatitis, hepatic events and follow up gastrointestinal events and infections is removed. Finally, the removal of the inverted black triangle as agreed other procedures is reflected in the RMP

Action: For adoption of PRAC Assessment Report

5.2.2. Elasmomeran - SPIKEVAX (CAP) - EMEA/H/C/005791/II/0062

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Submission of an updated RMP (version 4.0) in order to remove 'anaphylaxis' as an important identified risk and 'interaction with other vaccines' as a safety concern in study mRNA-1273-P904 (study 1) (listed as a category 3 study in the RMP): a post-authorisation active surveillance safety study using secondary data to monitor real-world safety of Spikevax (COVID-19 mRNA-1273 vaccine) in Europe - an enhanced pharmacovigilance study to provide additional evaluation of adverse events of special interest (AESI) and emerging validated safety signals in European populations and electronic database

assessment of use in pregnant women, following the outcome of MEA 004.4 adopted in January 2022; to implement the WHO⁵-approved international non-proprietary name (INN) 'elasomeran'. In addition, the MAH updated the milestones for studies mRNA-1273-P301, mRNA-1273-P203, mRNA-1273-P201, mRNA-1273-P901, mRNA-1273-P903 and mRNA-1273-P910 and added study mRNA-1273-P911 to the RMP. Annex II of the product information is updated accordingly

Action: For adoption of PRAC Assessment Report

5.2.3. Tolvaptan - JINARC (CAP) - EMEA/H/C/002788/II/0036

Applicant: Otsuka Pharmaceutical Netherlands B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of an updated RMP (version 15.0) in order to reflect the outcome of a substantial amendment to a protocol previously agreed for study 156-12-299 (listed as a category 1 study): a 7.5-year, multicentre, non-interventional PASS to characterise and quantify the identified risk of idiosyncratic liver injury in Jinarc (tolvaptan) treated patients with autosomal dominant polycystic kidney disease (ADPKD) in routine clinical practice, as concluded in procedure PSA/S/0078.1 finalised in February 2021. Annex II is updated accordingly. In addition, the MAH took the opportunity to correct an oversight/editorial error in the package leaflet

Action: For adoption of PRAC Assessment Report

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

5.3.1. (1R,2S,5S)-N-((1S)-1-cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido) butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide, ritonavir - PAXLOVID (CAP) - EMEA/H/C/005973/II/0007

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study C4671010 (listed as a category 3 study in the RMP): a phase 1, non-randomized, open label study to assess the pharmacokinetics, safety and tolerability of PF-07321332 boosted with ritonavir (Paxlovid) in adults with moderate hepatic impairment and individuals with normal hepatic function. The RMP (version 2.0) has also been submitted

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

5.3.2. Agalsidase alfa - REPLAGAL (CAP) - EMEA/H/C/000369/II/0117

Applicant: Takeda Pharmaceuticals International AG Ireland Branch

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Update of sections 4.2 and 6.6 of the SmPC in order to add self-administration by a

⁵ World Health Organization

trained patient and/or a caregiver as a new method of administration. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information. The RMP (version 0.1) is updated accordingly

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

5.3.3. Albutrepenonacog alfa - IDELVION (CAP) - EMEA/H/C/003955/II/0059, Orphan

Applicant: CSL Behring GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.2, 4.8 and 5.1 of the SmPC in order to update information and amend the frequencies of adverse drug reactions (ADRs) based on the final results from study CSL654_3003 (listed as a category 3 study in the RMP): an open-label, multicentre, uncontrolled study to evaluate the safety, pharmacokinetics and clinical response of recombinant factor IX albumin fusion protein (rIX-FP) with regard to the prevention and treatment of bleeding in previously untreated patients (PUPs) with haemophilia B. The package leaflet is updated accordingly. The RMP (version 4.0) has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information and update the list of local representatives in the package leaflet

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

5.3.4. Besilesomab - SCINTIMUN (CAP) - EMEA/H/C/001045/II/0015

Applicant: CIS BIO International

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Submission of the final report from study AG-2012 (listed as a category 3 study in the RMP): a non-interventional controlled survey on the impact of Scintimun (besilesomab) administered for scintigraphic imaging on diagnostic thinking and management of patient with suspicion of peripheral osteomyelitis (in fulfilment of MEA 08.4). The RMP (version 15) is updated accordingly

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

5.3.5. Brexucabtagene autoleucel - TECARTUS (CAP) - EMEA/H/C/005102/II/0019, Orphan

Applicant: Kite Pharma EU B.V., ATMP⁶

PRAC Rapporteur: Menno van der Elst

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update the safety and efficacy information based on 24-month follow-up data from all treated patients in cohort 1 of pivotal study KTE-C19-102 (ZUMA-2): a phase 2, multicentre, open-label study evaluating the safety and efficacy of KTE-X19 (brexucabtagene autoleucel) in subjects with relapsed or refractory (r/r) mantle cell lymphoma (MCL). This submission is in fulfilment of specific obligation SOB 004 to confirm the long-term efficacy and safety of Tecartus (brexucabtagene autoleucel) in adult patients with r/r MCL. In addition, the MAH took the

⁶ Advanced therapy medicinal product

opportunity to make minor editorial changes in the SmPC. The RMP (version 2.1) has also been submitted

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

5.3.6. Buprenorphine - BUVIDAL (CAP) - EMEA/H/C/004651/II/0017

Applicant: Camurus AB

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension of indication to include treatment of moderate to severe chronic pain in patients with opioid dependence. As a consequence, sections 4.1, 4.2, 4.5, 5.1 and 6.6 of the SmPC are updated. 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

5.3.7. Burosumab - CRYSVITA (CAP) - EMEA/H/C/004275/II/0023, Orphan

Applicant: Kyowa Kirin Holdings B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include treatment of fibroblast growth factor 23 (FGF23)-related hypophosphataemia in tumour-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumours that cannot be curatively resected or localised in patients aged 1 year and over, based on data from two ongoing open-label clinical studies, namely: 1) study UX023T-CL201: a phase 2 open-label trial to assess the efficacy and safety of burosumab in subjects with TIO or epidermal nevus syndrome (ENS)-associated osteomalacia, 2) study KRN23-002: a phase 2 open-label trial to assess the efficacy and safety of burosumab in patients with TIO or ENS (144-week data and 88-week data respectively). 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 4.0) are updated accordingly. The MAH also applied for one additional year of market protection

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

5.3.8. Caplacizumab - CABLIVI (CAP) - EMEA/H/C/004426/II/0035, Orphan

Applicant: Ablynx NV

PRAC Rapporteur: Jan Neuhauser

Scope: Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on increased risk of bleeding and to add blood and lymphatic system disorders to the list of adverse drug reactions (ADRs) with a frequency not known based on a safety evaluation report. The package leaflet and the RMP (version 2.0) are updated accordingly

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

5.3.9. Carglumic acid - CARBAGLU (CAP) - EMEA/H/C/000461/II/0044

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Ana Sofia Diniz Martins

Scope: Update of sections 4.2 and 4.4 of the SmPC in order to include information on the impact of renal impairment on systemic exposures to Carbaglu (carglumic acid) based on final results from study A: a phase 1, multicentre, open-label, parallel-group adaptive pharmacokinetic single dose study of oral Carbaglu (carglumic acid) in subjects with normal and varying degrees of impaired renal function. The package leaflet is updated accordingly. The RMP (version 2.2) has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the product information

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

5.3.10. Cemiplimab - LIBTAYO (CAP) - EMEA/H/C/004844/II/0026

Applicant: Regeneron Ireland Designated Activity Company (DAC)

PRAC Rapporteur: Menno van der Elst

Scope: Extension of indication to include monotherapy treatment of adult patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 3.0) are updated in accordance

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

5.3.11. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/II/0075

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Update of section 5.1 of the SmPC in order to include updated efficacy information based on the 6 months follow-up 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 (ChAdOx1-S [recombinant])). The RMP (version 5.1) has also been submitted. The MAH removed the important identified risk of anaphylaxis from the list of safety concerns, updated the routine and additional pharmacovigilance activities section and took the opportunity to implement other administrative updates

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

5.3.12. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0072

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Extension of indication to include treatment of paediatric patients aged ≥ 6 to < 18 years with relapsed or refractory systemic anaplastic lymphoma kinase (ALK)-positive

anaplastic large cell lymphoma (ALCL) and with unresectable, recurrent, or refractory ALK-positive inflammatory myofibroblastic tumour (IMT) based on the results from: 1) study ADVL0912: a phase 1/2 study of crizotinib, an oral small molecule inhibitor of ALK and C-Met, in children with relapsed/refractory solid tumours and anaplastic large cell lymphoma; 2) study A8081013: a phase 1b open-label study of the safety and clinical activity of crizotinib in tumours with genetic events involving the ALK gene locus. 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 8.0) are updated in accordance. In addition, the MAH took the opportunity to update the anatomical therapeutic chemical (ATC) code for crizotinib. Moreover, the MAH took the opportunity to implement a minor change in the list of local representatives in the package leaflet

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

5.3.13. Dexamethasone - NEOFORDEX (CAP) - EMEA/H/C/004071/II/0017/G

Applicant: Laboratoires CTRS

PRAC Rapporteur: Tiphaine Vaillant

Scope: Grouped variations consisting of: 1) submission of an updated RMP (version 4.3) to remove the score line for sub-division of the 40 mg tablet (as a completion of a category 3 activity) and consequent deletion of the 20 mg posology, including a direct healthcare professional communication (DHPC); 2) other quality variations. In addition, the MAH used the opportunity to update sections from Module 3 of the dossier with editorial changes

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

5.3.14. Dalbavancin - XYDALBA (CAP) - EMEA/H/C/002840/II/0043

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Rugile Pilviniene

Scope: Extension of indication to the paediatric population (aged 3 months to < 18 years) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) based on the interim results from the study DUR001-306: a phase 3, multicentre, open-label, randomized, comparator controlled trial of the safety and efficacy of dalbavancin versus active comparator in paediatric subjects with ABSSSI, together with data from three phase 1 pharmacokinetic studies (A8841004, DUR001-106, and DAL-PK-02). Consequently, the sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2 and 6.6 of the SmPC were updated. The package leaflet is updated accordingly. In addition, the applicant took the opportunity to make minor editorial amendments and to bring the product information in line with the latest quality review of documents (QRD) (version 10.2). The RMP (version 7.0) has also been submitted

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

5.3.15. Dapivirine - DAPIVIRINE VAGINAL RING 25 MG (Art 58⁷) - EMEA/H/W/002168/II/0016

Applicant: International Partnership for Microbicides Belgium AISBL

PRAC Rapporteur: Jan Neuhauser

Scope: Update of Annex II in order to replace the current post-authorisation efficacy study (PAES) IPM 055 (listed as a category 1 study in the RMP): a phase 4, open label, multicentre efficacy trial in healthy human immunodeficiency virus (HIV)-negative young women aged 18-25 years, with the implementation study: dapivirine vaginal ring implementation in a real-world setting in young women. The RMP (version 0.9) is updated accordingly

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

5.3.16. Darolutamide - NUBEQA (CAP) - EMEA/H/C/004790/II/0009

Applicant: Bayer AG

PRAC Rapporteur: Jan Neuhauser

Scope: Extension of indication to include treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel, based on final results from study 17777 (ARASENS): a randomized, double-blind, placebo-controlled phase 3 study designed to demonstrate the superiority of darolutamide in combination with docetaxel over placebo in combination with docetaxel in overall survival (OS) in patients with metastatic hormone-sensitive prostate cancer (mHSPC). As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated in accordance. The MAH also requested one additional year of market protection

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

5.3.17. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/II/0060

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of atopic dermatitis in paediatric patients from 6 months to <6 years of age based on final results from study R668-AD-1539: a phase 2/3 study investigating the pharmacokinetics, safety, and efficacy of dupilumab in patients aged ≥6 months to <6 years with moderate-to-severe atopic dermatitis. As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 7.0) are updated in accordance

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

⁷ Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

5.3.18. Finerenone - KERENDIA (CAP) - EMEA/H/C/005200/II/0001/G

Applicant: Bayer AG

PRAC Rapporteur: Menno van der Elst

Scope: Grouped variations consisting of: 1) extension of indication to include the treatment of chronic kidney disease (CKD) and for the prevention of cardiovascular (CV) events in adults with CKD (regardless of the stage of albuminuria) associated with type 2 diabetes mellitus (T2DM), based on results from study 17530 (FIGARO-DKD): a randomized, double-blind, placebo-controlled, parallel-group, multicentre, event-driven phase 3 study to investigate the efficacy and safety of finerenone on the reduction of cardiovascular morbidity and mortality in subjects with T2DM and the clinical diagnosis of diabetic kidney disease in addition to standard of care. As a consequence, sections 4.1, 4.8, 5.1, 5.2 of the SmPC are updated. The package leaflet and the RMP (version 2.1) are updated accordingly. In addition, the MAH took the opportunity to introduce editorial changes in the SmPC; 2) update of section 5.2 of the SmPC based on the results of study 21429: a phase 1 drug interaction study of finerenone with rosuvastatin; 3) submission of the results of study 21325: a phase 1 bioequivalence (BE) study assessing BE between finerenone 2 x 10 mg tablets and 20 mg tablet in Japanese healthy male adult participants

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

5.3.19. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0070

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of the existing indication on chronic lymphocytic leukaemia (CLL) to include combination treatment with venetoclax for previously untreated patients based on efficacy and safety data from: 1) study GLOW: a phase 3 trial testing ibrutinib and venetoclax for people with untreated CLL or small lymphocytic lymphoma (SLL); 2) study PCYC-1142-CA (CAPTIVATE): a phase 2 study of the combination of ibrutinib plus venetoclax in subjects with treatment-naïve CLL/SLL. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated in accordance. The package leaflet and the RMP (version 18.4) are updated accordingly. In addition, the MAH included a justification to support one year-extension of the marketing protection period

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

5.3.20. Ibrutinib - IMBRUVICA (CAP) - EMEA/H/C/003791/II/0073

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Extension of indication to include treatment with Imbruvica (ibrutinib) in combination with bendamustine and rituximab (BR) of adult patients with previously untreated mantle cell lymphoma (MCL) who are unsuitable for autologous stem cell transplantation, based on final results from study PCI-32765MCL3002 (SHINE) (listed as a category 3 study in the RMP): a randomized, double-blind, placebo-controlled phase 3 study of ibrutinib in combination with BR in subjects with newly diagnosed MCL. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet

and the RMP (version 19.1) are updated in accordance

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

5.3.21. [Ivacaftor, tezacaftor, elexacaftor - KAFTRIO \(CAP\) - EMEA/H/C/005269/II/0024, Orphan](#)

Applicant: Vertex Pharmaceuticals (Ireland) Limited

PRAC Rapporteur: Martin Huber

Scope: Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on interim results from clinical study VX17-445-105 (study 105) (listed as a category 3 study in the RMP): a phase III, open label extension study to evaluate the long-term safety and efficacy of Kaftrio (ivacaftor/tezacaftor/elexacaftor) in cystic fibrosis (CF) subjects homozygous for F508del (F/F genotype) or heterozygous for F508del and a minimal function (MF) mutation (F/MF genotypes). The RMP (version 6.1) has also been submitted. In addition, the MAH took the opportunity to implement minor corrections and editorial changes in the product information

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

5.3.22. [Lonoctocog alfa - AFSTYLA \(CAP\) - EMEA/H/C/004075/II/0042](#)

Applicant: CSL Behring GmbH

PRAC Rapporteur: Sonja Hrabcik

Scope: Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final results from study 3001 (listed as a category 3 study in the RMP): an open label, multicentre extension study to assess the safety and efficacy of Afstyla (lonoctocog alfa) in subjects with severe haemophilia A. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet. The RMP (version 6.0) is updated accordingly

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

5.3.23. [Lumasiran - OXLUMO \(CAP\) - EMEA/H/C/005040/II/0008, Orphan](#)

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Update of sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC in order to clarify administration instructions, remove an existing warning on metabolic acidosis in patients with severe or end stage renal impairment, update the description of adverse reactions injection site reactions, abdominal pain and immunogenicity, update efficacy and pharmacokinetic information based on: 1) interim results from study ALN-GO1-005 (ILLUMINATE-C) (listed as a category 3 study in the RMP): a single arm study to evaluate efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in patients with advanced primary hyperoxaluria type 1 (PH1); 2) available long-term efficacy and safety data from ongoing studies: study ALN-GO1-003 (ILLUMINATE-A): a phase 3 randomized, double-blind, placebo-controlled study with an extended dosing period to evaluate the efficacy and safety of lumasiran in children and adults with PH1 and study ALN-GO1-004

(ILLUMINATE-B): an open-label study to evaluate the efficacy, safety, pharmacokinetics, and pharmacodynamics of lumasiran in infants and young children with primary PH1; 3) study ALN-GO1-002: a phase 2, multicentre, open-label, extension study to evaluate the long-term administration of ALN-GO1 (lumasiran) in patients with PH. The package leaflet and the RMP (version 1.1) are updated in accordance

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

5.3.24. Luspatercept - REBLOZYL (CAP) - EMEA/H/C/004444/II/0009, Orphan

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Extension of indication in β -thalassaemia to include adult patients with non-transfusion dependent β -thalassaemia (NTDT) for Reblozyl (luspatercept). As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the package leaflet

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

5.3.25. Macitentan - OPSUMIT (CAP) - EMEA/H/C/002697/II/0046, Orphan

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Eva Segovia

Scope: Update of sections 4.6 and 5.3 of the SmPC in order to introduce additional data on male fertility based on literature search and global safety database. The RMP (version 13.1) has also been submitted

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

5.3.26. Mercaptamine - PROCYSBI (CAP) - EMEA/H/C/002465/X/0035, Orphan

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Extension application to introduce a new pharmaceutical form associated with two new strengths (75 and 300 mg gastro-resistant granules). The RMP (version 7.2) is updated in accordance

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

5.3.27. Nivolumab - OPDIVO (CAP) - EMEA/H/C/003985/II/0117

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Extension of indication to include Opdivo (nivolumab) in combination with platinum-based chemotherapy for neoadjuvant treatment of adult patients with resectable stage IB-IIIa non-small cell lung cancer (NSCLC), based on results from study CA209816: a

randomised, open-label, phase 3 trial of nivolumab plus ipilimumab or nivolumab plus platinum-doublet chemotherapy versus platinum-doublet chemotherapy in early-stage NSCLC. As a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC are updated. The package leaflet and the RMP (version 27.0) are updated in accordance

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

5.3.28. Obinutuzumab - GAZYVARO (CAP) - EMEA/H/C/002799/II/0047, Orphan

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Submission of the final report from study BO21223/GALLIUM (listed as a category 3 study in the RMP): an open-label, international, multicentre, randomized, phase 3 study to investigate the efficacy and safety of obinutuzumab administration at standard infusion rate plus chemotherapy followed by obinutuzumab maintenance therapy for responders (G-chemo arm) compared with rituximab plus chemotherapy followed by rituximab maintenance therapy for responders (R-chemo arm) in patients with previously untreated advanced indolent non-Hodgkin's lymphoma (iNHL). The RMP (version 9.0) has also been submitted

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

5.3.29. Octocog alfa - KOVALTRY (CAP) - EMEA/H/C/003825/II/0038

Applicant: Bayer AG

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of sections 4.8 and 5.1 of the SmPC to include data from study LEOPOLD kids part B: a long-term efficacy open-label programme in severe haemophilia A disease (previously submitted as an Art 46; an addendum on biomarker data is included in this submission) and extension study results. In addition, an editorial revision in section 4.2 and a clarification in section 6.5 of the SmPC are proposed. The package leaflet is updated accordingly. The MAH took the opportunity to correct a typo in the Greek product information. The RMP (version 4.1) is updated and brought in line with revision 2.0.1 of the guidance on the format of RMP in the EU (template)

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

5.3.30. Pralsetinib - GAVRETO (CAP) - EMEA/H/C/005413/II/0002/G

Applicant: Roche Registration GmbH

PRAC Rapporteur: Annika Folin

Scope: Grouped variations consisting of: 1) extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic rearranged during transfection (RET)-mutant medullary thyroid cancer for Gavreto (pralsetinib) based on the efficacy and safety data obtained from pivotal study BO42863 (ARROW): a phase 1/2 study of the highly-selective RET inhibitor, BLU-667, in patients with thyroid cancer, non-small cell lung cancer (NSCLC) and other advanced solid tumours. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC

are updated. Furthermore, some minor changes to the product information have been implemented in line with the latest anticancer guidelines recommendations; 2) extension of indication to include monotherapy treatment of adult and paediatric patients 12 years of age and older with locally advanced or metastatic RET fusion-positive thyroid cancer for Gavreto (pralsetinib) based on the efficacy and safety data obtained from pivotal study BO42863 (ARROW). As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2 and 5.3 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly

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

5.3.31. Ribociclib - KISQALI (CAP) - EMEA/H/C/004213/II/0035

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final overall survival (OS) analysis from study A2301 (MONALEESA-2) (listed as a category 3 study in the RMP): a phase 3, randomized, double-blind, placebo-controlled, multicentre study of ribociclib in combination with letrozole in postmenopausal women with hormonal receptor + (HR+), human epidermal growth factor receptor-2 negative (HER2-), locoregionally recurrent or metastatic breast cancer who had not received previous systemic therapy for advanced disease, and based on an updated pooled safety dataset including: 1) study MONALEESA-2; 2) study MONALEESA-3: a randomized double-blind, placebo-controlled study of ribociclib in combination with fulvestrant for the treatment of men and postmenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer who have received no or only one line of prior endocrine treatment; 3) study MONALEESA-7: a phase 3 randomized, double-blind, placebo-controlled study of LEE011 or placebo in combination with tamoxifen and goserelin or a non-steroidal aromatase inhibitor (NSAI) and goserelin for the treatment of premenopausal women with hormone receptor positive, HER2-negative, advanced breast cancer (in fulfilment of MEA 004). The package leaflet and the RMP (version 6.0) are updated accordingly

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

5.3.32. Tagraxofusp - ELZONRIS (CAP) - EMEA/H/C/005031/II/0009, Orphan

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Submission of the final report from study 20255431 (CRL-263114) (listed as a category 3 study in the RMP): a non-interventional, post-authorisation study on blood brain barrier (BBB) models in order to determine a potential toxicity biomarker to further investigate the risk of choroid plexus lesions - a characterisation of fixed choroid plexus samples from primate study MPI-2231-007 by immunohistochemistry with diphtheria toxin (DT), interleukin-3 receptor (CD123), interleukin-3 (IL-3) and immunoglobulin G (IgG) (in fulfilment of MEA 002). The RMP (version 2.0) is updated accordingly

Refer also to 10.1.1.

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

5.3.33. Tenofovir alafenamide - VEMLIDY (CAP) - EMEA/H/C/004169/II/0038

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Submission of the final week 192 report from study GS-US-320-3912 (listed as a category 3 study in the RMP): a phase 2, randomized, open label study to evaluate the efficacy and safety of tenofovir alafenamide (TAF) versus tenofovir disoproxil fumarate (TDF)-containing regimens in subjects with chronic hepatitis B virus (HBV) infection and stage 2 or greater chronic kidney disease who have received a liver transplant'. The RMP (version 8.1) has also been submitted

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

5.3.34. Tixagevimab, cilgavimab - EVUSHELD (CAP MAA) - EMEA/H/C/005788/II/0001

Applicant: AstraZeneca AB

PRAC Rapporteur: Kimmo Jaakkola

Scope: Extension of indication to include treatment of adults and adolescents aged 12 years and older weighing at least 40 kg with coronavirus (COVID-19), who do not require supplemental oxygen, based on interim results from study D8851C00001 (TACKLE): an ongoing, randomised, double-blind, placebo-controlled, multicentre study assessing the safety and efficacy of a single 600 mg dose of AZD7442 (× 2 intramuscular (IM) injections) compared with matching placebo for the treatment of mild to moderate COVID-19 in non-hospitalised adults. As a consequence, sections 4.1, 4.2, 4.8, 4.9, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and labelling are updated in accordance. The RMP (version 2 succession 1) has also been submitted

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

5.3.35. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/II/0012

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include monotherapy treatment of adult patients with locally advanced or metastatic epidermal growth factor receptor 2 (HER2)-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior anti-HER2-based regimen for Enhertu (trastuzumab deruxtecan) based on final results from: 1) study DS8201-A-J202 (DESTINY Gastric01): a phase 2, multicentre, open-label study of trastuzumab deruxtecan (DS-8201a) in subjects with HER2-expressing advanced gastric or gastroesophageal junction adenocarcinoma; 2) study DS8201-A-U205 (DESTINY Gastric02): a phase 2, open-label, single-arm trial of trastuzumab deruxtecan (DS 8201a) in HER2-positive, unresectable or metastatic gastric or GEJ adenocarcinoma subjects who have progressed on or after a trastuzumab-containing regimen. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 1.1) are updated accordingly. In addition, changes regarding the dosing recommendation for corticosteroid treatment and the protection of the infusion bag from light have been introduced

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

5.3.36. Trastuzumab deruxtecan - ENHERTU (CAP) - EMEA/H/C/005124/II/0014

Applicant: Daiichi Sankyo Europe GmbH

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Extension of indication to include treatment of adult patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer who have received one or more prior anti-HER2-based regimens. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet and the RMP (version 1.2) are updated accordingly

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

5.3.37. Upadacitinib - RINVOQ (CAP) - EMEA/H/C/004760/II/0020/G

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Grouped variations consisting of: 1) update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on 'hypersensitivity' and to add it to the list of adverse drug reactions (ADRs) with a frequency not known; 2) update of section 4.8 of the SmPC in order to add 'non-melanoma skin cancer (NMSC)' to the list of adverse drug reactions (ADRs) with a frequency uncommon. The package leaflet and the RMP (version 9.0) are 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. Acalabrutinib - CALQUENCE (CAP) - PSUSA/00010887/202110

Applicant: AstraZeneca AB

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.2. Aclidinium bromide, formoterol fumarate dihydrate - BRIMICA GENUAIR (CAP); DUAKLIR GENUAIR (CAP) - PSUSA/00010307/202111

Applicant(s): AstraZeneca AB

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.3. [Alglucosidase alfa - MYOZYME \(CAP\) - PSUSA/00000086/202109](#)

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.4. [Aliskiren - RASILEZ \(CAP\); aliskiren, hydrochlorothiazide - RASILEZ HCT⁸ - PSUSA/00000089/202109](#)

Applicant(s): Noden Pharma DAC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.5. [Alpelisib - PIQRAY \(CAP\) - PSUSA/00010871/202111](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.6. [Autologous CD34⁺ enriched cell fraction that contains CD34⁺ cells transduced with retroviral vector that encodes for the human adenosine deaminase \(ADA\) complementary deoxyribonucleic acid \(cDNA\) sequence - STRIMVELIS \(CAP\) - PSUSA/00010505/202111](#)

Applicant: Orchard Therapeutics (Netherlands) BV, ATMP⁹

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.7. [Axicabtagene ciloleucel - YESCARTA \(CAP\) - PSUSA/00010703/202110](#)

Applicant: Kite Pharma EU B.V., ATMP¹⁰

PRAC Rapporteur: Anette Kirstine Stark

⁸ European Commission (EC) decision on the withdrawal of the marketing authorisation (MA) for Rasilez HCT dated 20 December 2021

⁹ Advanced therapy medicinal product

¹⁰ Advanced therapy medicinal product

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.8. Benralizumab - FASENRA (CAP) - PSUSA/00010661/202111

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.9. Bezlotoxumab - ZINPLAVA (CAP) - PSUSA/00010576/202110

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.10. Buprenorphine¹¹ - SIXMO (CAP) - PSUSA/00010778/202111

Applicant: L. Molteni & C. dei Fratelli Alitti Societa di Esercizio S.p.A.

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.11. Cefiderocol - FETCROJA (CAP) - PSUSA/00010849/202111

Applicant: Shionogi B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.12. Ceftaroline fosamil - ZINFORO (CAP) - PSUSA/00010013/202110

Applicant: Pfizer Ireland Pharmaceuticals

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹¹ Implant(s) only

6.1.13. [Cobicistat, elvitegravir, emtricitabine, tenofovir alafenamide - GENVOYA \(CAP\) - PSUSA/00010449/202111](#)

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.14. [Conestat alfa - RUCONEST \(CAP\) - PSUSA/00000873/202110](#)

Applicant: Pharming Group N.V

PRAC Rapporteur: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.15. [Crizanlizumab - ADAKVEO \(CAP\) - PSUSA/00010888/202111](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.16. [Daratumumab - DARZALEX \(CAP\) - PSUSA/00010498/202111](#)

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.17. [Darifenacin - EMSELEX \(CAP\) - PSUSA/00000933/202110](#)

Applicant: Zr Pharma& GmbH

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.18. [Denosumab¹² - PROLIA \(CAP\) - PSUSA/00000954/202109](#)

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Ulla Wändel Liminga

¹² Indicated for osteoporosis and for bone loss associated with hormone ablation in prostate cancer only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.19. Dinutuximab beta - QARZIBA (CAP) - PSUSA/00010597/202111

Applicant: EUSA Pharma (Netherlands) B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.20. Dostarlimab - JEMPERLI (CAP) - PSUSA/00010931/202110

Applicant: GlaxoSmithKline (Ireland) Limited

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.21. Drospirenone, estetrol - DROVELIS (CAP); LYDISILKA (CAP) - PSUSA/00010938/202111

Applicant(s): Chemical Works of Gedeon Richter Plc. (Gedeon Richter Plc.) (Drovelis), Estetra SRL (Lydisilka)

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.22. Durvalumab - IMFINZI (CAP) - PSUSA/00010723/202110

Applicant: AstraZeneca AB

PRAC Rapporteur: David Olsen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.23. Eculizumab - SOLIRIS (CAP) - PSUSA/00001198/202110

Applicant: Alexion Europe SAS

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.24. Edoxaban - LIXIANA (CAP); ROTEAS (CAP) - PSUSA/00010387/202110

Applicant(s): Daiichi Sankyo Europe GmbH (Lixiana), Berlin Chemie AG (Roteas)

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.25. Emicizumab - HEMLIBRA (CAP) - PSUSA/00010668/202111

Applicant: Roche Registration GmbH

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.26. Etelcalcetide - PARSABIV (CAP) - PSUSA/00010533/202111

Applicant: Amgen Europe B.V.

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.27. Flutemetamol (¹⁸F) - VIZAMYL (CAP) - PSUSA/00010293/202110

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.28. Follitropin alfa - BEMFOLA (CAP); GONAL-F (CAP); OVALEAP (CAP) - PSUSA/00001463/202110

Applicant(s): Gedeon Richter Plc. (Bemfola), Merck Europe B.V. (Gonal-f), Theramex Ireland Limited (Ovaleap)

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.29. Follitropin alfa, lutropin alfa - PERGOVERIS (CAP) - PSUSA/00001464/202110

Applicant: Merck Europe B.V.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.30. Fostamatinib - TAVLESSE (CAP) - PSUSA/00010819/202110

Applicant: Instituto Grifols, S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.31. Givosiran - GIVLAARI (CAP) - PSUSA/00010839/202111

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.32. Glasdegib - DAURISMO (CAP) - PSUSA/00010859/202111

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.33. Hepatitis B surface antigen - HEPLISAV B (CAP) - PSUSA/00010919/202111

Applicant: Dynavax GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.34. Ibrutinib - IMBRUVICA (CAP) - PSUSA/00010301/202111

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nikica Mirošević Skvrce

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.35. Idarucizumab - PRAXBIND (CAP) - PSUSA/00010435/202110

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.36. Insulin detemir - LEVEMIR (CAP) - PSUSA/00001750/202110

Applicant: Novo Nordisk A/S
PRAC Rapporteur: Marie Louise Schougaard Christiansen
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.37. Insulin glargine, lixisenatide - SULIQUA (CAP) - PSUSA/00010577/202111

Applicant: sanofi-aventis groupe
PRAC Rapporteur: Menno van der Elst
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.38. Irinotecan¹³ - ONIVYDE PEGYLATED LIPOSOMAL (CAP) - PSUSA/00010534/202110

Applicant: Les Laboratoires Servier
PRAC Rapporteur: David Olsen
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.39. Ivacaftor, tezacaftor, elexacaftor - KAFTRIO (CAP) - PSUSA/00010868/202110

Applicant: Vertex Pharmaceuticals (Ireland) Limited
PRAC Rapporteur: Martin Huber
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.40. Ixazomib - NINLARO (CAP) - PSUSA/00010535/202111

Applicant: Takeda Pharma A/S
PRAC Rapporteur: Annika Folin
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

¹³ Liposomal formulation(s) only

6.1.41. Ketoconazole¹⁴ - KETOCONAZOLEHRA (CAP) - PSUSA/00010316/202111

Applicant: HRA Pharma Rare Diseases

PRAC Rapporteur: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.42. Larotrectinib - VITRAKVI (CAP) - PSUSA/00010799/202111

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.43. Letermovir - PREVYMIS (CAP) - PSUSA/00010660/202111

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.44. Lopinavir, ritonavir - ALUVIA (Art 58¹⁵) - EMEA/H/W/000764/PSUV/0115

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUR procedure

Action: For adoption of recommendation to CHMP

6.1.45. Lopinavir, ritonavir - KALETRA (CAP) - PSUSA/00001905/202109

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.46. Lumasiran - OXLUMO (CAP) - PSUSA/00010884/202111

Applicant: Alnylam Netherlands B.V.

¹⁴ Centrally authorised product(s) only

¹⁵ Article 58 of Regulation (EC) No 726/2004 allows the Committee for Medicinal Products for Human Use (CHMP) to give opinions, in co-operation with the World Health Organisation (WHO) on medicinal products for human use that are intended exclusively for markets outside of the European Union (EU)

PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.47. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - PSUSA/00010607/202110

Applicant: Pfizer Europe MA EEIG
PRAC Rapporteur: Jean-Michel Dogné
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.48. Midostaurin - RYDAPT (CAP) - PSUSA/00010638/202110

Applicant: Novartis Europharm Limited
PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.49. Miglustat - ZAVESCA (CAP) - PSUSA/00002062/202110

Applicant: Janssen-Cilag International N.V.
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.50. Nintedanib¹⁶ - OFEV (CAP) - PSUSA/00010319/202110

Applicant: Boehringer Ingelheim International GmbH
PRAC Rapporteur: Nikica Mirošević Skvrce
Scope: Evaluation of a PSUSA procedure
Action: For adoption of recommendation to CHMP

6.1.51. Onasemnogene abeparvovec - ZOLGENSMA (CAP) - PSUSA/00010848/202111

Applicant: Novartis Gene Therapies EU Limited, ATMP¹⁷
PRAC Rapporteur: Ulla Wändel Liminga
Scope: Evaluation of a PSUSA procedure

¹⁶ Respiratory indication(s) only

¹⁷ Advanced therapy medicinal product

Action: For adoption of recommendation to CAT and CHMP

6.1.52. Ozanimod - ZEPOSIA (CAP) - PSUSA/00010852/202111

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Maria del Pilar Rayon

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.53. Padeliporfin - TOOKAD (CAP) - PSUSA/00010654/202111

Applicant: STEBA Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.54. Pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - FOCLIVIA (CAP); pre-pandemic influenza vaccine (H5N1) (surface antigen, inactivated, adjuvanted) - AFLUNOV (CAP) - PSUSA/00010008/202110

Applicant(s): Seqirus S.r.l

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.55. Para-aminosalicylic acid¹⁸ - GRANUPAS (CAP) - PSUSA/00010171/202110 (with RMP)

Applicant: Eurocept International B.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.56. Parathyroid hormone - NATPAR (CAP) - PSUSA/00010591/202110

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Rhea Fitzgerald

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

¹⁸ Centrally authorised product(s) only

6.1.57. Pazopanib - VOTRIENT (CAP) - PSUSA/00002321/202110

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.58. Pemigatinib - PEMAZYRE (CAP) - PSUSA/00010923/202110

Applicant: Incyte Biosciences Distribution B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.59. Potassium citrate, potassium hydrogen carbonate - SIBNAYAL (CAP) - PSUSA/00010932/202110

Applicant: Advicenne

PRAC Rapporteur: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.60. Prasterone¹⁹ - INTRAROSA (CAP) - PSUSA/00010672/202111

Applicant: Endoceutics S.A.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.61. Prucalopride - RESOLOR (CAP) - PSUSA/00002568/202110

Applicant: Takeda Pharmaceuticals International AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.62. Ebola Zaire vaccine (live, attenuated) - ERVEBO (CAP) - PSUSA/00010834/202111

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Menno van der Elst

¹⁹ Pessary, vaginal use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.63. Relugolix, estradiol, norethisterone acetate - RYEQO (CAP) - PSUSA/00010942/202111

Applicant: Gedeon Richter Plc.

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.64. Remdesivir - VEKLURY (CAP) - PSUSA/00010840/202111

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.65. Rituximab - BLITZIMA (CAP); MABTHERA (CAP); RIXATHON (CAP); RIXIMYO (CAP); RUXIENCE (CAP); TRUXIMA (CAP) - PSUSA/00002652/202111 (without RMP)

Applicant(s): Celltrion Healthcare Hungary Kft. (Blitzima, Truxima), Pfizer Europe MA EEIG (Ruxience), Roche Registration GmbH (MabThera), Sandoz GmbH (Rixathon, Riximyo)

PRAC Rapporteur: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.66. Rurioctocog alfa pegol - ADYNOVI (CAP) - PSUSA/00010663/202111

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.67. Selpercatinib - RETSEVMO (CAP) - PSUSA/00010917/202111

Applicant: Eli Lilly Nederland B.V.

PRAC Rapporteur: Menno van der Elst

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.68. Setmelanotide - IMCIVREE (CAP) - PSUSA/00010941/202111

Applicant: Rhythm Pharmaceuticals Netherlands B.V.

PRAC Rapporteur: Marek Juracka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.69. Sotagliflozin - ZYNQUISTA²⁰ - PSUSA/00010766/202110

Applicant: Guidehouse Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For discussion

6.1.70. Stiripentol - DIACOMIT (CAP) - PSUSA/00002789/202111

Applicant: Biocodex

PRAC Rapporteur: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.71. Susoctocog alfa - OBIZUR (CAP) - PSUSA/00010458/202111

Applicant: Baxalta Innovations GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.72. Talazoparib - TALZENNA (CAP) - PSUSA/00010781/202110

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Marcia Sofia Sanches de Castro Lopes Silva

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.73. Talimogene laherparepvec - IMLYGIC (CAP) - PSUSA/00010459/202110

Applicant: Amgen Europe B.V., ATMP²¹

²⁰ European Commission (EC) decision on the withdrawal of the marketing authorisation (MA) for Zynquista dated 22 March 2022

²¹ Advanced therapy medicinal product

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CAT and CHMP

6.1.74. Tenofovir alafenamide - VEMLIDY (CAP) - PSUSA/00010575/202111

Applicant: Gilead Sciences Ireland UC

PRAC Rapporteur: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.75. Tofacitinib - XELJANZ (CAP) - PSUSA/00010588/202111 (with RMP)

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.76. Trastuzumab - HERCEPTIN (CAP); HERZUMA (CAP); KANJINTI (CAP); OGI VRI (CAP); ONTRUZANT (CAP); TRAZIMERA (CAP); ZERCEPAC (CAP) - PSUSA/00003010/202109

Applicant(s): Accord Healthcare S.L.U. (Zercepac), Amgen Europe B.V., BRED A (Kanjinti), Celltrion Healthcare Hungary Kft. (Herzuma), Pfizer Europe MA EEIG (Trazimera), Roche Registration GmbH (Herceptin), Samsung Bioepis NL B.V. (Ontruzant), Viatrix Limited (Ogivri)

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.77. Tucatinib - TUKYSA (CAP) - PSUSA/00010918/202110

Applicant: Seagen B.V.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.78. Vestronidase alfa - MEPSEVII (CAP) - PSUSA/00010709/202111

Applicant: Ultragenyx Germany GmbH

PRAC Rapporteur: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.79. Volanesorsen - WAYLIVRA (CAP) - PSUSA/00010762/202111

Applicant: Akcea Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.1.80. Zinc acetate dihydrate - WILZIN (CAP) - PSUSA/00003145/202110

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Rhea Fitzgerald

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. Bosentan - STAYVEER (CAP); TRACLEER (CAP); NAP - PSUSA/00000425/202111

Applicants: Janssen-Cilag International N.V. (Stayveer, Tracleer), various

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.2. Carbidopa, entacapone, levodopa - CORBILTA (CAP); LEVODOPA/CARBIDOPA/ENTACAPONE ORION (CAP); STALEVO (CAP); NAP - PSUSA/00000547/202110

Applicants: Orion Corporation (Corbilta, Levodopa/Carbidopa/Entacapone Orion, Stalevo), various

PRAC Rapporteur: Kirsti Villikka

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.3. Methotrexate - JYLAMVO (CAP); NORDIMET (CAP); NAP - PSUSA/00002014/202110

Applicants: Nordic Group B.V. (Nordimet), Therakind (Europe) Limited (Jylamvo), various

PRAC Rapporteur: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.4. Posaconazole - NOXAFIL (CAP); NAP - PSUSA/00002480/202110

Applicants: Merck Sharp & Dohme B.V. (Noxafil), various

PRAC Rapporteur: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CHMP

6.2.5. Sevelamer - RENAGEL (CAP); RENVELA (CAP); SEVELAMER CARBONATE WINTHROP (CAP); NAP - PSUSA/00002697/202110

Applicants: Genzyme Europe BV (Renagel, Renvela, Sevelamer Carbonate Winthrop), various

PRAC Rapporteur: Jean-Michel Dogné

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. ¹³C-methacetin (NAP) - PSUSA/00010846/202110

Applicant(s): various

PRAC Lead: Adam Przybylkowski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.2. Acetylsalicylic acid, bisoprolol (NAP) - PSUSA/00010287/202111

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.3. Acitretin (NAP) - PSUSA/00000051/202110

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.4. Amlodipine, perindopril (NAP) - PSUSA/00000179/202110

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.5. Azelastine, fluticasone (NAP) - PSUSA/00010067/202110

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.6. Benzalkonium chloride, chlorhexidine digluconate (NAP) - PSUSA/00010070/202111

Applicant(s): various

PRAC Lead: Rugilė Pilvinienė

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.7. Benzydamine (NAP) - PSUSA/00000375/202110

Applicant(s): various

PRAC Lead: Amelia Cupelli

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.8. Brimonidine²² (NAP) - PSUSA/00000430/202109

Applicant(s): various

PRAC Lead: Ronan Grimes

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

²² Non-centrally authorised product(s) only

6.3.9. Brimonidine, timolol (NAP) - PSUSA/00000431/202109

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.10. Clevidipine (NAP) - PSUSA/00010288/202111

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.11. Clindamycin (NAP) - PSUSA/00000795/202110

Applicant(s): various

PRAC Lead: Sonja Hrabcik

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.12. Dexketoprofen (NAP) - PSUSA/00000997/202110

Applicant(s): various

PRAC Lead: Eva Segovia

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.13. Dextromethorphan (NAP) - PSUSA/00001009/202111

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.14. Diclofenac²³ (NAP) – PSUSA/00001048/202109

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

²³ Systemic formulation(s) only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.15. Diclofenac, omeprazole (NAP) - PSUSA/00010461/202109

Applicant(s): various

PRAC Lead: Anette Kirstine Stark

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.16. Drospirenone (NAP) - PSUSA/00010853/202111

Applicant(s): various

PRAC Lead: Annika Folin

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.17. Erythromycin, tretinoin (NAP) - PSUSA/00001259/202110

Applicant(s): various

PRAC Lead: Anna Mareková

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.18. Ethinylestradiol, norgestimate (NAP) - PSUSA/00001313/202110

Applicant(s): various

PRAC Lead: Marie Louise Schougaard Christiansen

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.19. Human coagulation factor VIII, human von Willebrand factor (NAP) – PSUSA/00001621/202110

Applicant(s): various

PRAC Lead: Brigitte Keller-Stanislawski

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.20. [Hydrochlorothiazide, olmesartan \(NAP\) - PSUSA/00002209/202110](#)

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.21. [Isopropyl alcohol, propyl alcohol, mecetronium ethyl sulfate \(NAP\) - PSUSA/00010108/202109](#)

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.22. [Lacidipine \(NAP\) - PSUSA/00001815/202110](#)

Applicant(s): various

PRAC Lead: Maia Uusküla

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.23. [Letrozole \(NAP\) - PSUSA/00001842/202110](#)

Applicant(s): various

PRAC Lead: Tiphaine Vaillant

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.24. [Magnesium hydroxide \(NAP\) - PSUSA/00001926/202110](#)

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.25. [Meningococcal group C polysaccharide conjugate vaccine \(NAP\) - PSUSA/00001971/202110](#)

Applicant(s): various

PRAC Lead: Jean-Michel Dogné

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.26. Methylphenidate (NAP) - PSUSA/00002024/202110

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.27. Milrinone (NAP) - PSUSA/00002064/202110

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.28. Olmesartan (NAP) - PSUSA/00002207/202110

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.29. Phloroglucinol (NAP), phloroglucinol, trimethylphloroglucinol (NAP) - PSUSA/00010355/202109

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.30. Piretanide (NAP) - PSUSA/00002433/202110

Applicant(s): various

PRAC Lead: Nathalie Gault

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.31. Polystyrene sulfonate (NAP) - PSUSA/00002472/202110

Applicant(s): various

PRAC Lead: Jana Lukačičinová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.32. Rabeprazole (NAP) - PSUSA/00002601/202110

Applicant(s): various

PRAC Lead: Jan Neuhauser

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.33. Rubidium (⁸²Rb) chloride (NAP) - PSUSA/00010806/202110

Applicant(s): various

PRAC Lead: Martin Huber

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.34. Soybean phospholipids²⁴ (NAP) – PSUSA/00010707/202110

Applicant(s): various

PRAC Lead: Željana Margan Koletić

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.35. Teicoplanin (NAP) - PSUSA/00002878/202111

Applicant(s): various

PRAC Lead: Eva Jirsová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.36. Tiotropium (NAP) - PSUSA/00002972/202110

Applicant(s): various

PRAC Lead: Menno van der Elst

²⁴ Oral use only

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.3.37. Zidovudine (NAP) - PSUSA/00003143/202109

Applicant(s): various

PRAC Lead: Jana Lukačšínová

Scope: Evaluation of a PSUSA procedure

Action: For adoption of recommendation to CMDh

6.4. Follow-up to PSUR/PSUSA procedures

6.4.1. Alectinib - ALECENSA (CAP) - EMEA/H/C/004164/LEG 004

Applicant: Roche Registration GmbH

PRAC Rapporteur: Jana Lukacisinova

Scope: Cumulative review of cases of QT prolongation reported with alectinib administration, including post-marketing, clinical trials and literature data, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010581/202107) adopted in February 2022

Action: For adoption of advice to CHMP

6.4.2. Coronavirus (COVID-19) vaccine (Ad26.COVID-S, recombinant) - JCOVDEN (CAP) - EMEA/H/C/005737/LEG 051

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Cumulative review of cases of coronary artery disease including myocardial infarction based on data from clinical trials, post-marketing data and literature, including (age) stratified observed/expected (O/E) analyses following the publication of an epidemiological study based on data from French national databases (EPI-Phare) suggesting a slightly increased risk for myocardial infarction with Jcovden (COVID-19 vaccine (Ad26.COVID-S, recombinant)), as requested in the conclusions of the ninth summary safety report (SSR) adopted in March 2022

Action: For adoption of advice to CHMP

6.4.3. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/LEG 103

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: Cumulative review of cases of pulmonary embolism (PE) and coronary artery disease including myocardial infarction based on data from clinical trials, post-marketing data and

literature, including (age) stratified observed/expected (O/E) analyses following the publication of an epidemiological study based on data from French national databases (EPI-Phare), together with a justification of used background rates

Action: For adoption of advice to CHMP

6.4.4. Laronidase - ALDURAZYME (CAP) - EMEA/H/C/000477/LEG 056

Applicant: Genzyme Europe BV

PRAC Rapporteur: Nathalie Gault

Scope: Detailed review of cases of hypersensitivity reactions, immunogenicity, infusion-site reaction, overdose, cases suggestive of overdose and use of laronidase by intrathecal route, as requested in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010581/202107) adopted in December 2021

Action: For adoption of advice to CHMP

6.5. Variation procedure(s) resulting from PSUSA evaluation

6.5.1. Dolutegravir - TIVICAY (CAP) - EMEA/H/C/002753/WS2268/0079; dolutegravir, abacavir, lamivudine - TRIUMEQ (CAP) - EMEA/H/C/002754/WS2268/0104; dolutegravir, lamivudine - DOVATO (CAP) - EMEA/H/C/004909/WS2268/0031; dolutegravir, rilpivirine - JULUCA (CAP) - EMEA/H/C/004427/WS2268/0044

Applicant: ViiV Healthcare B.V.

PRAC Rapporteur: Martin Huber

Scope: Update of section 4.8 of the SmPC to add 'weight increased' with a frequency common based on available data/results from study RESPOND (International Cohort Consortium of Infectious Disease): a prospective, multi-cohort collaboration study of people living with human immunodeficiency virus (HIV) across Europe and Australia as requested in the conclusions of the post-authorisation measures (LEG procedures) adopted in February 2022 that followed a request adopted in the conclusions of the PSUR single assessment (PSUSA) procedure (PSUSA/00010075/202101) finalised in September 2021. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement a minor editorial change in the German SmPC for Juluca (dolutegravir/rilpivirine)

Action: For adoption of PRAC Assessment Report

6.6. Expedited summary safety reviews²⁵

6.6.1. Coronavirus (COVID-19) vaccine (recombinant, adjuvanted) - NUVAXOVID (CAP) - EMEA/H/C/005808/MEA 014.2

Applicant: Novavax CZ, a.s.

²⁵ Submission of expedited summary safety reports for review in addition to the requirements for submission of PSUR(s) falling within the pandemic period and requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC

PRAC Rapporteur: Brigitte Keller-Stanislawski

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

Action: For adoption of PRAC Assessment Report

6.6.2. [Elasomeran - SPIKEVAX \(CAP\) - EMEA/H/C/005791/MEA 011.12](#)

Applicant: Moderna Biotech Spain, S.L.

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: Thirteenth expedited summary safety report (SSR) for Spikevax (elasomeran) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

6.6.3. [Tozinameran - COMIRNATY \(CAP\) - EMEA/H/C/005735/MEA 002.13](#)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Fourteenth expedited summary safety report (SSR) for Comirnaty (tozinameran) during the coronavirus disease (COVID-19) pandemic

Action: For adoption of PRAC Assessment Report

7. Post-authorisation safety studies (PASS)

7.1. Protocols of PASS imposed in the marketing authorisation(s)²⁶

7.1.1. [Lomitapide - LOJUXTA \(CAP\) - EMEA/H/C/PSA/S/0083.1](#)

Applicant: Amryt Pharmaceuticals DAC

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to PSA/S/0083 [substantial amendment to a protocol previously agreed in November 2013 for lomitapide observational worldwide evaluation registry to evaluate the occurrence and outcomes of pregnancy in females of reproductive potential treated with lomitapide] as per the request for supplementary information (RSI) adopted in March 2022

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

7.1.2. [Teduglutide - REVESTIVE \(CAP\) - EMEA/H/C/PSA/S/0082.1](#)

Applicant: Shire Pharmaceuticals Ireland Limited

²⁶ In accordance with Article 107n of Directive 2001/83/EC

PRAC Rapporteur: Marie Louise Schougaard Christiansen

Scope: MAH's response to PSA/S/0082 [substantial amendment to a protocol previously agreed in July 2019 (PSA/S/0040) for study TED-R13-002: a prospective, multicentre registry for patients with short bowel syndrome] as per the request for supplementary information (RSI) adopted in February 2022

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

7.1.3. Valproate²⁷ (NAP) - EMEA/H/N/PSP/J/0074.5

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

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to PSP/J/0074.4 [interim report for a joint observational study to evaluate and identify the best practices for switching of valproate in clinical practice, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in January 2022

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

7.2. Protocols of PASS non-imposed in the marketing authorisation(s)²⁸

7.2.1. Crizanlizumab - ADAKVEO (CAP) - EMEA/H/C/004874/MEA 004.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 004 [protocol for study CSEG101A2405 (listed as a category 3 study in the RMP): a non-interventional PASS - registry-based study to assess long-term safety and pregnancy outcomes in patients with sickle cell disease (SCD) using crizanlizumab] as per the request for supplementary information (RSI) adopted in December 2021

Action: For adoption of advice to CHMP

7.2.2. Eptinezumab - VYEPTI (CAP) - EMEA/H/C/005287/MEA 004

Applicant: H. Lundbeck A/S

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: Protocol for study 19756N: a long-term cardiovascular safety and real-world use of eptinezumab - an observational, historical cohort study of patients initiating eptinezumab in routine clinical practice

Action: For adoption of advice to CHMP

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

²⁸ In accordance with Article 107m of Directive 2001/83/EC, supervised by PRAC in accordance with Article 61a (6) of Regulation (EC) No 726/2004

7.2.3. Linaclotide - CONSTELLA (CAP) - EMEA/H/C/002490/MEA 009.5

Applicant: Allergan Pharmaceuticals International Limited

PRAC Rapporteur: Martin Huber

Scope: Substantial amendment to a protocol previously agreed for PASS EVM-18888: linaclotide safety study assessing the complications of diarrhoea and associated risk factors in selected European populations with irritable bowel syndrome with constipation (IBS-C) for Constella (linaclotide) 290µg capsule (protocol version 10.0)

Action: For adoption of advice to CHMP

7.2.4. Lonapegsomatropin - LONAPEGOMATROPIN ASCENDIS PHARMA (CAP) - EMEA/H/C/005367/MEA 001

Applicant: Ascendis Pharma Endocrinology Division A/S

PRAC Rapporteur: Martin Huber

Scope: Protocol for study VV-SUB-056752: a prospective, non-interventional, long-term, safety study of patients treated with lonapegsomatropin to further characterise the potential long-term safety risks of lonapegsomatropin in patients treated with under real-world conditions in the post-marketing setting [final results expected in July 2033]

Action: For adoption of advice to CHMP

7.2.5. Neratinib - NERLYNX (CAP) - EMEA/H/C/004030/MEA 003.2

Applicant: Pierre Fabre Medicament

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 003.1 [protocol for study PUMA-NER-7402: a non-interventional study exploring the safety of neratinib among breast cancer patients to characterise the incidence and duration of diarrhoea in a real world setting, to describe patient characteristics, incidence rates and duration of diarrhoea, to describe use of loperamide and other concomitant anti-diarrhoeal medication, describe adherence to neratinib therapy, assess the impact of neratinib therapy on patient self-reported, health related quality of life and their ability to perform their activities of daily living and to further assess and characterise adverse events hepatic, cardiac, pulmonary, reproductive and developmental toxicity] as per the request for supplementary information (RSI) adopted in May 2020

Action: For adoption of advice to CHMP

7.2.6. Patisiran - ONPATTRO (CAP) - EMEA/H/C/004699/MEA 003.3

Applicant: Alnylam Netherlands B.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 003.2 [update to a previously agreed protocol and interim study report for study ALN-TTR02-010: patisiran- lipid nanoparticle (LNP) pregnancy surveillance programme (PSP) to collect primary data on pregnant women from the US, the

United Kingdom (UK), France, Spain, Italy, Portugal and Germany, and other potential countries, who have been exposed to patisiran during the exposure window, defined as 12 weeks prior to their last menstrual period (LMP), or at any time during pregnancy as well as to collect and analyse information pertaining to pregnancy complications and birth outcomes in women exposed to patisiran during pregnancy] as per the request for supplementary information (RSI) adopted in January 2022

Action: For adoption of advice to CHMP

7.2.7. Ponesimod - PONVORY (CAP) - EMEA/H/C/005163/MEA 001.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 001 [protocol for study PCSNSP004001 (listed as a category 3 study in the RMP): ponesimod pregnancy outcomes enhanced monitoring (POEM) - pregnancy outcomes programme utilising enhanced pharmacovigilance monitoring to evaluate the potential risk of reproductive and embryofetal toxicity in pregnant women exposed to ponesimod (from initial opinion/marketing authorisation)] as per the request for supplementary information (RSI) adopted in January 2022

Action: For adoption of advice to CHMP

7.2.8. Ponesimod - PONVORY (CAP) - EMEA/H/C/005163/MEA 004.1

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Anette Kirstine Stark

Scope: MAH's response to MEA 004 [protocol for study PCSNSP003693 (listed as a category 3 study in the RMP): a survey among healthcare professionals (neurologists treating patients with multiple sclerosis (MS) along with MS specialist nurses) in selected European countries to evaluate knowledge and behaviours required for the safe use of ponesimod] as per the request for supplementary information (RSI) adopted in December 2021

Action: For adoption of advice to CHMP

7.2.9. Rivaroxaban - XARELTO (CAP) - EMEA/H/C/000944/MEA 049.1

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study 22194 (listed as a category 3 study in the RMP): a multi-national, observational, cross-sectional study to evaluate the effectiveness of risk minimisation measures (RMM) provided to physicians and parents/caregivers (P/C) of children for the use of Xarelto (rivaroxaban) oral suspension for the treatment of venous thromboembolism (VTE) and to provide insight on the risk of medication errors (MEs) in routine clinical practice (feasibility report assessed by PRAC in July 2021 (MEA 049))

Action: For adoption of advice to CHMP

7.2.10. [Rivaroxaban - XARELTO \(CAP\) - EMEA/H/C/000944/MEA 049.2](#)

Applicant: Bayer AG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Protocol for study 22195 (listed as a category 3 study in the RMP): an observational, longitudinal, multi-source drug utilisation safety study to evaluate the drug use patterns and safety of rivaroxaban oral suspension in children under two years with venous thromboembolism (feasibility report assessed by PRAC in July 2021 (MEA 049))

Action: For adoption of advice to CHMP

7.2.11. [Sacubitril, valsartan - ENTRESTO \(CAP\) - EMEA/H/C/004062/MEA 002.8](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Substantial protocol amendment and fifth interim report for study CLCZ696B2014 (PASS 1) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to characterise the risk of angioedema and other specific safety events of interest in association with the use of Entresto/Neparvis (sacubitril/valsartan) in adult patients with heart failure

Action: For adoption of advice to CHMP

7.2.12. [Sacubitril, valsartan - NEPARVIS \(CAP\) - EMEA/H/C/004343/MEA 002.5](#)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Anette Kirstine Stark

Scope: Substantial protocol amendment and fifth interim report for study CLCZ696B2014 (PASS 1) (listed as a category 3 study in the RMP): a non-interventional post-authorisation European multi-database safety study to characterise the risk of angioedema and other specific safety events of interest in association with the use of Entresto/Neparvis (sacubitril/valsartan) in adult patients with heart failure

Action: For adoption of advice to CHMP

7.2.13. [Tozinameran - COMIRNATY \(CAP\) - EMEA/H/C/005735/MEA 017.3](#)

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

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

statistical analysis plan (SAP)] as per the request for supplementary information (RSI) adopted in March 2022

Action: For adoption of advice to CHMP

7.2.14. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 041.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 041 [protocol for study C4591036 (former paediatric heart network study): a safety surveillance study of myocarditis and myopericarditis associated with Comirnaty (tozinameran) in persons less than 21 years of age to characterize the clinical course, risk factors, long-term sequelae, and quality of life in children and young adults under 21 years with acute post-vaccine myocarditis] as per the request for supplementary information (RSI) adopted in February 2022

Action: For adoption of advice to CHMP

7.2.15. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 047.1

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: MAH's response to MEA 047 [protocol for study C4591038 (listed as a category 3 study in the RMP): a post conditional approval active surveillance study among individuals in Europe receiving the Pfizer BioNTech coronavirus disease 2019 (COVID-19) vaccine to investigate natural history of post-vaccination myocarditis and pericarditis] as per request for supplementary information (RSI) adopted in May 2022

Action: For adoption of advice to CHMP

7.3. Results of PASS imposed in the marketing authorisation(s)²⁹

7.3.1. Valproate (NAP) - EMEA/H/N/PSR/J/0036

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

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: MAH's response to PSR/J/0036 [results for a joint survey among healthcare professionals (HCP) to assess knowledge of HCP and behaviour with regards to pregnancy prevention programme (PPP) as well as receipt/use of a direct healthcare professional communication (DHPC) and educational materials and survey among patients to assess knowledge of the patients with regards to PPP as well as receipt/use of educational materials, as required in the outcome of the referral procedure under Article 31 of Directive 2001/83/EC on valproate-containing products completed in February 2018 (EMEA/H/A-31/1454)] as per the request for supplementary information (RSI) adopted in October 2021

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

²⁹ In accordance with Article 107p-q of Directive 2001/83/EC

information (RSI))

7.4. Results of PASS non-imposed in the marketing authorisation(s)³⁰

7.4.1. Alirocumab - PRALUENT (CAP) - EMEA/H/C/003882/II/0068

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Update of section 4.8 of the SmPC based on the final results from study OBS14697 (listed as a category 3 study in the RMP): a non-interventional, retrospective drug utilisation study (DUS) to assess in Europe the effectiveness of the dosing recommendation and to describe patterns of alirocumab utilisation in real world clinical practice (in fulfilment of MEA 019.8). In addition, the MAH took the opportunity to implement editorial changes in the product information

Action: For adoption of PRAC Assessment Report

7.4.2. Crizotinib - XALKORI (CAP) - EMEA/H/C/002489/II/0075

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Tiphaine Vaillant

Scope: Submission of the final report for study A8081062 (listed as a category 3 study in the RMP): a non-interventional, descriptive study of potential sight threatening event and severe visual loss following exposure to crizotinib (in fulfilment of MEA 024)

Action: For adoption of PRAC Assessment Report

7.4.3. Empagliflozin - JARDIANCE (CAP) - EMEA/H/C/002677/WS2196/0063; empagliflozin, linagliptin - GLYXAMBI (CAP) - EMEA/H/C/003833/WS2196/0042; empagliflozin, metformin - SYNJARDY (CAP) - EMEA/H/C/003770/WS2196/0060

Applicant: Boehringer Ingelheim International GmbH

PRAC Rapporteur: Eva Segovia

Scope: Update of section 4.4 of the SmPC to delete the warning on lower limb amputations based on the results from the final meta-analysis report of study 1245.171 (listed as a category 3 study in the RMP): a meta-analysis of amputation risk in empagliflozin studies, namely: 1) study 1245.25 (EMPA-REG OUTCOME): a study in patients with type 2 diabetes mellitus (T2DM) and increased cardiovascular risk; 2) study 1245.110 (EMPEROR- HFpEF): a study in patients with chronic heart failure (HF) with preserved ejection fraction; 3) study 1245.121 (EMPEROR- HFrEF): a study in patients with chronic HF with reduced ejection fraction. The package leaflet and the RMP (version 17 for Jardiance, version 11 for Synjardy and version 6 for Glyxambi) are updated accordingly. The conduct of this meta-analysis was requested to MAHs of all sodium-glucose co-transporter-2 (SGLT2)-containing products as part of the outcome of the referral procedure (EMA/H/A-20/1419) under Article 20 of

³⁰ 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

Regulation (EC) No 726/2004 finalised in 2016

Action: For adoption of PRAC Assessment Report

7.4.4. Flutemetamol (¹⁸F) - VIZAMYL (CAP) - EMEA/H/C/002557/II/0029

Applicant: GE Healthcare AS

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study GE067-027 (listed as a category 3 study in the RMP): a non-interventional PASS to evaluate the effectiveness of Vizamyl (flutemetamol (¹⁸F)) reader training in Europe. The submission also includes a comprehensive root-cause analysis on the contributing factors having an impact on reader performance as requested by PRAC. The RMP (version 3.1) is updated accordingly and includes relevant updates to reflect the completion of study GE067-028 on the use pattern of Vizamyl (flutemetamol (¹⁸F)) in post-authorisation setting in the EU, as previously assessed in MEA 003.3

Action: For adoption of PRAC Assessment Report

7.4.5. Hepatitis B surface antigen - HEPLISAV B (CAP) - EMEA/H/C/005063/II/0015

Applicant: Dynavax GmbH

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of the final report from study HBV-26 (listed as a category 3 study in the RMP): a post-marketing observational surveillance study to evaluate the incidence of new-onset immune-mediated diseases, herpes zoster, and anaphylaxis in recipients of Heplisav B (hepatitis B surface antigen) with recipients of another hepatitis B vaccine. The RMP (version 1.3) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.6. Meningococcal group B vaccine (recombinant, adsorbed) - TRUMENBA (CAP) - EMEA/H/C/004051/II/0040

Applicant: Pfizer Europe MA EEIG

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study B1971052 (listed as a category 3 study in the RMP): a population-based, non-interventional cohort study utilising administrative healthcare claims data assessing pregnancy and birth outcome after exposure to Trumenba (meningococcal group B vaccine (recombinant, adsorbed)) (in fulfilment of MEA 001)

Action: For adoption of PRAC Assessment Report

7.4.7. Naltrexone hydrochloride, bupropion hydrochloride - MYSIMBA (CAP) - EMEA/H/C/003687/II/0054

Applicant: Orexigen Therapeutics Ireland Limited

PRAC Rapporteur: Martin Huber

Scope: Submission of the final report from study NB-542 (listed as a category 3 study in the RMP): a cross-sectional survey aimed to evaluate the effectiveness of the Mysimba (naltrexone hydrochloride/bupropion hydrochloride) physician prescribing checklist (PPC) among physicians in the EU. The RMP (version 12.6) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.8. Rotavirus vaccine (live, oral) - ROTARIX (CAP) - EMEA/H/C/000639/II/0125

Applicant: GlaxoSmithKline Biologicals S.A.

PRAC Rapporteur: Jean-Michel Dogné

Scope: Submission of the final report from study EPI-ROTA-052 BOD EU SUPP (201433) (listed as a category 3 study in the RMP): an observational community-based strain surveillance study to monitor the potential emergence and spread of novel rotavirus (RV) strains throughout Europe. The RMP (version 23) is updated accordingly

Action: For adoption of PRAC Assessment Report

7.4.9. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/II/0091

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: Submission of the final safety registry report from study CNTO1275PSO4007: pregnancy research initiative - exposure to ustekinumab during pregnancy: a review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers (in fulfilment of MEA 024). The RMP (version 22.1) is updated accordingly

Action: For adoption of PRAC Assessment Report

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

7.5.1. Abatacept - ORENCIA (CAP) - EMEA/H/C/000701/MEA 048.10

Applicant: Bristol-Myers Squibb Pharma EEIG

PRAC Rapporteur: Kimmo Jaakkola

Scope: Annual update report on recruitment for study IM101240 (listed as a category 3 study in the RMP): an observational registry of abatacept in patients with juvenile idiopathic arthritis (JIA registry) to explore the long-term safety of abatacept treatment for JIA in routine clinical practice by quantifying the incidence rates of serious infections, autoimmune disorders and malignancies [final registry report expected by 2029]

Action: For adoption of advice to CHMP

7.5.2. Adalimumab - HUMIRA (CAP) - EMEA/H/C/000481/MEA 065.12

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Ulla Wändel Liminga

Scope: Thirteenth interim annual report for study P10-023, a psoriasis patient registry: a 10-year, post-marketing observational study to assess the long-term safety of Humira (adalimumab) in adult patients with chronic plaque psoriasis (PS)

Action: For adoption of advice to CHMP

7.5.3. Alemtuzumab - LEMTRADA (CAP) - EMEA/H/C/003718/MEA 007.12

Applicant: Sanofi Belgium

PRAC Rapporteur: Anette Kirstine Stark

Scope: Seventh annual progress report for study OBS13434: a prospective, multicentre, observational PASS to evaluate the long-term safety profile of Lemtrada (alemtuzumab) treatment in patients with relapsing forms of multiple sclerosis (MS) and to determine the incidence of adverse events of special interest (AESIs)

Action: For adoption of advice to CHMP

7.5.4. Cangrelor - KENGREXAL (CAP) - EMEA/H/C/003773/MEA 002.5

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Amelia Cupelli

Scope: MAH's response to MEA 002.4 [second interim report for study DFIDM-1801 (ARCANGELO (i)tAlian 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] as per the request for supplementary information (RSI) adopted in January 2022

Action: For adoption of advice to CHMP

7.5.5. Filgrastim - FILGRASTIM HEXAL (CAP) - EMEA/H/C/000918/MEA 007.12

Applicant: Hexal AG

PRAC Rapporteur: Menno van der Elst

Scope: Eleventh annual report for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation

Action: For adoption of advice to CHMP

7.5.6. Filgrastim - ZARZIO (CAP) - EMEA/H/C/000917/MEA 007.12

Applicant: Sandoz GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Eleventh annual report for study EP06-501 (SMART): a non-interventional, prospective, long-term safety data collection of Zarzio/Filgrastim Hexal (filgrastim) in

healthy unrelated stem cell donors undergoing peripheral blood progenitor cell (PBPC) mobilisation

Action: For adoption of advice to CHMP

7.5.7. Mercaptamine - CYSTADROPS (CAP) - EMEA/H/C/003769/MEA 001.4

Applicant: Recordati Rare Diseases

PRAC Rapporteur: Eva Segovia

Scope: Second annual report for study CYT-DS-001 (listed as a category 3 study in the RMP): an open-label longitudinal PASS to assess the safety of Cystadrops (mercaptamine) in paediatric and adult cystinosis patients in long term use

Action: For adoption of advice to CHMP

7.5.8. Ofatumumab - KESIMPTA (CAP) - EMEA/H/C/005410/MEA 003

Applicant: Novartis Ireland Limited

PRAC Rapporteur: Amelia Cupelli

Scope: First annual interim report for COMB157G2399 (ALITHIOS) study (listed as a category 3 study in the RMP): an open-label, single arm, multicentre extension study evaluating long-term safety, tolerability and effectiveness of ofatumumab in subjects with relapsing multiple sclerosis

Action: For adoption of advice to CHMP

7.5.9. Inclisiran - LEQVIO (CAP) - EMEA/H/C/005333/MEA 004.1

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Kimmo Jaakkola

Scope: First annual interim report for study CKJX839A12011: a non-interventional PASS to estimate the proportion of major congenital malformations among pregnancies exposed to inclisiran during pregnancy reported to Novartis amongst (i) live births and (ii) live births plus still births plus termination of pregnancy for foetal anomaly (TOPFA) - Inclisiran pregnancy outcomes intensive monitoring (PRIM)

Action: For adoption of advice to CHMP

7.5.10. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 001.4

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Third 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

Action: For adoption of advice to CHMP

7.5.11. Romosozumab - EVENITY (CAP) - EMEA/H/C/004465/MEA 002.4

Applicant: UCB Pharma S.A.

PRAC Rapporteur: Tiphaine Vaillant

Scope: Third 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

Action: For adoption of advice to CHMP

7.5.12. Sarilumab - KEVZARA (CAP) - EMEA/H/C/004254/MEA 002.6

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Eva Segovia

Scope: Third interim report for a safety surveillance programme using existing EU rheumatoid arthritis (RA) registries conducted in four countries: Germany (German Register for Rheumatoid Arthritis Observation of Biologic Therapy (RABBIT) (OBS15180)), Spain (Spanish Registry for Adverse Events for Biological Therapy in Rheumatic Diseases (BIOBASASER) (6R88-RA-1720)), Sweden (Register for Antirheumatic Therapies in Sweden (ARTIS) (OBS15220)) and UK (British Society for Rheumatology Biologicals Register (BSRBR) (6R88-RA-1634))

Action: For adoption of advice to CHMP

7.5.13. Selexipag - UPTRAVI (CAP) - EMEA/H/C/003774/MEA 001.7

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Nathalie Gault

Scope: Fifth annual interim report for PASS AC-065A401 (EXPOSURE): an observational cohort study of pulmonary arterial hypertension (PAH) patients newly treated with either Uptravi (selexipag) or any other PAH-specific therapy in routine clinical practice

Action: For adoption of advice to CHMP

7.5.14. Teriflunomide - AUBAGIO (CAP) - EMEA/H/C/002514/MEA 005.4

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Martin Huber

Scope: MAH's response to MEA 005.3 [1] eighth annual progress report for pregnancy registry OBS13499 (US/CA): teriflunomide pregnancy outcome exposure registry: a 'teratology information specialists (OTIS)' autoimmune diseases in pregnancy project, 2) fifth annual progress report for OBS12751 (international): an international pregnancy exposure registry of women with multiple sclerosis (MS) exposed to Aubagio (teriflunomide)] as per request for supplementary information (RSI) adopted in February

2022

Action: For adoption of advice to CHMP

7.5.15. Tisagenlecleucel - KYMRIA³¹ (CAP) - EMEA/H/C/004090/ANX 003.8

Applicant: Novartis Europharm Limited, ATMP³¹

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Fifth semi-annual report for study CCTL019B2401: a non-interventional PASS to further characterise the safety, including long-term safety, of Kymriah (tisagenlecleucel) based on data from a disease registry in acute lymphoblastic leukaemia (ALL) and diffuse large B-cell lymphoma (DLBCL) patients (European Society for Blood and Marrow Transplant Society Registry (EBMT) data only)

Action: For adoption of advice to CAT and CHMP

7.5.16. Tozinameran - COMIRNATY (CAP) - EMEA/H/C/005735/MEA 011.5

Applicant: BioNTech Manufacturing GmbH

PRAC Rapporteur: Menno van der Elst

Scope: Interim report for study C4591010: a post-approval active surveillance safety study to monitor real-world safety of Comirnaty (tozinameran) vaccine in the EU

Action: For adoption of advice to CHMP

7.5.17. Ustekinumab - STELARA (CAP) - EMEA/H/C/000958/MEA 045.8

Applicant: Janssen-Cilag International N.V.

PRAC Rapporteur: Rhea Fitzgerald

Scope: MAH's response to MEA 045.7 [second interim report for study RRA-20745: an observational PASS to describe the safety of ustekinumab and other Crohn's disease treatments in a cohort of patients with Crohn's disease] as per the request for supplementary information (RSI) adopted in January 2022

Action: For adoption of advice to CHMP

7.5.18. Venetoclax - VENCLYXTO (CAP) - EMEA/H/C/004106/MEA 002.9

Applicant: AbbVie Deutschland GmbH & Co. KG

PRAC Rapporteur: Eva Jirsová

Scope: Second interim analysis report and fourth study progress report for study P16 -562 (listed as a category 3 study in the RMP): a prospective observational study to assess the long-term safety profile of venetoclax in a Swedish cohort of chronic lymphocytic leukaemia (CLL) patients

Action: For adoption of advice to CHMP

³¹ Advanced therapy medicinal product

7.6. Others

7.6.1. Coronavirus (COVID-19) vaccine (ChAdOx1-S [recombinant]) - VAXZEVRIA (CAP) - EMEA/H/C/005675/MEA 007.5

Applicant: AstraZeneca AB

PRAC Rapporteur: Jean-Michel Dogné

Scope: MAH's response to MEA 007.4 [statistical analysis plan (SAP) for study D8111R00006: a post-authorisation/post-marketing observational study using existing secondary health data sources to evaluate the association between exposure to Vaxzevria (AZD1222) and safety concerns] as per the request for supplementary information adopted in February 2022

Action: For adoption of advice to CHMP

7.6.2. Fentanyl - INSTANYL (CAP) - EMEA/H/C/000959/LEG 028.5

Applicant: Takeda Pharma A/S

PRAC Rapporteur: Tiphaine Vaillant

Scope: Sixth six-monthly update on the development of the child-resistant multi-dose nasal spray DoseGuard as requested in the conclusions of procedure R/0049 finalised in April 2019

Action: For adoption of advice to CHMP

7.6.3. Natalizumab - TYSABRI (CAP) - EMEA/H/C/000603/MEA 071.1

Applicant: Biogen Netherlands B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: MAH's response to MEA 071 [feasibility assessment for study OXON 214-04 (listed as a category 3 study in the RMP): an observational study utilising data from EU national multiple sclerosis (MS) registries to estimate the incidence of anti-natalizumab antibody among patients who receive subcutaneous administration (SC) of natalizumab for treatment of relapsing remitting MS in order to investigate immunogenic potential of SC administration (from X/0116)] as per the request for supplementary information (RSI) adopted in December 2021

Action: For adoption of advice to CHMP

7.6.4. Reslizumab - CINQAERO (CAP) - EMEA/H/C/003912/MEA 005.7

Applicant: Teva B.V.

PRAC Rapporteur: Brigitte Keller-Stanislawski

Scope: Submission of an updated feasibility report for study C38072-AS-50027 as a MAH's response to MEA 005.6 [protocol for study C38072-AS-50027 (listed as category 3 study in the RMP): a long-term non-interventional study comparing the potential risk of malignancy

in severe asthma patients treated with reslizumab and patients not treated with reslizumab using secondary administrative healthcare data] as per the request for supplementary information (RSI) adopted in March 2020

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. Velmanase alfa - LAMZEDE (CAP) - EMEA/H/C/003922/S/0025 (without RMP)

Applicant: Chiesi Farmaceutici S.p.A.

PRAC Rapporteur: Jan Neuhauser

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. Crizanlizumab - ADAKVEO (CAP) - EMEA/H/C/004874/R/0008 (without RMP)

Applicant: Novartis Europharm Limited

PRAC Rapporteur: Jean-Michel Dogné

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.2.2. Larotrectinib - VITRAKVI (CAP) - EMEA/H/C/004919/R/0024 (without RMP)

Applicant: Bayer AG

PRAC Rapporteur: Rugile Pilviniene

Scope: Conditional renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3. Renewals of the marketing authorisation

8.3.1. Concentrate of proteolytic enzymes enriched in bromelain - NEXOBRID (CAP) - EMEA/H/C/002246/R/0056 (without RMP)

Applicant: MediWound Germany GmbH

PRAC Rapporteur: Martin Huber

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.2. Dupilumab - DUPIXENT (CAP) - EMEA/H/C/004390/R/0053 (without RMP)

Applicant: sanofi-aventis groupe

PRAC Rapporteur: Kimmo Jaakkola

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.3. Lacosamide - LACOSAMIDE ACCORD (CAP) - EMEA/H/C/004443/R/0015 (without RMP)

Applicant: Accord Healthcare S.L.U.

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.4. Letermovir - PREVYMIS (CAP) - EMEA/H/C/004536/R/0027 (with RMP)

Applicant: Merck Sharp & Dohme B.V.

PRAC Rapporteur: Kirsti Villikka

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: Gen.Orph

PRAC Rapporteur: Ulla Wändel Liminga

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

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

Applicant: STEBA Biotech S.A

PRAC Rapporteur: Maia Uusküla

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.7. Ritonavir - RITONAVIR MYLAN (CAP) - EMEA/H/C/004549/R/0015 (without RMP)

Applicant: Mylan Pharmaceuticals Limited

PRAC Rapporteur: Liana Gross-Martirosyan

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.8. Tacrolimus – TACFORIUS (CAP) – EMEA/H/C/004435/R/0010 (with RMP)

Applicant: Teva B.V.

PRAC Rapporteur: Ronan Grimes

Scope: 5-year renewal of the marketing authorisation

Action: For adoption of advice to CHMP

8.3.9. Trientine - CUPRIOR (CAP) - EMEA/H/C/004005/R/0018 (without RMP)

Applicant: Orphalan

PRAC Rapporteur: Ana Sofia Diniz Martins

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

9.1.1. Risk-based programme for routine pharmacovigilance inspections of marketing authorisation holders connected with human centrally authorised products

Scope: Pharmacovigilance inspection programme 2022-2025 (first revision for 2022)

Action: For adoption

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

10.1.1. Tagraxofusp - ELZONRIS (CAP) - EMEA/H/C/005031/II/0009, Orphan

Applicant: Stemline Therapeutics B.V.

PRAC Rapporteur: Menno van der Elst

Scope: PRAC consultation on the final report from study 20255431 (CRL-263114) (listed as a category 3 study in the RMP): a non-interventional post-authorisation study on blood brain barrier (BBB) models in order to determine a potential toxicity biomarker to further investigate the risk of choroid plexus lesions - a characterisation of fixed choroid plexus samples from primate study MPI-2231-007 by immunohistochemistry with diphtheria toxin (DT), interleukin-3 receptor (CD123), interleukin-3 (IL-3) and immunoglobulin G (IgG) (in fulfilment of MEA 002). The RMP (version 2.0) is updated accordingly

See also 5.3.32.

Action: For adoption of advice to CHMP

10.2. Timing and message content in relation to Member States' safety announcements

None

10.3. Other requests

None

10.4. Scientific Advice

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

11. Other safety issues for discussion requested by the Member States

11.1. Safety related variations of the marketing authorisation

11.1.1. N(2)-L-alanyl-L-glutamine (NAP) - DE/H/xxxx/WS/1108

Applicant: MAH Fresenius Kabi Deutschland GmbH (Dipeptamin)

PRAC Lead: Martin Huber

Scope: PRAC consultation on a worksharing variation procedure evaluating the data from spontaneous reports, literature, clinical trials and updated guidelines on the use of N(2)-L-alanyl-L-glutamine, as discussed at PRAC and agreed by CMDh following the conclusion of the PSUSA procedure (PSUSA/00003158/202103) concluded in December 2021, on request of Germany

Action: For adoption of advice to Member States

11.2. Other requests

None

12. Organisational, regulatory and methodological matters

12.1. Mandate and organisation of the PRAC

12.1.1. PRAC membership

Action: For information

12.1.2. Vote by proxy

Action: For information

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. Healthcare Professionals Working Party (HCPWP) and Patients and Consumers Working Party (PCWP) - Nomination of PRAC representative(s)

Action: For adoption

12.3.2. Healthcare Professionals Working Party (HCPWP) and Patients and Consumers Working Party (PCWP) - work plan 2022-2025

Action: For discussion

12.4. Cooperation within the EU regulatory network

12.4.1. Coronavirus (COVID-19) pandemic - update

Action: For discussion

12.4.2. PRAC strategic review and learning meeting (SRLM) under the French presidency of the European Union (EU) Council – Paris, France, 22 - 24 June 2022 - agenda

PRAC lead: Tiphaine Vaillant, Nathalie Gault

Action: For discussion

12.5. Cooperation with International Regulators

None

12.6. Contacts of the PRAC with external parties and interaction with the Interested Parties to the Committee

12.6.1. Coronavirus (COVID-19)-medicines monitoring: CONSIGN³² consortium project – COVID-19 infection and medicines in pregnancy – update

PRAC lead: Sabine Straus, Ulla Wändel Liminga

Action: For discussion

12.7. PRAC work plan

None

³² Covid-19 infectiOn aNd medicineS In pregnancy

12.8. Planning and reporting

None

12.9. Pharmacovigilance audits and inspections

12.9.1. Pharmacovigilance systems and their quality systems

None

12.9.2. Pharmacovigilance audits

None

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

12.10.1. Periodic safety update reports

None

12.10.2. Granularity and Periodicity Advisory Group (GPAG)

PRAC lead: Menno van der Elst, Maia Uusküla

Action: For discussion

12.10.3. PSURs repository

None

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

Action: For adoption

12.11. Signal management

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

PRAC lead: Menno van der Elst

Action: For discussion

12.11.2. Signal and safety analytics project

Action: For discussion

12.12. Adverse drug reactions reporting and additional reporting

12.12.1. Management and reporting of adverse reactions to medicinal products

None

12.12.2. Additional monitoring

None

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

Action: For adoption

12.13. EudraVigilance database

12.13.1. Activities related to the confirmation of full functionality

None

12.14. Risk management plans and effectiveness of risk minimisations

12.14.1. Risk management systems

None

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

None

12.15. Post-authorisation safety studies (PASS)

12.15.1. Post-authorisation Safety Studies – imposed PASS

None

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

None

12.16. Community procedures

12.16.1. Referral procedures for safety reasons

None

12.17. Renewals, conditional renewals, annual reassessments

None

12.18. Risk communication and transparency

12.18.1. Public participation in pharmacovigilance

None

12.18.2. Safety communication

None

12.19. Continuous pharmacovigilance

12.19.1. Incident management

None

12.20. Impact of pharmacovigilance activities

12.20.1. Good Pharmacovigilance Practice (GVP) – mid-year update

PRAC Lead: Sabine Straus

Action: For discussion

12.21. Others

12.21.1. Coronavirus (COVID-19) vaccines - benefit-risk contextualisation of COVID-19 vaccines in the EU

Action: For discussion

12.21.2. Data analysis and real-world interrogation network (DARWIN EU) – selection of studies supportive for PRAC decision-making to be performed in DARWIN EU year 1

Action: For discussion

12.21.3. EMA-funded studies - coronavirus (COVID-19) lessons learnt and future perspectives for PRAC decision-making

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/